

Protocol Article

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Collaboration between the Danish and Swedish hernia registers – a study protocol

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ABSTRACT

INTRODUCTION. The most common laparo-endoscopic groin hernia repair techniques are TEP (total extraperitoneal) and TAPP (transabdominal preperitoneal) repair. Despite geographic proximity, Swedish surgeons distinctively favour TEP, whereas Danish surgeons prefer TAPP. The aim of this study is to analyse the risk of reoperation for recurrence after TAPP, TEP and Lichtenstein repair using data from two nationwide registers. We also aim to discuss advantages of international collaboration between nationwide registers.

METHODS. All groin hernia operations registered as TEP, TAPP or Lichtenstein repair in the Swedish Hernia Register and the Danish Hernia Database between January 2004 and December 2020 will be included. Cumulative hazard rate of reoperation for recurrence will be estimated using Cox-regression analyses adjusted for age and anatomy.

CONCLUSION. Approximately 400,000 operations are estimated to have been registered prospectively in the inclusion period in the registers. The merging of two nationwide registers was made possible owing to close cooperation between the register steering committees and by obtaining the necessary approvals. This unique collaboration between nationwide registers will make it possible to compare the risk of reoperation for recurrence after TAPP, TEP and Lichtenstein repair on an international level. In future, similar collaboration may be established to explore other outcomes such as complication rates and chronic pain.

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TRIAL REGISTRATION. not relevant.

Worldwide, approximately 20 million patients undergo inguinal hernia repair annually [1]. In Sweden and Denmark, around 16,000 and 8,000 groin hernia operations are performed every year, respectively. Among these, 4,600 (39%) in Sweden and 4,500 (65%) in Denmark were performed using laparo-endoscopic techniques in 2020 [2, 3]. In Sweden, the total extraperitoneal approach (TEP) is the main laparo-endoscopic repair of choice, whereas Danish surgeons prefer the transabdominal preperitoneal approach (TAPP). **The international guideline for groin hernia management** recommends that the choice of technique is based on the surgeon's skills, education and experience [1]. Current evidence cannot uniformly recommend one type of laparoscopic repair over the other. Among 4,552 operations, TAPP was superior to TEP with regard to complications, operating time and conversion rate [4]. Additionally, a meta-analysis of 27 randomised controlled trials found a higher recurrence rate after TEP than after TAPP [5]. However, when analysing data from 17,587 operations in the Herniated Hernia Register, no significant differences between TEP and TAPP were found [6].

In Sweden, the risk of reoperation for recurrence after TEP and TAPP was found to be around 2.5% at two-year follow-up in the 2011-2020 period. The corresponding risk of reoperation for recurrence after Lichtenstein repair was just above 1% [2, 7]. Similar results have been found in Denmark [8].

Due to the above-described national differences in preference of laparo-endoscopic technique, data from either country alone cannot identify any difference in risk of reoperation for recurrence between TAPP and TEP. However, by merging data from the two national quality registers, clinically significant differences may be visualised.

The aim of this paper is to show that it is possible to analyse and compare the risk of reoperation for recurrence between TAPP, TEP and Lichtenstein by merging data from two national hernia registers.

METHODS

The Swedish Hernia Register and the Danish Hernia Database

The Swedish Hernia Register (SHR) became operational in 1992 and is a non-mandatory quality register. Today, its registration rate is approximately 98% of all groin hernia operations in Sweden. Data are registered prospectively after each operation and include parameters such as time on waiting list, patient characteristics, hernia anatomy, primary/recurrent hernia, method of repair, anaesthesia and complications.

The Danish Hernia Database (DHDB) was established in 1998 and collects prospective nationwide data. The primary aim of the DHDB is to reduce the risk of recurrence and improve outcomes after hernia repair. Surgeons are obliged to register repairs immediately after surgery. The register included 90% of all operations in 2015 [9]. The main included parameters are sex, age and perioperative data such as repair method, hernia type (inguinal or femoral), hernia subtype

(medial/lateral), use of mesh and side (left or right) [9].

Both registers use a personal identity number, which makes it possible to follow patients over time regardless of where they are re-operated [10].

Total extraperitoneal approach

In TEP repair, the preperitoneal space is reached directly without entering the abdominal cavity [11]. A TEP repair includes placing a mesh in the pre-peritoneal space. The TEP technique is occasionally described as more complex and has a steeper learning curve than TAPP repair [12].

Transabdominal preperitoneal approach

In TAPP repair, the pre-peritoneal space is reached laparoscopically via the abdomen [13]. The peritoneum is incised and the hernia orifices are visualised. The mesh is placed between the abdominal wall and the peritoneum. This technique inevitably carries the risk of any intraabdominal approach, including accidental injury of abdominal organs.

Lichtenstein repair

The tension-free inguinal hernia repair was first described by Irving Lichtenstein in 1986 [14]. A mesh was inserted covering the defect in the transversalis fascia, reconstructing the posterior wall of the inguinal canal [14]. Owing to modifications of the technique, a consensus meeting in Sweden agreed on the term "open anterior mesh repair". A detailed description of this repair is published at the SHR webpage. Similarly, in Denmark, a consensus on the Lichtenstein technique was reached in the late nineties through several extensive discussion meetings hosted by the DHDB. The consensus reached is available on the DHDB website. In this article, "open anterior mesh repair" is replaced by Lichtenstein enabling comparison with the DHDB.

Inclusion criteria

All primary groin hernia repairs registered as TEP, TAPP or Lichtenstein in the SHR and DHDB between January 2004 and December 2020 will be included in the study. Patients 18 years or older will be included.

Exclusion criteria

Repairs with missing or incomplete data on anatomy or method of operation will be excluded. Repairs registered in the database as recurrences will be excluded.

Population

The study cohort will include approximately 400,000 patients who underwent groin hernia surgery between 2004 and 2020 in Sweden and Denmark. In 2019, 15,821 groin hernia operations were performed in Sweden. Among these, 5,853 (37%) patients had a laparo-endoscopic repair, of which 1,011 were TAPP and 4,842 were TEP repairs [2]. In 2016, 8,694 patients underwent groin hernia surgery in Denmark. Among these, 4,442 (51%) patients had a laparoscopic repair and almost all of

these were TAPP (97%) [15].

External validity

In Sweden, 10% of affiliated surgical units are randomly selected for validation of register records annually. Approximately 98% of groin hernia operations performed in Sweden are registered in the SHR [16]. In Denmark, the coverage is around 90% of all hernia repairs [8]. Patients are included irrespective of sex and comorbidities. External validity is therefore high.

Patient information and informed consent

In Sweden, all patients are informed of their participation in the register and may actively choose not to participate, withdraw their informed consent and delete their data from the register. In Denmark, no informed consent is needed for registration of groin hernia operations.

Variables

The variables registered vary with time within and between the registers. Variables of importance to our study that were found to be equivalent in both registers are: right/left side, unilateral/bilateral, TEP/TAPP/Lichtenstein, elective/emergency, primary/recurrent, male/female, age at operation, time to reoperation, recurrence/death, method of anaesthesia, inguinal/femoral and medial/lateral.

Primary endpoint

The primary endpoint is cumulative hazard rate of reoperation for recurrence for TEP, TAPP and Lichtenstein repair, analysed using a Cox regression model.

Secondary endpoints

Cumulative hazard rate of reoperation for recurrence for laparo-endoscopic versus Lichtenstein repair, overall and separately analysed for males and females.

Sample size calculation

The hypothesis is that the risk of reoperation for recurrence is equivalent for the two laparo-endoscopic techniques. Furthermore, we anticipate that the reoperation for recurrence rate after Lichtenstein repair compared with laparo-endoscopic repair is lower for men than for women. The sample size calculation is based on the overall re-operation rates in previous publications from the SHR and the DHDB. Assuming that the risk of reoperation for recurrence for both TEP and TAPP repair is 2% after two years, a non-inferior limit of 0.50% and a power of 90%, the minimum sample size are estimated to be 30,000 patients with 15,000 in each group. $p \leq 0.05$ will be considered statistically significant.

Data analyses/statistics

Demographics for the included patients will be presented in Table 1 in the final study report; separately for males and females and classified by TEP, TAPP and Lichtenstein repair. Parameters

include but are not limited to anatomy, age, unilateral/bilateral, method of repair, anaesthesia and time to follow-up.

The total number of procedures and crude reoperation for recurrence rate will be presented Table 2 in the final study report; separately for sex and presented by TEP, TAPP and Lichtenstein repair. Cumulated re-operation rates will be demonstrated by Kaplan-Meier plots and compared with a Log Rank test. Cumulative risk of reoperation for recurrence will be analysed using a cox-proportional hazard model. Using this model, the hazard rates of the groups have to be proportional. If not, we will stratify by this variable. TEP will be compared with TAPP and illustrated Table 3 and Figure 1 in the final study report, whereas both laparo-endoscopic procedures (TEP and TAPP) will be compared with Lichtenstein repair in Table 4 and Figure 2 in the final study report. Registered operations with missing values for method of repair, hernia anatomy and primary/recurrent hernia will be excluded from the analyses. When missing values occur, we assume that they are missing at random and thereby not affecting the results.

Sex is planned to be analysed separately because of the known sex-related difference in risk of reoperation for recurrence. The effects of patients' age, method of repair, hernia anatomy and mode of admission (elective/emergency) will be estimated in the Cox regression model.

Ethical considerations

Approval was obtained from the Regional Ethics Board of Gothenburg (Dnr 416-17). Under Danish law, ethical committee approval is not required for this type of study. All patients included in the SHR are informed and participation is entirely voluntary. In contrast, the registration is mandatory in Denmark. Data included in the study are de-identified. The participation in the register and thereby in this study will not affect the treatment of the patient in any manner. Data will be presented groupwise without any possibility to identify individual patients.

Regulatory and methodological issues

Obstacles need to be overcome when merging register data within countries and even more so across nations. First of all, the national cohorts must be considered comparable. If differences are found between TEP and TAPP, this might be due to differences in the cohorts. Despite the geographical proximity of Sweden and Denmark, some demographic differences exist, i.e. the life expectancy is higher for Swedish men (80.7 years) than for Danish men (78.6 years) [17]. There is, however, little or no reason to believe that the small demographic differences between Denmark and Sweden would affect the risk of reoperation for recurrences after groin hernia surgery.

The variables registered have varied within and between the registers. Variables have been added and withdrawn over time. We have chosen to include data from 2004 and onwards in an attempt to avoid such biases and to avoid old data to interfere with modern results.

Trial registration: not relevant.

DISCUSSION

Even though more than 20 years have passed since the introduction of TEP and TAPP, the literature remains inconclusive with regards to the superiority of one of the techniques in terms of risk of reoperation for recurrence. Thus, the choice of surgical technique is often based upon local tradition. With this multinational register study, this question may be answered with some certainty and high external validity.

Register studies carry several strengths and limitations. Strengths include the unique amount of data, the fact that data are collected prospectively and are readily available. Furthermore, nationwide coverage increases the external validity. Weaknesses include the variation of the validity of data, the fact that data were not reported for this study's specific purpose and that definitions may vary during the study period [18]. Merging two national registers adds important considerations for the analyses. This study, it might be argued, compares the outcome of Swedish and Danish surgeons. To reduce this bias, we have included the Lichtenstein repair in the analysis. The Lichtenstein repair is performed in both countries and will therefore serve as a reference.

The Lichtenstein repair is advocated by Swedish surgeons. When analysing the effect of more advanced techniques, such as TEP or TAPP, the importance of a national coverage cannot be overestimated. This study will reveal what occurs when all surgeons within a country apply a surgical technique, not only the experts as has been shown in randomised controlled trials and register studies with selected patients and surgeons.

When comparing TAPP, TEP and Lichtenstein, differences in the demographics of patients also need to be considered. Besides the obvious demographics that are available in the database, less obvious patient characteristics and surgeon preferences are not available in large-scale datasets. A risk may exist of confounding by indications if indications for TEP in Sweden were different from those of TAPP in Denmark. In Denmark, TAPP is increasingly used, also for primary inguinal hernias. The same trend is seen for TEP in Sweden [2]. Therefore, we believe that the risk of confounding by indication remains minor in this study.

The large study populations accumulated in the databases of the registers will allow us to establish clinically significant differences in rare events such as risk of reoperation for recurrence. Conversely, the large cohorts will most probably produce in a number of statistically significant differences that may not be clinically relevant.

The true incidence of recurrence is difficult to estimate. Recurrence rate exceeds the reoperation rate for recurrence by almost 40% [19]. The surrogate endpoint used in this study is therefore reoperation for recurrence as these are considered clinically relevant recurrences. The author group consists of Danish and Swedish surgeons, and it is our impression that the indication for reoperation for recurrence does not differ between the two nations, and this factor should therefore not interfere with the results.

CONCLUSION

The aim of this study is to investigate the risk of reoperation for recurrence after TEP, TAPP and Lichtenstein repair in a large cohort with high external validity.

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