

Onstep repair of inguinal hernias

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3. Andresen K, Burcharth J, Fonnes S, Hupfeld L, Rothman JP, Deigaard S, Winther D, Errebo M, Therkildsen R, Hauge D, Sørensen FS, Bjerg J, Rosenberg J. Short term outcome after Onstep versus Lichtenstein technique for inguinal hernia repair: results from a randomized clinical trial. *Hernia* 2015;19:871-7
4. Andresen K, Burcharth J, Fonnes S, Hupfeld L, Rothman JP, Deigaard S, Winther D, Errebo M, Therkildsen R, Hauge D, Sørensen FS, Bjerg J, Rosenberg J. Sexual dysfunction after inguinal hernia repair with Onstep versus Lichtenstein technique: a randomized clinical trial. *Surgery* 2017;161:1690-5
5. Andresen K, Burcharth J, Fonnes S, Rothman JP, Hupfeld L, Deigaard S, Winther D, Errebo M, Therkildsen R, Hauge D, Sørensen FS, Bjerg J, Rosenberg J. Chronic pain after inguinal hernia repair with the Onstep versus the Lichtenstein technique, results of a double blinded randomized clinical trial. *Langenbecks Arch Surg* 2016;402:213-8
6. Andresen K, Laursen J, Rosenberg J. Difficulties and problematic steps in teaching the Onstep technique, results from a focus group interview. *Surg Res Pract* 2016;2016:4787648

INTRODUCTION

Background

Inguinal hernias occur either because of weakening in the groin or a pre-existing condition such as a persistent processus vaginalis [7]. The hernia orifice allows a protrusion of the peritoneum, containing either bowel or intra-abdominal fat. It is estimated

that more than 20 million people are having an inguinal hernia repair annually worldwide [8]. In Denmark alone, approximately 10,000 repairs are done annually [9], with the majority being male [10]. The life-time risk of developing an inguinal hernia among men is estimated to be as high as 27% [7]. Therefore, inguinal hernia repairs are among the most common procedures within surgery and accounts for a high number of patients with symptoms and potential complications.

The first description of inguinal hernia dates back to the Ebers Papyrus from around 1555 BC. The treatment for an inguinal hernia would then be a truss or bandages [11]. When the surgical repair of inguinal hernia started to come into use, the main problem was a high risk of recurrence. Therefore, the focus was to lower the risk of recurrence. Nowadays, the recommendation world-wide is to use a mesh when repairing an inguinal hernia [7]. In Denmark, two mesh based techniques are almost exclusively being used; the open Lichtenstein technique and the laparoscopic approach [12].

The single most used inguinal hernia repair technique in USA is the Lichtenstein repair or a modification [7]. Until recently, the Lichtenstein was also the most widely used in Denmark, but now accounting for around 50% of repairs [12]. The first description of the technique was published in 1989 [13]. A key-point of the repair is the tension free principle, with no tension on the structures in or around the inguinal canal. Tension was thought to be a contributing factor to the high recurrence rates found after sutured repairs. An incision is made on top of the inguinal canal, which is entered, the spermatic cord is mobilized, and the hernia is identified and returned to the abdominal cavity. A mesh is inserted and fixated with sutures. The introduction of the mesh-based techniques resulted in decreased recurrence rates and the standardized Lichtenstein technique was taken up by surgeons worldwide, making it one of the mostly used mesh-based repair techniques for inguinal hernias [7].

After reduction in the recurrence rates, focus shifted towards other complications, chronic pain being the most significant. Chronic post-herniorrhaphy pain is defined as pain from the operated area lasting for more than six months after the repair [14]. The prevalence of substantial pain-related impairment of function six months after Lichtenstein treatment has been found to be 16% [15, 16]. Chronic pain and discomfort occurs after Lichtenstein's repair as well as laparoscopic repair and has been investigated in studies worldwide [17, 18]. Furthermore, laparoscopic repair also has a potential problem with the learning curve [19]. The risk of chronic pain after laparoscopic repaired compared with Lichtenstein repair has been found to be reduced, however, not disappearing [20]. Up to 8% of patients operated with a laparoscopic repair experienced some degree of chronic pain in a large comparative study [15].

Because of the issues with chronic pain, surgeons are constantly developing and searching for better surgical methods.

Throughout history of hernia repair, numerous methods have been described and tested [21]. In 2013, two Portuguese surgeons published the results of their initial experience with 700 patients that had been operated with a new technique called Onstep [22]. Access to the inguinal canal is obtained through an open approach, but the incision is moved cranially, compared with the Lichtenstein technique, and is minimized to only 3-4 cm. Dissection is carried out to the external oblique fascia that is opened. Care is taken not to incise the internal oblique, and blunt dissection is used towards the inguinal canal. The spermatic cord is mobilized and the hernia is returned to the abdomen. A perforation is made in the transversalis fascia medially close to the pubic bone, the preperitoneal space is reached, and a gauze is inserted to facilitate blunt dissection in the pre-peritoneal space, thus creating space for the medial part of the mesh. The mesh for the Onstep repair is the Polysoft® mesh or the Onflex® mesh (figure 1). The mesh is teardrop-formed and the medial broad part is placed in the preperitoneal space after removal of the gauze. The lateral part of the mesh is placed around the spermatic cord between the internal and external oblique. The mesh is not sutured to any structures. It is held in place by being closed around the spermatic cord and by being placed through the perforation in the fascia transversalis (figure 1) [22, 23]. The avoidance of sutures was thought to contribute to the reduced risk of chronic pain.

The initial results published by the Portuguese surgeons were excellent with almost no recurrences and no patients experiencing chronic pain at one year follow up [22]. These results are extraordinary and a follow-up conducted a few years later confirmed the results [24].

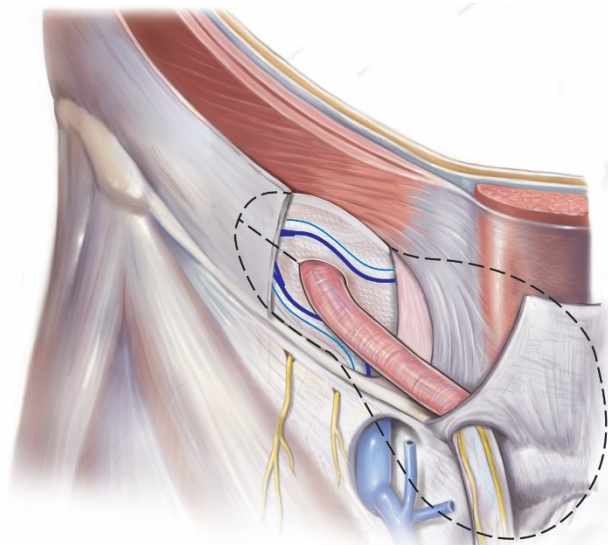


Figure 1. The right groin area is shown with an Onflex® mesh inserted by the Onstep technique. Laterally the mesh is placed between the internal and external oblique and medially the mesh is placed in the preperitoneal space. No sutures are fixating the mesh to the tissue. The spermatic cord is seen passing through a slit in the mesh.

Hypothesis and objectives

The objective of this PhD-project was to investigate the Onstep technique for the repair of inguinal hernias with focus on outcomes relating to pain and discomfort. The aim was to investigate the technique outside the departments of the inventors and compare it with the Lichtenstein technique. It was hypothesized that patients would experience less pain in the early postopera-

tive period, less chronic pain at 6 and 12 months follow-up, as well as less pain during sexual activity.

The overall aim was to clarify whether the Onstep technique should be implemented on a larger scale outside the departments of the inventors.

METHODOLOGICAL CONSIDERATIONS

Ethical considerations

When conducting research, no matter the design, ethics need consideration. For a systematic review, bias can be introduced in the design [25]. If bias is introduced on purpose, to demonstrate a certain point, it could make a systematic review unethical. It has also been suggested that a systematic review only should include studies that follow certain ethical standards, however, this has not been implemented. No permissions are needed to conduct a systematic review and authors or publishers of included studies in a systematic review do not need to give approval. Authors of systematic reviews have to be careful in their presentation and interpretation of results, because the level of evidence from a systematic review is considered to be high. However, the level of evidence is only high if the systematic review is done correctly and the included studies are of good quality [26].

In clinical interventional studies, the principle of equipoise is important and window of equipoise needs to be open for a study to be considered ethically justified. The principle relates to the situation where the intervention under investigation as well as the comparator are considered equal because of a lack of evidence needed to conclude one to be superior to the other [27]. In the studies included in this thesis, patients were randomized between the Lichtenstein repair and Onstep repair, because we believed that there was not enough evidence to conclude superiority of one procedure over the other. Therefore, it was ethically acceptable to randomize patients because we did not truly know which repair would result in better outcomes. Besides the window of equipoise, The Declaration of Helsinki has to be followed, especially focusing on informed consent and minimizing harms [28]. All interventional studies in Denmark need approval by The Ethical Committee. The approval is mandatory before inclusion of patients in an interventional study [29]. From the ethics perspective, a sample size calculation is also needed. If an insufficient number of patients are included, the study might be inconclusive, and participants will have been bothered and potentially harmed for no reason. Furthermore, if the study is including more than needed to show superiority of one treatment over the other, too many patients are exposed to potential harms [30].

Ethical approvals are not needed when conducting research based on focus-group-interviews in Denmark. However, there are still ethical issues relating to the interviews [31]. There is a risk of over-disclosure, meaning that participants in a focus group might be led to disclose issues that they normally would not discuss with other people. If the researchers are not handling these disclosures appropriately, the study could be considered unethical. Furthermore, it is important to stress to all participants that everything said during a focus group interview is confidential. In cases where sensitive topics are being discussed, psychological stress can arise as well. In the focus group study in this thesis we discussed surgeons' experiences relating to the training of other surgeons, which we considered a "safe" topic and therefore risks of over-disclosure or psychological stress to be minimal.

The studies in this thesis were all ethically justified and the required approvals from the ethics committee were obtained.

Method of systematic review

The systematic review in this thesis is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline [32]. When reporting a systematic review in accordance with the guideline, one will be encouraged to also conduct the review in a specific way. There is also a guideline for the reporting of a protocol for a systematic review called the PRISMA-Protocol (PRISMA-P) guideline [33]. It is important to have a protocol and a well-defined hypothesis before the start of a systematic review in order to draw valid conclusions. In order to increase transparency and avoid duplication of work, a systematic review should be registered, like a clinical trial, on the PROSPERO website [34, 35].

A systematic review starts with a formulated aim and research question. Then the search strategy is developed in order to try to identify all potential relevant studies. It is important that several databases are being sought [36], because even though there is considerable overlap, each database might have a unique set of citations relevant for the study. We searched PubMed, Cochrane database, and Embase. Besides the electronic searches, we also added a snow-ball search. In a snow-ball search the reference lists of manuscripts in the review are screened for identification of additional relevant articles [37].

A screening process followed the search. Two researchers independently assessed all identified records on title and abstract and made a judgment about in- or exclusion from the review. After screening on title and abstract full text manuscripts were retrieved and read for final judgment as whether to include the records. Thereafter, data extraction was done. When the data had been extracted, the results were summarized in text and tables. The online platform Covidence was used for organizing the work process (www.covidence.org).

A meta-analysis is a quantitative extension to a systematic review, where results of two or more trials are combined and effect size is estimated across the studies. There are several reasons not to conduct a meta-analysis. It is important to ensure that only comparable studies are pooled in the same analysis, meaning that there need to be a high level of clinical as well as statistical homogeneity. If this is not the case, one should refrain from conducting a meta-analysis [38]. Another problem can be bias in the included studies since the meta-analysis has a risk of combining and thereby enlarging these errors and producing a wrong result. Furthermore, a meta-analysis is only based on identified, available literature. Thereby, results from studies that have not been published or found during the search will not be part of the meta-analysis. This can overestimate or underestimate the effect of an intervention compared with the effect in the normal daily setting [38, 39].

Since the aim of the review was to clarify which methods existed, it was decided that a meta-analysis was not relevant. Instead of a meta-analysis, the results of the included records are presented in a summary tables and with a narrative synthesis [40]. A narrative synthesis is a description of the results but without making a combined and pooled estimate of the effect.

Method of randomized clinical trial

For the randomized clinical trial in this thesis, the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline was followed [41]. The CONSORT-statement was originally for randomized clinical trials of pharmacological therapies. Therefore, an extension was made for randomized trials of non-pharmacologic treatments [42]. An issue with non-pharmacological treatment such as massage, physiotherapy, and surgery, is standardization

of the arms of the trial. Therefore, the extended CONSORT-statement includes items such as description of standardization of treatment, training of personnel, and centres' volume.

A randomized clinical trial can provide high level of evidence as long as certain standards are followed. The Centre of Evidence Based Medicine in Oxford has updated their guide to evidence levels to a table [26, 43]. Randomized trials are level 2 evidence, but can be upgraded to level 1 "if there is a large or very large effect size" [43]. When several randomized trials can be combined in a systematic review it will be level 1 evidence.

The protocol for a randomized clinical trial needs to be approved by several authorities before patient inclusion. The protocol has to conform to the Good Clinical Practice guidelines if the study is investigating a medical therapy and the ISO standard 14155:2012, if the study is testing a device [29, 44]. For investigation of surgical interventions there is not yet a legal requirement to follow these specific standards. However, the protocol still needs approval by the ethics committee. Before inclusion of the first patient, the study should be registered in a publicly available database such as clinicaltrials.gov [45]. The registration contains information from the protocol regarding primary outcome and methods of analysis, aim of study etc. The registration increases transparency and will minimize data dredging. Registration of trials will also allow other researchers to either contribute to the ongoing study or design their study accordingly.

In the randomized trial, the screening, identification, and recruitment of potential participants can be difficult. For the randomized clinical trial in this thesis, participants were included from the outpatient clinics for patients with hernias at participating hospitals. Participants were informed and allowed time to process information and give their consent to participate or decline participation. If they chose not to participate in the study, it would not influence their treatment.

The randomization list should be created by someone not including patients so the allocation is concealed until the participants are allocated to either arm of the study. If possible, patients, outcome assessors, and healthcare providers around the patients should be blinded to the allocation. Blinding is a way of minimizing the risk of biases and prejudice regarding the treatment effect to influence the care and behavior of both patients and care givers. Furthermore, it is advised to have a blinded data analysis. When a trial is conducted with several centres, it is recommended that each centre provides patients to the intervention group as well as to the control group. In our study, this was done with the use of block-randomization. The block-size was six participants, meaning that for every six patients included, three were allocated to intervention and three were allocated to control. Thereby, when a centre had included six patients, they would have operated three participants with each method.

The follow-up has to be standardized and pre-defined in the protocol. In this randomized trial we used questionnaires, clinical examination, and phone interviews. Patient reported outcomes like these are increasingly important from decision-makers' point of view, and their use has been shown to improve quality of care [46].

Method of qualitative focus group interview

The focus group interview in this thesis is reported according to the Consolidated Criteria for Reporting Qualitative Research (COREQ) guideline [47]. The purpose of COREQ is to facilitate transparency in the reporting and thereby allowing readers and other researchers to evaluate the quality of the study.

A qualitative study seeks to identify thoughts, feelings, opinions, frustrations etc. among informants. These issues cannot be measured on a scale, an instrument, or with questionnaires, but needs to be investigated through the analysis of words, expressions, interactions, etc. A qualitative study can then inform the construction of a scale or questionnaire. The unit of analysis is a phenomena and a qualitative study is explorative by nature. It can be used to identify important issues that need to be further investigated, e.g. in a randomized clinical trial.

Transferability of the results of a focus group interview is desirable, meaning that the results can be “transferred” or used to understand a similar problem or phenomena in a similar group of people [48]. However, generalizability of the findings of qualitative studies is discussed among researchers and classic statistical generalization cannot be done with the results of a qualitative study [48]. To ensure a phenomenon has been thoroughly investigated in a study, data saturation should be reached [49]. Data saturation is defined as the situation where the addition of further information (addition of more groups or persons to the study) is unlikely to confer further insight. Data saturation is reached when no new themes arise when a new group is added to the study.

The focus group interview in this thesis was supported by a pre-developed interview guide (table 2). An interviewer and an observer were present during the interview that was recorded and later transcribed verbatim. The transcribed interview was then analysed by qualitative content analysis where themes were identified. We used a conventional content analysis where pre-conceived categories were avoided [50]. First the interview was read in its whole, then words and sentences were labelled and categorized into meaning clusters that were condensed, coded, and formulated into themes. The themes are the results of the study.

STUDY PRESENTATION

Study I: Open preperitoneal groin hernia repair with mesh: a qualitative systematic review.

Multiple methods for the repair of inguinal hernias exist [21]. One concept is to use the pre-peritoneal space for the placement of a mesh. The pre-peritoneal space lies posterior to the muscles in the abdominal wall but anterior to the peritoneal lining. The idea of placing a mesh in this plane is to avoid mesh in the groin area, where there is a risk of damaging the nerves.

The aim of this study was to identify and present open pre-peritoneal methods that have been reported in the medical literature. The aim was to provide an overview of the methods and evidence. No comparisons between the different open pre-peritoneal methods were planned.

Methods

This study was a systematic review. PubMed, Cochrane database of clinical trials and Embase were searched. The search string included terms related to “pre-peritoneal”, the names of some methods, and “groin hernia”. The full search string can be found in the published article [1]. The protocol was developed before the start of the study and registered on PROSPERO [34]. Screening of articles was done in accordance with the description mentioned earlier. Besides the systematic search of databases, a so-called snow-ball search was also conducted [37]. No meta-analyses were planned.

Results

The initial search identified 2296 records. After removing of duplicates and screening of title and abstract, 162 articles were retrieved for full text screening and 67 articles were included. Nine surgical methods were identified: Onstep [22], Trans Inguinal Pre-Peritoneal (TIPP) [51], Kugel [52], Trans Rectus Sheath Pre Peritoneal [53], Nyhus [54], Ugahary [55], Horton/Florence [56], Stoppa [57], and Read [58]. Several different meshes were used, some with reinforcement in the border and some were regular flat meshes. Fixation ranged from no fixation in some methods to suture fixation in others. The recurrence rates were in general reported in the lower end, see table 1. No comparison of pain across the studies was done because of different lengths of follow-up as well as different assessment methods of pain.

Method	No of patients	Recurrence <i>n/total n (%)</i>	Follow-up <i>months</i>
Onstep [22]	945	18/945 (1.9)	1-60
TIPP [51]	3,243	39/3,243 (1.2)	6-63
Kugel [52]	4,781	80/4,781 (1.7)	3-60
TREPP [53]	982	11/982 (1.1)	24
Nyhus [54]	444	9/444 (2.0)	24-72
Ugahary [55]	366	23/366 (6.3)	2 (1-4)
H/F [56]	157	2/157 (1.3)	2-18
Stoppa [57]	1,036	20/1,036 (1.9)	12-66
Read [58]	327	8/327 (2.4)	24-82

Table 1. The nine different identified pre-peritoneal techniques from the systematic review. H/F = Horton and Florence. For more details, please refer to the published paper [1].

Discussion/limitations

It is safe to conclude, that the pre-peritoneal techniques in general seem to provide good results regarding pain and discomfort, but more studies are needed. No meta-analysis was conducted for this systematic review, because levels of heterogeneity were too high and because the aim of the study was to present which methods are published in the literature.

For systematic reviews there is a risk that some relevant papers have not been identified. Language can be a factor since the researcher might not be proficient in all relevant languages. In our case we only included papers reported in English or Scandinavian languages. Furthermore, there is a risk that reports with negative or harmful results are not published, so called publication bias. “Grey literature” outside peer reviewed journals could have been considered. However, we choose to only include peer reviewed literature to ensure a certain quality of the papers.

Even though a technique has a specific “recipe” and name, it can be modified and changed through time [59]. We might not have identified all modifications made to some of the methods throughout the years. Besides the standardization of the technique there are also variations in the types of mesh within the methods of repair. There are other factors such as the patient demographics, the use of sutures, and the way of dissecting etc. that can influence the results.

It is difficult to standardize techniques, patients, and hernias, and assessment needs to be done in a standardized setting. Ideally, the surgeons should perform both the procedure under investigation as well as the procedure used for the control group, in order to try to minimize the effect of the surgeon. Because it was difficult to compare the results across the studies, and because we did not aim to do a meta-analysis, the assessment and recommendations across studies are limited. Therefore, we did not compare the techniques. It would be difficult to combine all these

methods into a meta-analysis which potentially could be performed as a network meta-analysis [60]. However, this field of research is characterized by smaller studies with varying degrees of follow-up as well as varying methods of assessment and therefore they seem too heterogeneous to combine into a (network-) meta-analysis.

Because we did not aim for a presentation of effect size, we decided not to do a formal bias assessment. We also avoided recommending one method over another. The aim was to present the methods that have been presented in the individual reports, and therefore we decided that bias would not need to be assessed within each study. There can still be publication bias since there may be other methods for placing a mesh in the preperitoneal plane that have not been published.

The quality of a systematic review can be judged by the "AMSTAR" (MeaSurement Tool for the Assessment of multiple systematic Reviews) checklist [36]. This review would receive a score of 4/11, where 11/11 would indicate high quality. However, the rather low score of 4/11 is not necessarily an indication of poor quality of the review, since the aim and design was different than reviews intended to be scored by the AMSTAR checklist.

Study II: Lichtenstein versus Onstep for inguinal hernia repair: protocol for a double-blind randomized trial.

A randomized clinical trial was needed in order to assess the Onstep method in comparison with an established method, and to investigate the method outside the inventors' hands. It was unknown if the Lichtenstein or the Onstep resulted in better outcomes. The protocol is needed to ensure transparency and by publishing the protocol this is enhanced. It is also recommended by the International Committee of Medical Journal Editors to make protocols publicly accessible [61].

The aim of the protocol article is to provide details of the design and specifically to give details of the sample-size calculation as well as insight into the statistical analysis plan.

Methods

This randomized clinical trial was approved by the ethical committee. Furthermore, it was registered on clinicaltrials.gov (NCT01753219). For this trial several primary outcomes were defined, each with a separate sample size calculation.

The four primary outcomes were: A) Proportion of patients with pain related impairment of function at six months follow-up; B) proportion of patients with pain at 12 months follow-up; C) proportion of patients with pain related impairment of sexual function; and D) early postoperative pain.

A sample size calculation was made for each of the four outcomes. A total of 282, 230, 110 and 22 patients were needed for outcomes A, B, C, and D, respectively. Therefore, it was planned to include 282 patients in order to obtain power enough for all primary outcomes.

Follow up was planned with the use of clinical examination, phone-interviews and validated questionnaires. Patients were followed up at 10 days, 30 days, 6 and 12 months post-operatively.

Discussion/Limitations

A limitation to the protocol article is that it was not reported according to Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guideline which is now recommended for reporting of protocols. The SPIRIT guideline was published in early 2013 [62, 63], and the protocol article was submitted in august the same year. We were not aware of the guideline before

the submission of the protocol, but believe the protocol to contain all relevant items.

The protocol article ensures transparency in the research processes, but protocols often need adjustments. However, it is not all journals that have a set-up to update the article and therefore protocol amendments might not be published alongside the protocol. Amendments should, however, be accessible on the trial registration platform.

Some researchers could be concerned that other research groups would "steal" their idea and conduct a similar trial. However, this would be valuable. If a similar trial is conducted, it would then be possible to combine studies with the same aim and outcome assessment in a meta-analysis and thereby it would be possible to reach level-1 evidence about the intervention [26].

Study III: Short term outcome after Onstep versus Lichtenstein technique for inguinal hernia repair.

Patients are eager to return to work and leisure activities as soon as possible following surgery. In the new World Guidelines, which are still in draft, there are no restrictions relating to postoperative activity following inguinal hernia repair [64]. Therefore, pain and discomfort are likely the most inhibiting factors preventing patients from returning to their normal daily lives after surgery.

The aim of this first report of the Onstep versus Lichtenstein trial was to investigate differences in the first 30 postoperative days regarding pain, return to work, and complications.

Methods

Patients were randomized to Onstep or Lichtenstein repair and blinded to the intervention. Because the incision of the Lichtenstein and the Onstep repair are in the same area, patients without medical background would not know if they received the Lichtenstein or the Onstep repair.

Patient discomfort was assessed both before surgery, with the use of standardized questionnaire, as well as on the first three days and on day 10 after surgery where participants were seen in the outpatient department for removal of stitches, and clinical examination. Patients were phoned on day 30 regarding complications and return to work, and reminded to fill out a questionnaire.

Complications were graded according to the Clavien-Dindo Classification [65]. The primary outcome for the study was pain measured on the visual analogue scale (VAS) on day 1. Twenty-two patients were needed in each arm according to sample size calculations.

Results

In total, 141 and 139 patients randomized to Lichtenstein or Onstep, respectively, were available for the 30-day follow-up analysis. VAS at day 1 was compared between the groups and no differences were found. Median VAS values were 18 and 16, respectively, $p = 0.778$. During mobilization pain rose to VAS = 52 for Lichtenstein and 48 for Onstep, $p = 0.615$. The pain diary investigating pain at day 1 to 3 and 10 was used to calculate the amount of pain by the use of Area Under the Curve (AUC) [66]. This revealed no differences between Onstep and the Lichtenstein procedures.

Twelve patients in the Lichtenstein group and 10 patients in the Onstep group experienced postoperative complications graded as I or II with the Clavien-Dindo classification. One patient in the Lichtenstein group experienced a grade 3a complication. There was one patient in each group experiencing a grade 3b complication (a complication requiring surgical intervention).

Recurrences were diagnosed among four patients in the first 10 days of follow-up; three in the Onstep group and one in the Lichtenstein group, $p=0.30$. At day 30, patients were asked about pain, but no significant differences were found. Also no significant differences were found in return to work or leisure activities.

A shorter duration of surgery was found for the Onstep repair, median 25 versus 33 minutes, $p<0.0005$.

Discussion/limitations

Onstep is a safe technique and has comparable results to the Lichtenstein technique regarding early postoperative outcomes. There is a need for longer follow-up.

It can be discussed whether the finding of no difference between the Onstep and the Lichtenstein group is due to a type 2 error. A type 2 error is the rejection of a true alternative hypothesis (a true difference). However, a type 2 error is unlikely since the study would be considered overpowered. Only 22 patients were needed in each group in order to identify the expected clinically relevant difference in pain between the Lichtenstein and the Onstep technique on postoperative Day 1, which was set at a 30% reduction in VAS from 34.1 mm [2]. With more than 100 persons available in each group the risk of type-2 error was therefore negligible. Thus, the two methods were equal regarding early postoperative pain.

These results differ from the results of the Portuguese study, which could be due to the relative inexperience that our surgeons had with the Onstep technique compared with the Lichtenstein technique. It was a requirement that surgeons had performed 10 Onstep procedures before they started operating patients for the Onstep group. However, this might be too few and the results may have differed if the surgeons had had more experience with the Onstep technique.

The most likely explanation for the lack of differences between the two groups is that open surgery per se in the groin hurts. It is painful to be operated with an open approach, no matter if it is the Onstep or the Lichtenstein technique. The tissue damage, the handling of the cord, and the insertion of a foreign body might all contribute to pain. Therefore, the Onstep technique can be said to not have a measurable benefit in the early postoperative period.

Study IV: Sexual dysfunction after inguinal hernia repair with Onstep versus Lichtenstein technique.

A specific issue following repair of inguinal hernias is pain during sexual activity. Pain during sexual activity has increasingly gained attention after it was described. It affects 20% after Lichtenstein repair [67], and has also been identified after laparoscopic repairs of inguinal hernias with rates of pain up to 10% [68]. A subgroup of patients experience pain during ejaculation, so called dysejaculation [69]. The dysejaculation can be severe enough to keep patients from engaging in sexual activity, but is rare [70]. It was thought that the Onstep repair would result in lower rates of pain during sexual activity than the Lichtenstein repair because it results in low rates of chronic pain [22, 24].

The aim of this study was to investigate differences in pain during sexual activity following Onstep versus Lichtenstein repair.

Methods

The method of this study is identical with other parts of the Onstep versus Lichtenstein trial regarding randomization and follow up. For pain during sexual activity, this study focused on pain at six months follow up. The questionnaire used relates to pain during sexual activity before and after surgery [67]. The primary

outcome was number of patients with pain during sexual activity at six months follow up. The sample size for this study was calculated to be two groups of 55 patients.

Results

In total, 129 patients from the Lichtenstein group and 130 patients operated with the Onstep repair were available for analysis. No differences were found between the groups regarding baseline characteristics. Seventeen patients (13%) that were operated using the Onstep technique, and 30 patients (23%) operated using the Lichtenstein technique, experienced pain during sexual activity at follow up, $p = 0.034$.

As a secondary outcome it was investigated if the preoperative pain during sexual activity affected the postoperative pain during sexual activity, and whether the repairs of the hernias would solve or diminish this issue. Among the patients that did not have pain during sexual activity before surgery, the Lichtenstein technique gave rise to this issue for 14 out of 70 patients (20%) compared with the Onstep technique, where seven out of 74 (9%) experienced this issue, $p = 0.073$.

When looking at the degree of pain, no patients in the Onstep group experienced moderate or severe pain during sexual activity compared with the Lichtenstein group, where four patients experienced moderate or severe pain. Dysejaculation was experienced by three patients in the Onstep group and four patients in the Lichtenstein group, $p = 0.72$.

Discussion/limitations

When comparing the Onstep and the Lichtenstein technique, it can be concluded that the Onstep repair results in less pain during sexual activity. Furthermore, it seems that the Onstep technique has a lower risk of inducing new pain during sexual activity compared with the Lichtenstein technique, however, not statistically significant. If a patient has pain during sexual activity as part of their complaints preoperatively, the surgeon might consider using the Onstep repair technique instead of the Lichtenstein technique based on these results.

In the questionnaire used, there were no assessments of level of sexual activity. If one group of patients had a higher level of sexual activity, they might experience more pain or vice versa. It might also be that some patients experience pain and then stopped having sexual activity and therefore did not report having pain during sexual activity. It could be considered to extend the questionnaire and investigate the level of sexual activity that patients have in order to correct for this in future studies. However, we do believe the results to be valid based on this questionnaire since the questionnaire has been used in several other publications and demonstrated good use, both in Denmark as well as internationally.

This finding of a significant difference could theoretically be because the study was "overpowered" in the sense that only 55 patients were needed in each arm according to the sample size calculation for identification of a clinically relevant difference [2]. Due to the other primary outcomes, 130 patients were available for analysis in each group thereby allowing us to identify a smaller difference than would be possible with only 55 patients in each group. However, the difference between 13% and 23% should be considered a clinically relevant difference and is not just a statistical significant difference caused by an overpowered study.

Patients can experience pain in the groin for a range of different reasons [71]. It is not with a hundred percent certainty that all patients with pain during sexual activity had pain related to the inguinal hernia repair. However, since this was a randomized trial,

the other possible reasons for having pain during sexual activity or having pain from the groin is expected to be equally distributed between the groups. Therefore, the difference can most likely be attributed to differences in the surgical techniques.

Study V: Chronic pain after inguinal hernia repair with the Onstep versus the Lichtenstein technique.

Chronic pain following inguinal hernia repair affects 16% of patients at six months follow up [15, 16].

The aim of this study was to investigate the chronic pain at six and 12 months follow up for patients operated with the Onstep or Lichtenstein repair.

Methods

This is the final study in the Onstep versus Lichtenstein trial where patients were randomized to Onstep or Lichtenstein repair. Pain was assessed at six and 12 months follow up by the use of questionnaires: The Activity Assessment Scale (AAS), the Inguinal Pain Questionnaire (IPQ) and the Carolinas Comfort Scale (CCS). All three questionnaires have been validated [72-74]. Patients were mailed the questionnaires. If they did not return the questionnaire they received a phone call kindly reminding them to return the questionnaire.

In total, 130 patients were needed in each group for six months follow up and 115 for 12 months follow up.

Results

From April 2013 to May 2014, 290 patients were included from the five participating departments. At six months, 129 patients from the Onstep group and 130 patients operated with the Lichtenstein technique were available for follow up. Regarding the two primary outcomes, which were pain at six and 12 months follow up, no differences were found. Fourteen patients in the Onstep group and 18 in the Lichtenstein group had pain related impairment of daily functions (AAS), $p = 0.49$. At the twelve months follow up 15 patients in the Onstep group and nine patients in the Lichtenstein group had pain related impairment of daily functions, $p = 0.18$. The VAS for pain showed no differences neither at six nor 12 months follow up. Neither did the CCS reveal any differences.

Regarding recurrences, six were found among the patients operated with Onstep and five were found among the patients operated with Lichtenstein, $p = 0.78$. For the recurrences diagnosed in the Onstep group, three occurred before day thirty. In the Lichtenstein group only one was diagnosed before day thirty.

Discussion/limitations

No differences were found regarding chronic pain at six and 12 months follow up between the Onstep and Lichtenstein technique. Thus, the Onstep technique does not increase the risk of chronic pain at six and 12 months follow up.

When investigating a new surgical method, there is a risk that parts of the results are not caused by the method, but instead because of limited experience among surgeons. This factor is difficult to remove from studies of surgical interventions. It could be that the results had been in favour of the Onstep technique if the surgeons had more experience with the Onstep technique. Surgeons had to perform ten procedures before they started operating patients for the study, which might have been too few. However, no learning curve study exists for the Onstep technique. The learning curve for Lichtenstein is suggested to be passed by 40 procedures [75]. For laparoscopic repair the learning curve has

been estimated to be 30-100 procedures [76]. Therefore, ten procedures might be too few.

Patients reported outcomes in questionnaires filled out once at six and once at 12 months after surgery. A limitation to a questionnaire is that answers can be influenced by how patients feel on the very day or hour of follow up. More measurements could have been done, e.g. once every week for a month, however, it was not feasible in the setup of this study. All questionnaires were validated and we had a validated Danish translation. Therefore, we believe that the use of questionnaires is appropriate for the assessment of the outcome.

No differences were found between the Onstep and the Lichtenstein technique for any of the questionnaires. It can therefore be concluded that surgeons after performing ten Onstep procedures can achieve results comparable to the Lichtenstein technique, even though surgeons had much more experienced with this technique.

Study VI: Difficulties and problematic steps in teaching the Onstep technique, a focus group interview.

When new surgical procedures are implemented, there is a need to train surgeons in the techniques. Traditionally, surgeons learn a procedure by observing and assisting multiple times. Then he/she gradually takes over parts of the procedure, and then conducts the procedure under supervision, and in the end, unsupervised. However, for a new technique, the surgeons need to move quickly from supervised training to "self-training" since it is not always possible to spend extended time with the expert. From experience with the Onstep technique it seems safe to quickly move to self-training. There are difficulties related to teaching surgeons a new technique in limited time.

The aim of the study was to investigate problems, issues, thoughts, and experiences from teachers that were training other surgeons in the Onstep technique.

Main question	
Opening	<i>Tell me about the experience of training others in the Onstep technique</i>
Instructions of others	<i>What are your experiences when instructing/teaching the Onstep technique?</i>
Compared with other techniques?	<i>What are the main differences when you are instructing/teaching this technique?</i>
Which surgeons?	<i>Who should be taught this technique? Who could/should teach/train others?</i>
Proficiency	<i>When are you ready for unsupervised procedures?</i>
Closure	<i>Something else we need to add?</i>

Table 2. Interview guide for the focus group interview. For more details please refer to the published paper [6].

Methods

We aimed at understanding the experience from the trainer's perspective when training surgeons in the Onstep technique. A qualitative study design, with a focus group interview, was used. Before the interview, an interview guide was developed and tested (Table 2).

The informants were an international group of experienced Onstep surgeons. The focus group took place in a comfortable setting without disturbances. The interview was recorded and

transcribed verbatim. The transcribed interviews were analysed by conventional content analysis [50].

Results

The analysis of the transcribed interview revealed four themes: Instruction of others, comfort, concerns/fear, and anatomy. The theme “instruction of others” covered three subthemes: experience, patient selection, and tailored teaching.

When instructing other surgeons, the trainer needs to consider the experience of the trainee. If the trainee was experienced in inguinal hernia repairs, it was easier to train them in the Onstep technique. The trainers found it important to have a proper patient selection, meaning that patients should be fit for the purpose of training. Patients should not have difficult or large hernias, or be too obese.

The trainers discussed both comfort for the trainees as well as comfort for themselves. When teaching in their own department they were in charge and more comfortable. However, they experienced that when teaching in the trainee’s departments, the trainees were more at comfort and possibly learned more.

The trainers were concerned about their reputation as surgeons/teachers and the reputation of the technique. The reasons for these concerns were the risk of complications. If complications occurred following training in the Onstep repair, it could be because the technique was bad or because the trainers were incapable and that could harm the reputation of the technique and/or the trainers.

Discussion/limitations

For experienced surgeons being trained by experienced trainers, a one-day training schedule in their department was an acceptable set up that allowed experienced surgeons that are being trained to move to self-training.

A limitation of this study was that only one group of international expert surgeons were available when discussing the Onstep technique. However, we ensured that data saturation was reached by keeping asking questions in order to ensure that no new ideas or items would come forward. The study might have benefitted by having another group of surgeons added. However, no other group was available for this, since no other surgeons, besides the interviewed, did training in the Onstep technique at the time of the study.

We only interviewed European surgeons, and there could be a difference in the socio-cultural context if implementing the Onstep technique in another context. This could limit the transferability of the results; however, the results can be used in a European context both north and south, since we had surgeons from both north and south of Europe.

The perspective from learners of the technique is missing from this study. That would be a different focus group interview, which is also needed, but does not fit into one report together with these results. A study of the trainee’s experience with learning the Onstep technique should investigate what they experience as their challenges, what keeps them from doing Onstep repairs, and what would enhance their take up and acceptance of the technique.

DISCUSSION

The findings of this PhD-thesis have several important implications. The systematic review demonstrated that there are multiple methods for the placement of a mesh in the pre-peritoneal space through an open procedure. In general, the results seem

promising and the use of the pre-peritoneal space seems justified although no meta-analysis was made. The Onstep versus Lichtenstein trial was reported in four publications that are all included in this thesis. First, the protocol article outlines the design and contains a detailed description of the sample size calculation as well as the analysis plan for the primary outcomes. Thereafter, the three papers describing short term pain and discomfort, pain during sexual activity, and finally chronic pain. The Onstep versus Lichtenstein trial demonstrated that in the short term, there is no benefit of the Onstep compared with the Lichtenstein technique, but also no additional harms related to the Onstep technique. In the long term, chronic pain was equal between methods. Relating to pain during sexual activity, patients operated with the Onstep technique had a more favourable outcome. Significantly fewer patients in the Onstep group experienced pain during sexual activity at the six months follow-up compared with the patients from the Lichtenstein group. The final study of the thesis, which was a focus group interview with experienced surgeons, found four themes to be important and challenging when teaching the Onstep technique: instruction of others, comfort, concerns/fear, and anatomy. The focus group interview provided insight and suggestions for the organization of training the Onstep technique.

The potential benefit of using the pre-peritoneal plane for placement of the mesh is the avoidance of the nerves (iliohypogastric nerve, ilioinguinal nerve, and the genital branch of the genitofemoral nerve) [77]. The nerves are spared during dissection since many of the preperitoneal methods does not enter through the inguinal canal. The nerves are also thought spared in the longer term since the mesh is placed preperitoneally, away from the nerves in the inguinal canal. In Denmark it is not recommended from the Danish Hernia Database to use these methods and there is almost no use of these pre-peritoneal open techniques [78]. However, the laparoscopic pre-peritoneal placement of a mesh has seen a dramatic increase and is now covering approximately 50% of inguinal hernia repairs in Denmark [12]. The limited use of the pre-peritoneal open techniques is possibly due to several factors. One factor is that it is not recommended by The Danish Hernia Database [78]. Another factor could be that the pre-peritoneal technique seems more difficult to teach and learn compared with the standardized Lichtenstein technique [13].

Regarding the early postoperative pain, no difference was found between the Lichtenstein and the Onstep repair [3]. This is probably because open groin surgery results in considerable early postoperative pain (median VAS during mobilization on day 1 was at around 50 mm) [3]. Another study comparing the Lichtenstein with the preperitoneal TIPP repair also did not find a difference in the early postoperative period [79]. Even laparoscopic repair results in significant levels of pain in the first postoperative days [80]. Early postoperative pain could be caused by the incision, the tissue damage and the manipulation of the hernia and the cord. The early pain is probably also maintained by inflammation in the tissue [81]. The pathophysiology for early and chronic pain or discomfort has not been investigated in this thesis. Furthermore, a relationship between early and chronic pain would be interesting to analyse with the current data. The transition from acute pain to chronic pain is not fully understood [82].

It can be discussed whether the issue of chronic pain is an important outcome. However, according to Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group, an outcome can be ranged according to its importance [83]. For inguinal hernia surgery, the chronic pain would be ranged as critical for making a decision [83]. There is no mortality

and rare occurrence of other morbidity related to inguinal hernia surgery. Therefore, chronic pain is nowadays the most important issue for both patients as well as surgeons when operating or having an inguinal hernia repair operated. It is interesting, that there is no difference between the Onstep and the Lichtenstein repair when it comes to chronic pain, neither at six nor 12 months follow-up. This is in direct contrast to the conclusion drawn from the Portuguese study [22, 24]. There could be several reasons for this lack of advantage using the Onstep repair in our study. One thing could be that there is a learning curve that surgeons had not passed. The two inventors are experienced hernia surgeons and their experience could possibly explain some of the advantages seen in the initial publication regarding the Onstep technique. Even though the technique was taught in a standardized way to others, there might be small details during the procedure that is missing, resulting in different outcomes. For surgeons to participate in our study, they had to have performed at least ten Onstep procedures. It could be discussed whether ten was enough, however, no data exists on the learning curve of the Onstep technique.

The Portuguese study was conducted in a different setting from our study. The Portuguese population was similar regarding age, but included 18% women [22]. Since women are at higher risk of experiencing chronic pain after inguinal hernia surgery [84], it is unlikely that the inclusion of women could explain the difference. Another possibility could be the different socio-cultural contexts. It has been demonstrated that cultural issues influence pain [85]. Maybe Portuguese patients are more resilient to pain. Furthermore, the assessment methods between our studies and the Portuguese study are different. Patients in the Portuguese study were seen at clinical follow-up and interview. In our study patients filled out validated questionnaires with items relating to different everyday situations. In the Portuguese study patients were asked if they had pain or not. They were asked by the surgeons that had operated them and maybe that made them reluctant to complain about eventual pain. It can be discussed whether clinical examination is better than a questionnaire. In our study patients filled out the questionnaires at home and there was no pressure on them to report more or less pain. Furthermore, they did not know whether they had had the Lichtenstein or the Onstep repair.

A clinical, significant difference was found when investigating pain during sexual activity, favoring the Onstep repair. One could argue that this difference was only found because the study was over-powered [86]. However, the difference between 23% and 13% would require 50 patients in each group in order to achieve significance. The effect is larger than the minimal clinically relevant difference that was defined before the start of the study where it was calculated that two times 54 patients were needed [2]. It was therefore concluded that the risk of pain during sexual activity following Onstep repair was lower than the risk of pain during sexual activity following Lichtenstein repair. Pain during sexual activity is rarely mentioned during clinical examination and surgeons should consider asking patients about this issue as well.

Maybe it would have been possible to demonstrate a benefit of the Onstep technique if patients at high risk of chronic pain had been included. Some patients are “high responders” to pain [87]. It is possible, that if a study only included high responders, a smaller benefit of a technique could be demonstrated. We did not include assessment of high/low responders in our study because we wanted to reflect the daily clinical setting where the assessment of pain response is not applicable. Quantitative sensory

testing is still investigational and too time consuming to be applicable in most clinics and even some studies [15].

Conclusion

In conclusion, the Onstep repair is one among several methods, where a mesh is placed in the preperitoneal plane, through an open approach. In this thesis the Onstep technique has been thoroughly investigated in comparison with the Lichtenstein technique, but the results have not been as promising as the initial studies from the inventors of the technique:

1. For acute postoperative pain, no differences were found between Onstep and Lichtenstein repair and the study was sufficiently powered to identify a difference, had it been there.
2. For chronic pain, no differences were found and the study was sufficiently powered and proper assessment tools were used.
3. For pain during sexual activity, it can be concluded that the Onstep repair is superior compared with the Lichtenstein repair and results in a reduced risk of pain during sexual activity.
4. Teaching and implementation of the Onstep technique needs attention and the results from the focus group interview should be used when planning training and implementation.

Based on the findings in this thesis, the Onstep technique could be implemented on a larger scale outside the departments of the inventors without resulting in increased risk of complications. Furthermore, the Onstep technique would possibly benefit patients by reducing the risk of pain during sexual activity compared with the Lichtenstein technique.

Perspectives and future studies

Results for the Onstep technique are promising and therefore Onstep could be considered an alternative to the standard open approach for inguinal hernias such as the Lichtenstein technique. Onstep is one among several other techniques that uses the preperitoneal space through an open approach such as the TREPP [88] or TIPP [89]. In the future, the Onstep could be included in the recommendations and guidelines for repair of primary hernias since it is equal to Lichtenstein regarding chronic pain, and superior to the Lichtenstein technique regarding pain during sexual activity [4]. It could also be considered if a region or country wanted to standardize their inguinal hernia repairs. In some countries there are many different methods in use and the standardization can be beneficial because it allows for better data collection, and it allows for higher levels of training in one technique. In such a setting the Onstep technique could be favourable because it is possible to teach to experienced surgeons during one-day training and the results are as good as or better than the Lichtenstein technique which is considered “gold standard” for open mesh-based repair in many places.

The Onstep technique can be used for recurrent hernias, not primarily operated with the Onstep technique, even though the mesh is placed in two planes; the pre-peritoneal plane as well as the lateral plane between the internal and external oblique. In the initial series from the inventors, 76 patients (11%) had a previous hernioplasty and this did not affect the overall excellent results [22]. However, the data available to support recommendations regarding the repair of recurrent hernias with the use of Onstep technique is still somewhat limited and could be explored further.

Mesh based repairs of inguinal hernias are recommended worldwide and there is, so far, no sutured repair technique that can compete with the mesh-based techniques, when implemented in general surgical practice/departments. Among the mesh

based techniques, Onstep is a valid competitor with results just as good as the Lichtenstein results.

If the Onstep technique is chosen as a recommended technique, it is important to focus on the implementation that needs tailoring [6, 90]. If the implementation is not done right, there is a risk that surgeons will start to make their own version of the Onstep technique and thereby not achieve the good results found in our studies where the method was standardized.

Some surgeons are warning against the use of the Onstep technique because it makes use of two planes; the pre-peritoneal plane and the plane between the internal and external oblique [91]. However, we have not identified any problems relating to the use of the two planes. Some concerns relate to the repair of recurrences because the recommendation is that if an anterior mesh based technique has recurred, the recurrence should be operated with a posterior technique such as the laparoscopic technique and vice versa [64]. In our department we have had some experience with recurrence after the Onstep technique and found that it is not a problem to repair a recurrent hernia after Onstep with the use of the laparoscopic technique. Open approach can also be used and the inventors of the technique recommend to do a re-Onstep for a recurrent Onstep repair [Lourenço A, da Costa RS. Personal communication]. Possible recurrence mechanism following Onstep repair is clarified in an earlier publication [92]. Most of the recurrences could be contributed to a lack of standardization of the technique or failure to comply with the recommendations relating to how to operate the Onstep repair. If these recommendations are followed, then the recurrence rate is likely to be within acceptable limits.

In the future, focus might shift more towards the surgeons and hernia repairs will probably be conducted by fewer surgeons, each performing more repairs. Hernia centres have been created in Germany [93] and the Shouldice Hospital in Canada is famous for its published results [94]. The good results from Shouldice Hospital might partly be attributable to some degree of patient selection [95], and partly attributable to the extensive training that their surgeons receive. For surgeons to operate in the Shouldice Hospital they have to assist in 50 procedures and then conduct 200 supervised operations before operating independently [96]. If this kind of training was implemented globally, the rate of chronic pain and recurrences might drop to a very low level. Most patients would also prefer a surgeon with extensive experience in the hernia repair technique. However, with the way surgery is organized nowadays it is not applicable or feasible in many places.

In the future, the Onstep repair could be a valid alternative to other mesh based open techniques. Whether or not it can compete with the laparoscopic inguinal hernia repair will be further clarified with the Onstep versus laparoscopy trial that is currently ongoing [97].

ENGLISH SUMMARY

Background

Inguinal hernias are a protrusion of the peritoneum through a weakening in the groin in which abdominal content (intestines or fat) can herniate and cause a bulge. Inguinal hernias can be painful and require surgery. Worldwide, approximately 20 million patients are operated each year, with 10,000 in Denmark. The repair of inguinal hernias causes pain and 16% of patients experience chronic pain six months after the standard, open, mesh based Lichtenstein technique. Therefore, surgeons are trying to improve the techniques by finding new ways of operating. The

Onstep method was a new method for the repair of inguinal hernias, presented along with excellent results regarding pain, recurrence and complications. However, the technique had not been tested outside the department of the inventors.

The overall aim was to clarify whether the Onstep technique should be implemented on a larger scale outside the departments of the inventors.

Methods and results

Six papers are included in this thesis: a systematic review, a protocol article, three reports on the Onstep versus Lichtenstein trial, and finally a focus group interview.

The systematic review identified nine different methods of placing a preperitoneal mesh through and open anterior approach. In general, the techniques seem to provide good results regarding pain and discomfort, but more studies are needed.

The protocol article describes the randomized, double blinded Onstep versus Lichtenstein study, with focus on the statistical analysis and sample size calculations. Four separate sample size calculations were conducted, making several primary outcomes possible.

The three reports of the Onstep versus Lichtenstein study reported on early postoperative outcomes, on chronic pain, and lastly on sexual dysfunction. The overall findings from the trial demonstrated that there were no differences between the Onstep and the Lichtenstein technique regarding early and chronic pain (30 days, six months, and 12 months). However, for the group of patients operated with the Onstep technique, fewer patients experienced pain during sexual activity.

The focus group interview was done with experienced surgeons teaching the Onstep technique. They described their experience, thoughts, and concerns regarding teaching the technique. The results from the focus group interview can be used to guide future trainings sessions.

Conclusion

In this thesis the Onstep technique has been investigated in comparison with the Lichtenstein technique, but the results have not been as promising as the initial studies from the inventors. However, implementation of the Onstep technique outside the departments of the inventors is unlikely to result in increased risk of complications. Furthermore, the Onstep technique could possibly benefit patients by reducing the risk of pain during sexual activity.

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