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Mesh hernia repair and male infertility. A retrospective register study.

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Abstract

Background Previous studies have suggested that the use of mesh in groin hernia repair may be associated with an increased risk for male infertility due to inflammatory obliteration of structures in the spermatic cord. In a recent study we could not find an increased incidence of involuntary childlessness. The aim of this study was to further evaluate this issue.

Methods Men born between 1950 and 1989, with a hernia repair registered in the Swedish Hernia Register between 1992 and 2007, were cross-linked with all men in the same age group with the diagnosis of male infertility according to the Swedish National Patient Register. The cumulative and expected incidences of infertility were analyzed. Separate multivariate logistic analyses, adjusted for age and years elapsed since the first repair, were performed for men with unilateral and bilateral repair, respectively.

Results 34,267 men were identified with a history of at least one inguinal hernia repair. 233 (0,7%) of these had been given the diagnosis of male infertility after their first operation. We did not find any differences between expected and observed cumulative incidences of infertility in men operated with hernia repair. Men with bilateral hernia repair had a slightly increased risk for infertility when mesh was used on either one or both sides. However, the cumulative incidence was less than 1%.

Conclusion Inguinal hernia repair with mesh is not associated with an increased incidence of, or clinically important risk for male infertility.

Introduction

Inguinal hernia is one of the most common conditions requiring surgical treatment. Hernia repair techniques have varied over the years. The last two decades have seen the use of alloplastic mesh-based tension-free methods gradually replacing traditional sutured techniques. Most surgeons regard mesh repair as the method of choice whether performed laparoscopically or by open technique. The low recurrence rate, short learning curve and rapid return to physical activity make it cost-effective and safe in the short as well as in the long run[1]. This is of importance not only for the patient but also for the social insurance system. The alloplastic mesh causes an inflammatory response and a foreign-body reaction in the adjacent tissues, and the resulting fibrosis of the inguinal wall is suggested to be the main reason for the stability of the repair and the low recurrence rate.

The complications of hernia surgery are much more common and severe in patients undergoing repair in a previously operated groin[2]. In most studies comparing different methods for groin hernia repair, the long-term recurrence rate is considered to be the most important single study outcome variable. So far little attention has been paid to method-specific complications. Mesh techniques, however, have reduced recurrence rates to such low

levels that other aspects have now become more important as outcome measures, including, chronic pain[3,4] and infertility.

A growing number of reports from animal studies have voiced the possibility that the use of mesh in male hernia repair may cause infertility due to obliteration of the vas deference (obstructive azoospermia) or obliteration of the blood vessels in the spermatic cord[5-8]. Results are inconsistent, even though most studies find inflammatory reactions to some extent in the funicular structures. Until now there are only a few human studies and case reports on this subject, which together include only a limited number of patients[9,10]. The conclusions and recommendations regarding hernia repair vary in these studies. Some authors do not favour the use of mesh, at least in young men[5,8] while others are still unsure whether or not this really is an important clinical problem[11] and often emphasize the need for more human studies. Finally a modified mesh method has been proposed to be safer regarding the so-called infertility problem[12].

In a recent prospective human register study we could not find any significant increase in the prevalence of involuntary childlessness after bilateral groin hernia repair with mesh, compared to non-mesh techniques and to the general age-matched male population. To our knowledge, this study is the largest study on this topic so far[13].

The purpose of this study was to further evaluate the risk for male infertility after groin hernia mesh repair, using a different approach, i.e. a retrospective study design in a large population-based cohort.

Material and methods

All men born between 1950 and 1989 who were registered with a hernia repair in the Swedish Hernia Register (SHR) between 1992 and 2007 were included in the study. Men with both hernia repair and the diagnosis infertility were identified by cross-linking the SHR with the Swedish National Patient Register[14] by searching for the diagnosis “male infertility” (ICD code N46.9). It was not possible to obtain the ICD subcodes (fifth position) for the etiology of infertility from the Swedish National Patient Register.

Cumulative incidence of infertility in men operated for groin hernia versus the general population

The observed cumulative incidence of infertility, estimated from the year after the first hernia repair, was compared with the expected cumulative incidence, i.e. the calculated incidence that would be expected if it was identical to the general age-matched Swedish male population.

The expected cumulative incidence was estimated by adding together the incidences of newly diagnosed infertility in the total Swedish male population each year after the hernia repair.

The incidence of infertility each year was determined by the ratio between the number of men with the diagnosis of infertility and the total number of men born within the same five-year stratum in Sweden. The total relevant population of Sweden was obtained from Statistics Sweden[15]. For men who had undergone more than one repair, the incidence was determined from the year after the first repair.

In the analyses, the men with at least one hernia repair were divided into five groups depending on the repair:

I. unilateral repair without mesh

II. unilateral repair with mesh

III. bilateral repair without mesh

IV. bilateral repair with mesh on one side

V. bilateral repair with mesh on both sides

Men who had undergone more than one repair on either side were included in a separate group since this constitutes a more heterogenic group and surgical trauma to the vas deferens may have been more extensive. No distinction was made between bilateral repair in one synchronous procedure and bilateral repairs on two separate occasions.

Mesh versus non-mesh repair and risk for infertility

Two separate multivariate logistic analyses with infertility as the dependent variable were performed, one for men who had undergone bilateral repair and one for men who had undergone unilateral repair. In both analyses adjustments were made for age (men born 1965 or later versus men born before 1965) and years elapsed since the first repair. In the analysis of men who had been bilaterally repaired, the laterality was treated as a three-stage ordinal scale (no mesh, mesh on one side and mesh on both sides).

Results

Altogether 42,775 repairs between 1992 and 2007 in 34,267 men born between 1950 and 1989 were identified in the Swedish Hernia Register (SHR) (Table 1). 233 of these men were also identified, according to the Swedish National Patient Register, with a diagnosis of “male infertility” (ICD code N46.9) registered the year after the first hernia repair and any time thereafter (Table 1).

Cumulative incidence of infertility in men operated for groin hernia versus the general population

Observed and expected cumulative incidences of infertility are presented in Table 1. None of the groups had an observed cumulative incidence of infertility greater than the expected cumulative incidence. For most groups, the cumulative incidence was even lower than that of the general population.

Mesh versus non-mesh repair and risk for infertility

In a multivariate logistic analysis of men operated bilaterally, with infertility as the dependent variable and adjusted for age and year elapsed since the repair, a significant difference was seen between men operated with mesh and men operated with suture repair ($p=0.030$). There was a higher risk for infertility in men who had undergone mesh repair.

In a corresponding multivariate logistic analysis of men operated unilaterally, mesh repair was not found to be significantly associated with an increased risk for infertility ($p=0.082$).

Power analysis

Assuming that bilateral mesh repair in fact increases the risk five-fold for developing infertility (from 0.64% to 3.2%), a population of 1,500 men would be sufficient to achieve a 90% chance of detecting a difference at the $p<0.05$ level.

Similarly, assuming that unilateral mesh repair increases the risk from 0.67% to 1.0%, a population of 20,000 men would be sufficient to achieve a 90% chance of detecting a difference at the $p<0.05$ level.

The sample sizes in the present study were sufficient to reach these levels (Table 1).

Discussion

This study indicates that male infertility is not a major clinical problem after mesh hernia repair. Even if the risk for infertility is slightly higher for men who have undergone bilateral mesh repair compared to those who have undergone sutured repairs, the cumulative incidence of infertility in this group of patients is so low that the advantages of the mesh technique in every other aspect outweigh this theoretical disadvantage. Thus, mesh techniques should still be considered the methods of choice for these patients.

The size of this retrospective register study is, by far, the largest published. The Swedish Hernia Register (SHR), which includes more than 90% of all inguinal hernia operations performed in Sweden, the Swedish National Patient Register and the unique Swedish personal number system allowing all Swedish citizens to be identified and traced, make this type of study possible in our country. We do not know of any other register or system that can repeat this study with the same number of subjects.

This study was designed to reveal any adverse effect of mesh hernia repair regarding male fertility. The design also made it possible to adjust for confounding factors. Although spermiogram, vasography and testicular biopsy would theoretically enable one to differentiate between the specific causes of infertility, the aim of the present study was not to identify the specific mechanisms behind any infertility incurred. Instead the diagnosis of male infertility was used as a surrogate for the incidence of obstructive azoospermia. In this respect it is possible that any difference in the cumulative incidence of infertility between mesh and non-mesh methods is in part the result of a vascular lesion affecting the testis and/or obstructive fibrosis affecting the vas deferens. The cumulative incidence of infertility in all groups was lower than expected. However, we do not know the true incidence since the rates are only based on men seeking health care for infertility. There may have been many more infertile men in the study group as well as in the control population without the desire to have children and thus never being diagnosed as infertile. There is no a priori reason to suspect that men in the study group sought health care for infertility in a different manner than men in the control population. Furthermore, most men with the infertility diagnosis were probably part of a couple being evaluated for infertility. There is no reason to believe that these men were given an infertility diagnosis if in fact the female part was the reason for the involuntary childlessness. However, if there existed a small proportion of men who were misclassified, there is no reason to believe that this misclassification would differ between the groups

The results of this study do not indicate that mesh repair increases the risk for male infertility to the extent that is clinically relevant. The relatively low incidence of infertility resulted in wide confidence intervals for some of the groups, but a potential increase in any of the groups would be so low that it lacks clinical relevance. The sample size provides sufficient statistical power to detect a hypothetical increase in the risk for infertility of up to 3.2% for men undergoing bilateral mesh repair and 1% for men undergoing unilateral mesh repair. Any undetected increase in risk below these levels is of very little clinical importance. Although men that had undergone bilateral mesh hernia repair had a significantly higher risk for infertility than men who had undergone bilateral repair without mesh on both sides, the incidence is still so low that this increase is to be considered of no clinical importance. The results of this study are thus in accordance with our previous prospective study[13] that showed no increased risk for involuntary childlessness in men that had undergone hernia repair using mesh techniques.

In Sweden polypropylene is the dominating alloplastic mesh material. Definitive conclusions regarding other mesh material can not be drawn.

The ultimate way of providing definite evidence on the issue of male infertility after mesh hernia repair would be to conduct a prospective randomised clinical controlled study, with detailed examination including semen analysis. Performing such a study would require a very large study sample and long follow-up. Assuming a cumulative incidence similar to that in the present study, a study population of more than 1000 men would be required to detect a significant difference in male infertility after mesh repair. Furthermore, such a study would

only provide valid results if based on young men with bilateral hernias. We believe that the discomfort for the men participating in such a study (including very personal tests) would make inclusion very difficult. Taking all these aspects into account, we believe that conducting a randomized study is not the way to go. It is our opinion that the present study, based on register data, together with our previous prospective study[13] provide strong evidence that groin hernia surgery using mesh does not cause any increase in the incidence of, nor any clinically important risk for male infertility.

We conclude that surgery for male groin hernia using mesh techniques may continue to be performed without major concern about the risk for male infertility.

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This study was approved by Umeå Ethics Review Board. The authors declare no conflict of interest. This study was partly presented as an abstract at the 4th International Hernia Congress, Joint meeting of the AHS and EHS, Berlin, Germany, September, 9th-12th, 20

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Table 1. Observed and expected cumulative incidences of infertility. Numbers are based on men born between 1950 and 1989 (N=34,267)

Group	**Number of men in the hernia register**	**Number of men diagnosed with infertility after the first registered hernia repair.**	**Observed cumulative incidence (%, 95% confidence interval)**	**Expected cumulative incidence (%)**
Operated unilaterally without mesh*	6281	57	0.91 (0.67-1.14)	1.03
Operated unilaterally with mesh*	22420	133	0.59 (0.49-0.69)	0.67
Operated bilaterally without mesh*	226	0	0 **	1.01
Operated bilaterally, mesh on one side*	346	3	0.87 (0-18.4)	1.05
Operated bilaterally, mesh on both sides*	2293	19	0.83 (0.46-1.20)	0.64
Repeated repairs on any side	2701	21	0.78 (0.45-1.11)	0.68

* No repeated repair on any side

** Confidence interval not applicable
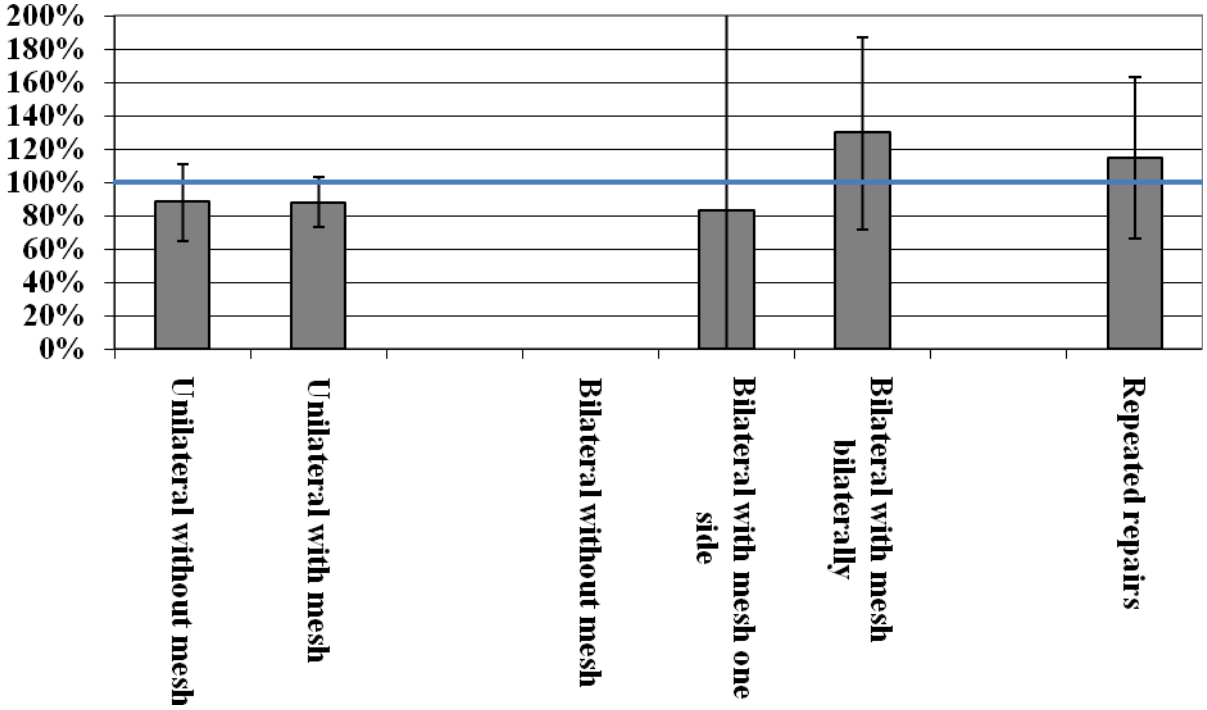
Figure 1. Observed rates of infertility adjusted for expected rates. The expected risk was estimated by adding the expected risk each year following the first repair determined from the ratio between the total number of men with the diagnosis of infertility each year with the total number of men born within the same five-year stratum in Sweden.