ONSTEP versus laparoscopy for inguinal hernia repair: protocol for a randomised clinical trial

Kristoffer Andresen, Jakob Burcharth & Jacob Rosenberg

ABSTRACT

INTRODUCTION: The optimal repair of inguinal hernias remains controversial. It is recommended that an inguinal hernia be repaired using a mesh, either with a laparoscopic or an open approach. In Denmark, the laparoscopic approach is used in an increasing number of cases. The laparoscopic repair has a learning curve of about 50-100 cases and decreases chronic pain, but slightly increases the risk of serious complications compared with open mesh repairs. Therefore, a simpler kind of operation is needed. The ONSTEP technique is a possible solution to this problem. The objective of the present randomised clinical trial described in this protocol is to evaluate chronic pain after inguinal hernia repair using the ONSTEP method versus the laparoscopic approach.

METHODS: This study is designed as a non-inferiority, two-arm, multicentre, randomised clinical trial, with a 1:1 allocation to ONSTEP or laparoscopic repair. Patients are recruited from surgical departments in Denmark and follow-up is one year. In total, 188 patients will be included.

DISCUSSION: This protocol describes one of the first randomised clinical trials investigating the ONSTEP technique. To our knowledge, it is the first clinical trial comparing the ONSTEP technique with the laparoscopic technique. The results from this study are needed before it can be decided whether the ONSTEP technique should replace the laparoscopic technique in general surgical practice.

FUNDING: This study has not received external funding.

TRIAL REGISTRATION: NCT01960777 (clinicaltrials.gov).

Inguinal hernia is a condition affecting millions of people worldwide, and it is estimated that 20 million repairs are performed annually [1]. The optimal repair for inguinal hernias has been sought for centuries, and it is recommended that an inguinal hernia should be repaired using either the Lichtenstein or the laparoscopic technique [2, 3].

The quality of repair for inguinal hernias has previously been evaluated in terms of recurrence rates. However, following the introduction of mesh repairs, the number of recurrences dropped and focus has shifted towards post-operative pain, both acute and chronic. Following repair of primary inguinal hernia, 11-17% of patients are affected by chronic pain interfering with their daily activities [4]. One of the advantages of the laparoscopic approach is that it diminishes the risk of acute and chronic pain. Chronic pain that impairs daily activities was found in 8.1% of patients six months after repair [5]. However, the laparoscopic repair requires dedicated technical skills from the operating surgeon with a learning curve of 50-100 repairs [6] and has a slight increase in the risk of serious complications compared with mesh repair [7]. Therefore, there is a need for a simpler operation with comparable outcomes that does not require the same learning curve or carries the same risk of serious complications as the laparoscopic repair. The ONSTEP technique is a possible solution to this problem, and the initial results are promising with no chronic pain and few recurrences [8].

Clinical studies are needed to evaluate this new technique and to investigate how it compares with laparoscopic repair. The objective of the present non-inferiority, randomised, clinical trial described here is to evaluate pain after inguinal hernia repair using the ONSTEP method versus the laparoscopic approach. Inclusion of patients has begun and is expected to conclude in the winter of 2015 and follow-up is expected to conclude in the winter of 2016.

METHODS

This study is designed as a non-inferiority, two-arm, multicentre, randomised clinical trial. Patients are recruited from surgical departments in Denmark and follow-up is one year.

Patients will be assessed for inclusion when they visit the outpatient clinic at the participating centres. See **Table 1** for inclusion and exclusion criteria. Following inclusion and signing of the informed consent form, the patient will be booked for an inguinal hernia repair.

Following inclusion, an envelope containing the patient's allocation will be opened. This is done prior to the day of surgery to facilitate planning of the surgical rooms since there is a difference in operating time and equipment between the two procedures. Patients will not be blinded in this study because of the obvious difference in surgical wounds between the procedures and because of the long follow-up. However, the persons conducting the data analysis will be blinded. An electronic randomisation list with fixed block size is created

PROTOCOL ARTICLE

Department of Surgery, Herlev Hospital, Denmark

Dan Med J 2015;62(12):A5169

TABLE 1

Inclusion and exclusion criteria.

Inclusion criteria
Male patient > 18 yrs of age
Primary groin hernia which requires surgical intervention
Eligible for both ONSTEP and laparoscopic repair performed in general anaesthesia
Exclusion criteria
Emergency procedures
ASA score > 3
Irreducible inguinoscrotal hernia
Local or systemic infection
Other abdominal hernias being operated at the same time or planned operated during follow-up
Previous surgery which has impaired the sensation in the groin area
BMI > 40 kg/m^2 or BMI < 20 kg/m^2
Daily intake of alcohol > 5 U[a]
Known disease which impairs central or peripheral nerve function
Concurrent malignant disease
Impairment of cognitive function (e.g. dementia)
Chronic pain which requires daily medication
Mental disorder which requires daily medication

ASA = American Society of Anesthesiologists physical status classification; BMI = body mass index; ONSTEP = open new simplified totally extraperitoneal
a) 1 U = 12 g pure alcohol.

for each participating centre, using *randomization.com*, and allocation is packed in consecutively numbered, sealed, opaque envelopes.

Surgeons have to be familiar with the ONSTEP or the laparoscopic technique. It is required that the surgeons have received dedicated training and have performed a minimum of ten ONSTEP procedures before operating patients for this study. This minimum requirement is set in order to minimise the learning curve effect, and it is based on prior experience from our department. Furthermore, it is a requirement that the surgeons have performed at least 50 laparoscopic repairs of inguinal hernia. This limit was set based on a Cochrane review concluding that the learning curve of the laparoscopic repair is likely to be 50 or more procedures [6].

Both techniques will be done with the patient in general anaesthesia. The ONSTEP technique will be done according to the description from the inventors of the technique [8]. In short, the ONSTEP technique is performed through a 4-cm horizontal incision approximately two fingers cranially to the pubic bone and two fingers laterally to the midline. At this place, the fascia of the external oblique is reached and the fascia is incised. Following the incision, the plane between the external and internal oblique is dissected digitally, see **Figure 1**. The spermatic cord is mobilised and lateral or medial hernias are identified. Before handling the hernias, a perforation in the fascia transversalis is made digitally, and a possible femoral hernia is visualised and withdrawn. The hernia is handled, the Polysoft mesh (Bard, Davol Inc., Warwick RI) is placed around the spermatic cord, and the slit in the mesh is closed with three interrupted sutures. No sutures are used to fixate the mesh. The mesh is placed medially in the preperitoneal space and laterally surrounding the spermatic cords between the internal and external oblique muscles.

The laparoscopic repair should be done as a transabdominal preperitoneal repair (TAPP) according to the guidelines described by the Danish Hernia Database [2]. The mesh should be at least 10 × 15 cm. Fixation of the mesh is done using absorbable tacks. Following removal of the laparoscopic ports, the skin is closed using sutures or staples.

Baseline characteristics of the patients are registered preoperatively. Outcomes will be assessed at the following time points: First, second, third, and tenth days post-operatively, and then at 30 days and at six and 12 months post-operatively. Patients are clinically evaluated on day ten, and questionnaires will be used preoperatively and on all follow-ups. The following questionnaires will be used in their validated Danish language versions: Activity Assessment Scale (AAS) [9], the Inguinal Pain Questionnaire (IPQ) [10], the visual analogue scale (VAS) for pain [11] and Carolina's Comfort Scale (CCS) [12].

For this study, it was decided to include three primary outcomes, and make three individual sample size calculations to ensure that enough power would be achieved to cover all three outcomes. This would give us the opportunity to report the results in three separate publications if found reasonable after final data analysis. The three primary outcomes are: 1) prevalence of pain-related impairment of function at six months assessed by the AAS, 2) prevalence of pain related impairment at the 12-month follow-up assessed by the AAS, and 3) early post-operative pain (30 days) assessed by the VAS for pain. Secondary outcomes include: AAS score on day 30, pain assessed by the IPQ, Carolinas comfort scale score, operative time (minutes), length of hospital stay, time to return to normal daily activities, and other long-term complications assessed at the six- and 12-month follow-up.

Sample size calculation based on prevalence of pain-related impairment of function at the six-month follow-up

In a previous study, using the AAS for outcome assessment, the prevalence of substantial pain-related impairment of function six months after TAPP repair was found

to be 8% [5]. In a cohort study, a prevalence of chronic pain at six months after ONSTEP treatment was 0% [8]. We may expect a higher prevalence of pain in this study for the ONSTEP group since the procedures are spread across more surgical departments. The expected prevalence of pain-related impairment is therefore set to 4%. Since the study is designed as a non-inferiority study, it was decided that a difference of 5.0 percentage points or less is equal to non-inferiority. This means that the 95% confidence interval for the difference in favour of the laparoscopic approach does not exceed 5%. The sample size is calculated using SPSS Sample Power version 3. Alpha is set to 5% (one-sided) and beta is set to 20%. This will require a sample size of 85 patients for two groups. Due to possible dropouts, nine patients will be added in each group, which is considered a safe estimate [13, 14]. This results in a total of 188 patients.

Prevalence of pain-related impairment of function at one-year follow-up

One year post-operatively we expect the pain to diminish in both groups compared with the six-month follow-up. We therefore expect 6% in the laparoscopic group and 2% in the ONSTEP group to experience pain-related impairment of function. This outcome will be analysed with the non-inferiority assumptions. It was decided that a difference of 5.0 points or less is unimportant. Alpha is set at 5% (one-sided) and beta is set at 20%. The required sample size needed will be two groups of 59 patients, a total of 118 patients. This sample is smaller than the sample for the outcome at six months, and therefore we do not need to increase sample size to clarify this outcome.

Pain in the early post-operative period

Results from a recently published study showed that 24 hours after surgery, patients operated by the laparoscopic technique had a mean VAS score of 1.4 cm with a standard deviation of 0.6 [15]. The early post-operative pain has not yet been investigated following the ONSTEP repair. We expect the early post-operative pain in the ONSTEP group to be similar to that of the laparoscopic group and to have a similar standard deviation. A difference of 0.5 cm on the VAS is considered acceptable, and this leads to the following assumptions: Early post-operative pain in the TAPP group mean (standard deviation, SD): 1.4 (0.6) cm. Early post-operative pain in the ONSTEP group, mean (SD): 1.4 (0.6) cm. With alpha set at 5% and beta set at 20%, the sample size needed is two groups of 19 patients, a total of 38. The study includes 188 patients and therefore this outcome should be covered by the included population.

Statistical analysis will be performed using both parametric and nonparametric statistics depending on distribution of data. A p-value of ≤ 0.05 is considered significant. Both *per protocol* as well as *intention to treat analyses* will be conducted.

Baseline characteristics of the participants will be reported as means and standard deviations or medians and ranges, depending on the distribution of data for continuous data, and as numbers and percentages for categorical data. No comparisons of baseline characteristics between groups are planned. The results from the AAS will be analysed by comparing the proportion of patients in each group with substantial pain-related impairment of function using Fisher's exact test. Furthermore, a confidence interval will be calculated for the percentages. A mean and standard deviation will be calculated for the AAS score in the two groups; and if appropriate, the groups will be compared using a t-test. The results of the sub-scales for the AAS (sedentary, ambulatory and work/exercise activities) will be analysed and reported.

The analysis of the visual analogue scale results will be done by comparing the mean in the two groups 24 hours post-operatively, using the t-test if appropriate. Furthermore, the results of the VAS for post-operative days one, two, three and ten will be summarised for each patient as the area under the curve [16] and compared with the t-test.

This trial does not put any participants at increased risk compared with standard treatment of inguinal hernias. The laparoscopic approach is widely used and surgeons performing the procedure in this trial will be well-trained. Furthermore, there is no evidence that the ONSTEP technique carries an increased risk of chronic pain, recurrence or serious complications. This study was approved by the Danish Data Protection Agency (HEH-2013-069) and by the Ethics Committee (H-1-2013-

FIGURE 1

Blunt dissection of the plane between the internal and external oblique.

084). The trial is registered at clinicaltrials.gov (NCT01960777). Negative as well as positive and inconclusive results will be published.

Trial registration: NCT01960777 (clinicaltrials.gov).

DISCUSSION

This protocol describes the first randomised clinical trial comparing the ONSTEP technique with a laparoscopic technique. The preliminary results of the ONSTEP technique are promising with no chronic pain at the one-year follow-up and no serious complications [8]. Furthermore, experience from our own department and from departments participating in the Onli trial shows that the ONSTEP technique is easy and fast to perform [17]. The learning curve has not yet been ordinarily assessed, but it seems short.

Patients operated with the laparoscopic technique generally experience less post-operative pain and less chronic pain than patients operated with open methods [7]. However, the laparoscopic technique carries a slightly increased risk of serious complications and is more time-consuming, more expensive and requires a long learning curve for the operating surgeon [7]. Therefore, the ONSTEP technique could be used instead of the laparoscopic technique if it turns out to be comparable in terms of pain and complications because it seems easier to learn and teach and it is less time-consuming with short operating times of around 20 minutes [8]. Therefore, this study is done as a non-inferiority trial with the aim of determining if the ONSTEP technique performs at par with the laparoscopic technique in terms of acute and chronic pain. The results of this study, together with the results of the ONSTEP versus Lichtenstein trial [18], can be used to guide the choice of surgical methods for future hernia patients. If the ONSTEP repair is demonstrated to be superior to Lichtenstein repair and equal to laparoscopic repair, then it may be the first choice for future patients. However some issues remain to be addressed, preferably in prospective studies, such as recurrence and learning curve. These issues are important when evaluating the ONSTEP technique, but are unfortunately beyond the scope of the ONSTEP versus laparoscopy study.

CONCLUSIONS

The randomised clinical trial described in this protocol was designed with the aim of showing non-inferiority comparing the ONSTEP technique with the laparoscopic technique. The results from this study, together with the results of the ongoing ONSTEP versus Lichtenstein study are needed to clarify if ONSTEP should be the first choice of repair for primary inguinal hernias.

CORRESPONDENCE: *Kristoffer Andresen.*
E-mail: kristofferandresen@gmail.com
ACCEPTED: 12 October 2015

CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

LITERATURE

1. Kingsnorth A. Treating inguinal hernias. BMJ 2004;328:59-60.
2. Rosenberg J, Bisgaard T, Kehlet H et al. Danish Hernia Database recommendations for the management of inguinal and femoral hernia in adults. Dan Med Bul 2011;58(2):C4243.
3. Simons MP, Aufenacker T, Bay-Nielsen M et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. Hernia 2009;13:343-403.
4. Bay-Nielsen M, Perkins FM, Kehlet H. Pain and functional impairment 1 year after inguinal herniorrhaphy: a nationwide questionnaire study. Ann Surg 2001;233:1-7.
5. Aasvang EK, Gmaehle E, Hansen JB et al. Predictive risk factors for persistent postherniotomy pain. Anesthesiol 2010;112:957-69.
6. Wake BL, McCormack K, Fraser C et al. Transabdominal pre-peritoneal (TAPP) vs totally extraperitoneal (TEP) laparoscopic techniques for inguinal hernia repair. Cochrane Database Syst Rev 2005;1:CD004703.
7. McCormack K, Scott NW, Go PM et al. Laparoscopic techniques versus open techniques for inguinal hernia repair. Cochrane Database Syst Rev 2003;1:CD001785.
8. Lourenço A, Soares da Costa R. Open new simplified totally extraperitoneal (ONSTEP) inguinal hernia repair: experience in two institutions. Hernia 2013;17:357-64.
9. McCarthy M Jr., Jonasson O, Chang C-H et al. Assessment of patient functional status after surgery. J Am Coll Surg 2005;201:171-8.
10. Franneby U, Gunnarsson U, Andersson M et al. Validation of an Inguinal Pain Questionnaire for assessment of chronic pain after groin hernia repair. Br J Surg 2008;95:488-93.
11. Breivik H, Borchgrevink PC, Allen SM et al. Assessment of pain. Br J Anaesth 2008;101:17-24.
12. Heniford BT, Walters AL, Lincourt AE et al. Comparison of generic versus specific quality-of-life scales for mesh hernia repairs. J Am Coll Surg 2008;206:638-44.
13. Campanelli G, Pascual MH, Hoeferlin A et al. Randomized, controlled, blinded trial of Tisseel/Tissucol for mesh fixation in patients undergoing Lichtenstein technique for primary inguinal hernia repair results of the TIMELI Trial. Ann Surg 2012;255:650-7.
14. Bittner R, Gmahle E, Gmahle B et al. Lightweight mesh and noninvasive fixation: an effective concept for prevention of chronic pain with laparoscopic hernia repair (TAPP). Surg Endosc 2010;24:2958-64.
15. Wang MG, Tian ML, Zhao XF et al. Effectiveness and safety of n-butyl-2-cyanoacrylate medical adhesive for noninvasive patch fixation in laparoscopic inguinal hernia repair. Surg Endosc 2013;27:3792-8.
16. Matthews JN, Altman DG, Campbell MJ et al. Analysis of serial measurements in medical research. BMJ 1990;300:230-5.
17. Andresen K, Burcharth J, Rosenberg J. The initial experience of introducing the Onstep technique for inguinal hernia repair in a general surgical department. Scand J Surg 2015;104:61-5.
18. Andresen K, Burcharth J, Rosenberg J. Lichtenstein versus Onstep for inguinal hernia repair: protocol for a double-blinded randomised trial. Dan Med J 2013;60(11):A4729.