Male infertility after mesh hernia repair. A prospective study.

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Abstract

Background Several animal studies have raised concern about the risk for obstructive azoospermia due to vasal fibrosis caused by the use of alloplastic mesh prosthesis in inguinal hernia repair. The aim of this study was to determine the prevalence of male infertility after bilateral mesh repair.

Methods In a prospective study, a questionnaire inquiring about involuntary childlessness, investigation for infertility and number of children was sent by mail to a group of 376 men aged 18 to 55 years, who had undergone bilateral mesh repair, identified in the Swedish Hernia Register (SHR). Questionnaires were also sent to two control groups, one consisting of 186 men from the SHR who had undergone bilateral repair without mesh, and one consisting of 383 men identified in the general population. The control group from the SHR was matched 2:1 for age and years elapsed since operation. The control group from the general population was matched 1:1 for age and marital status

Results The overall response rate was 525/945 (56%). Method of approach (anterior or posterior), type of mesh and testicular status at the time of the repair had no significant impact on the answers to the questions. Nor did subgroup analysis of the men 40 years or younger reveal any significant differences.

Conclusion The results of this prospective study in men do not support the hypothesis that bilateral inguinal hernia repair with alloplastic mesh prosthesis causes male infertility at a significantly greater rate than those operated without mesh.

Introduction

Groin hernia repair in men is one of the most common surgical procedures throughout the world. Over the past 20 years, the use of mesh bioprosthesis in hernia repair has increased rapidly. Currently the open and laparoscopic, mesh-based, tension-free surgical methods dominate. Among the advantages of mesh repair are low recurrence rate, short learning curve and rapid return to physical activity. The use of alloplastic mesh prosthesis in inguinal hernia repair is thus cost-effective for the patient as well as for the health care and social insurance system.

It is well known that alloplastic mesh causes an inflammatory response and a foreign-body reaction in adjacent tissues. The resulting fibrosis of the inguinal wall is suggested to be one of the reasons for the low recurrence rate. Whether or not the mesh is applied from an anterior approach, e.g. according to the Lichtenstein technique[1], or from a posterior approach, as in laparoscopic repair, the mesh is placed in direct contact to the spermatic cord. Several animal studies in various species have reported that the structures of the spermatic cord also react to the mesh[2-6], especially the edge of the mesh[3]. Thickening of the wall of the vas deferens with narrowing and obstruction of the lumen at the site of the mesh but not proximal to it have been observed and discussed[3]. In contrast others have found proximal dilatation but no thickening of the wall of the vas deferens[2]. Decreased arterial perfusion in the testis[5,7] and spermatic venous thrombosis[4] have also been reported.. One study has shown beneficial effects on the integrity of the vas deferens when using lightweight mesh[3] whereas another study did not find any difference in inflammation and fibrosis comparing heavyweight with lightweight mesh[8].

During the past 10 years, a few reports suggested that the use of mesh for male inguinal hernia repair could cause male infertility, most often by obstructive azoospermia[9,10]. Men operated with bilateral mesh hernia repair or men with unilateral repair and impairment of the contralateral testis have been considered to be at the greatest risk. Some authors even suggest that the risk for infertility after mesh repair is of such importance that surgeons should not generally recommend this technique for young men. Because most of these reports are based on a limited number of cases[9,10], their conclusions have been questioned, and some consider the studies inadequate and not valid enough for more explicit conclusions[11]. In contrast, the avoidance of hernia recurrence is still considered to be of major importance[12]. The discussion has been further complicated by the notion that operation for inguinal hernia may instead improve male fertility. There has also been discussion whether or not the proposed risk is of such importance that some or all patients undergoing hernia surgery should be informed in detail preoperatively, even if this may cause some to choose a method associated with greater risk for recurrence and long-term pain[10,11]. Recommendations have also been made to leave the cremaster muscle intact as a protective layer[4] and to dissect the spermatic cord carefully and meticulously, to avoid damaging its structures[13]. A technique for reestablishing patency in the vas deferens has also been described[14].

Most authors agree that we are still not sure if the risk for postoperative infertility is relevant, and more human studies have been requested[3,11,15]. The frequency and clinical relevance of

azoospermia after mesh hernia repair has, to our knowledge, not been evaluated in any large prospective study. The purpose of this study was to determine the prevalence of infertility, measured as involuntary childlessness, in men who hypothetically may run a high risk for azoospermia, i.e. those in fertile age who have undergone bilateral mesh hernia repair.

Methods

The present study is based on data from the Swedish Hernia Register (SHR), which covers many different parameters, including data on method of repair, type of mesh used and testicular status at the time of the hernia repair. The register covers almost 100 % of hernia repairs performed in Sweden (www.incanet.se/Svenskt-Brackregister) and at present more than 180 000 repairs have been recorded. Because every Swedish citizen can be traced by their unique personal registration number, any further repair on the same patient, performed in Sweden, can be traced and cross-checked with the National Population Register.

Two groups were assembled from the SHR, one consisting of patients operated bilaterally with mesh, and one group consisting of men operated bilaterally without mesh. The groups were matched for age and time elapsed since last repair. Because bilateral repairs without mesh were much less frequent than repairs with mesh, thereby limiting the size of the study, this group was identified first. The mesh group was then matched to the non-mesh group two cases to one. Included were men aged 18-55 years. Men who had undergone more than one repair in the same groin were excluded.

A second control group, matched for age and marital status, was assembled from the National Population Register. This control group consisted of one subject for each man operated bilaterally with mesh.

In April 2009, all men in the three groups received the same questionnaire by mail. The questionnaire included the questions listed in Table 2. There was also an additional question inquiring about previous hernia repair addressed to the controls assembled from the general population. Three weeks after the questionnaire was distributed a reminder was sent to non-responders.

The difference in numbers of children born after the last repair was tested with Student's t-test. For all other questions the differences between the groups were tested with chi-square test. A p-value of less than 0.05 was considered significant. The results for continuous variables are presented as mean + standard deviation (SD) if not stated otherwise. For categorical data, absolute numbers in addition to percentages are provided. All three groups were included in comparisons regarding the first two questions (involuntary childlessness and investigations for infertility the last five years). The remaining questions were not applicable for the control group from the general population.

Results

Altogether 192 men aged 18-55 years operated bilaterally without mesh were identified in the SHR. These men were matched 1:2 with 384 men operated bilaterally with mesh and 1:2 with 384 men from the general population. There were 8 men in the bilateral mesh repair group, 6 men in the non-mesh bilateral repair group, and one in the general population group who had emigrated or deceased by the time the questionnaire was administrated.

The response rates were 232/376 (62%) in the bilateral mesh repair group, 112/186 (60%) in the bilateral non-mesh repair group and 181/383 (53%) in the control group. All data presented are based on the responders. Responders and non-responders did not differ in age and marital status (Table 1). Mean age in the bilateral mesh repair group was 42.3 years ±8.8 years, 43.4 years ±8.8 years in the bilateral suture repair group, 43.1 years ±8.1 years in the control group. Altogether 179 (33%) were 40 years of age or younger when they answered the questionnaire. There was no significant difference in age between the two hernia repair groups and the control group. Mean time elapsed since the last repair in the two groups from the SHR was 6.9 years, ±3.3 years. There was no significant difference in time elapsed since the last repair between the two groups. Testicular atrophy or absence of the testicle on the side operated was noted in 6 (1.1%) of the repairs. Light-weight meshes were used in 17 patients (4.9%) of the mesh repairs. The mesh repairs were performed via an anterior approach in 435 (80%) patients and via a posterior approach, open, or laparoscopic, in 111 (20%) patients. There were 16 (8%) subjects in the control group assembled from the general population who stated that they had undergone hernia repair.

There were no significant differences between the groups for any of the questions, including questions inquiring about involuntary childlessness, infertility investigation, and number of children (Table 2). Subgroup analysis of men 40 years or younger did not reveal any significant differences. Method of approach (anterior or posterior), type of mesh, and testicular status at the time of the repair had no significant impact on the answers to the questionnaire.

Discussion

The results of this prospective study in men do not support the hypothesis that inguinal hernia repair with mesh causes male infertility at a significantly greater rate than those operated without mesh. The men included in the analysis, *i.e.* young men who had undergone repair on both sides using alloplastic mesh prosthesis, represent a group that hypothetically runs the greatest risk of infertility if the use of mesh has a substantial impact on the risk for obstructive azoospermia. Because no increase in risk was seen after bilateral mesh repair, unilateral use of mesh should be even safer as far as infertility is concerned. The findings were also confirmed by the results of a subgroup analysis of the youngest men in our study.

The study was not designed to determine whether bilateral hernia surgery in males increases the risk for infertility per se, but rather to explore the effect of the mesh. Our results do not indicate that there is a substantial risk with those methods included in our study.

Infertility is a serious complication, especially in young men who may later wish to conceive a child. It cannot be ruled out that the relatively high rate of non-responders obscures a risk increase not detected in the study. Nevertheless, these results do not indicate that the risk of infertility is of such magnitude that the mesh technique should be avoided in young men. The advantages of the mesh-method appears to outweigh potential drawbacks, at least outside centers specialized in non-mesh inguinal hernia repair with comparable recurrence rates. Increasing the use of non-mesh methods would most likely lead to an unwanted increase in recurrences and more reoperations, because the introduction of mesh repairs has decreased the rate of recurrences[12]. A reoperation may be even more traumatic to the spermatic cord than any primary repair, whether it is with or without mesh.

The more radical dissection along the spermatic cord and resection of cremaster muscles required to perform a sutured repair may, in fact, be more harmful than the mesh itself. It may be argued that the trauma and ischemia to the vas caused by the more extensive dissection is associated with a greater risk for injury to the vas deferens than the fibrosis caused by the mesh. Our study, however, did not provide any statistical evidence for this hypothesis.

In mesh operations, the recommendation of using the intact cremasteric muscle as a protective layer for the spermatic cord structures is theoretically preferable and recommended by some[4]. This is possible only when the mesh is placed over the posterior wall. Regarding to infertility, our study found no differences between the mesh methods, but the study design was not done to answer that question and we do not know exactly how the spermatic cord and the cremasteric muscle was treated in each Lichtenstein operation. Moreover the Lichtenstein group is numerically very dominating in our material.

In the control group from the general population, 7% stated that they had experienced a period of one year of involuntary childlessness (Table 2). The sample size of the study responders was sufficient to achieve a statistical power of 80% to detect a hypothetical doubled risk in the mesh repair group at the $p<0.05$ level. Considering the fact that the men in the bilateral mesh group actually gave less positive responses than the control groups to most of the questions, the statistical power is even stronger than so. The risk of these findings being the result of a Type II error is, thus, relatively small, at least if a risk increase greater than a factor of two is assumed.

Our study does have some limitations. Not unexpectedly and probably due to the fact that many of the questions concerned matters that may be perceived as quite intimate, the response rate was relatively low, despite the reminder. Although it cannot be excluded that the prevalence of infertility may have differed between responders and non-responders, the groups did not differ in terms of age or marital status. Whereas the willingness to answer the questionnaire may be affected by a history of involuntary childlessness, there is no obvious reason to believe that it could be affected by the method of hernia repair. The risk of a systematic selection bias decreasing the difference between the mesh group and non-mesh

group is small, although the overall prevalence of infertility may have been affected by selection of responders.

We are well aware of the fact that the etiologies of involuntary childlessness are multiple and involve both partners; however the power of the study was sufficient to detect a hypothetical influence from the use of mesh despite a high background prevalence of involuntary childlessness.

Analyze of the spermiogram would of cause have been an even more reliable method to diagnose male infertility, but when designing the study, we expected that method to be to intimate and thereby giving us a response rate making the result useless.

The risk for infertility after mesh repair, as proposed by other authors[4,5,9,10], has been regarded as an important question. Our results indicate that at the informed consent, the surgeon should not focus on the infertility problem. To advise a man to undergo a hernia repair with a mesh-method must be regarded as a recommendation based on the most recent clinical evidence.

In our opinion cryopreservation of sperm prior to hernia surgery in young men, with or without mesh, is not necessary. It may be indicated in selected cases before bilateral inguinal hernia surgery and also when doing unilateral operations in men with a medical history and clinical findings indicative of testicular dysfunction or abnormalities of the vas deferens on the contralateral side. This concept includes testicular atrophy and a history of previous surgery that could have harmed the testicle or the vas deferens. Local legal circumstances and health-care policies may also have to be taken into consideration when deciding on cryopreservation of sperm. Finally, the decision must be taken by the patient together with the surgeon responsible. Cost-effectiveness will also be taken into account in those countries where the national health care system covers the cost and in those countries where economic resources are very limited.

In conclusion, the study showed no increase in involuntary childlessness in men who had undergone bilateral mesh repair. Although it cannot be ruled out that there may be a minor increase in risk not detected in this study, it is very unlikely that this increase would be great enough to outweigh all advantages of mesh repairs in comparison with sutured repairs. In our opinion based on the results of this study, mesh repair could continue to be the method of choice in hernia surgery.

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Table 1. Marital status

	Operated bilaterally with mesh	**Operated bilaterally without mesh**	**Controls from the general population**
Married	107 (46.1%)	50 (44.6%)	95 (47.0%)
Unmarried	95 (40.9%)	47 (42.0%)	93 (46.0%)
Divorced	30 (12.9%)	15 (13.4%)	14 (6.0%)
Total	232 (100%)	112 (100%)	202 (100%)

Table 2. Outcome of the questionnaire

	Operated bilaterally with mesh		**Operated bilaterally without mesh**		**Controls from the general population**	
	Positive responses/ Total number of responders	% (95% confidence interval)	Positive responses/ Total number of responders	% (95% confidence interval)	Positive responses/ Total number of responders	% (95% confidence interval)
1. Have you had a period of at least one year of involuntary childlessness during the last five years?	15/232	6.5 (3.3-9.6)	10/111	9.0 (3.7-14.3)	14/201	7.0 (3.4-10.5)
2. Have you undergone investigation for infertility the last five years?	6/229	2.6 (0.6-4.7)	5/112	4.5 (0.6-8.3)	9/201	4.5 (1.6-7.3)
3. Did you have any children prior to the hernia repair?	120/228	52.6 (46.2-59.1)	61/111	55.0 (45.7-64.2)	Not applicable	
4. Did you have a period of at least one year of involuntary childlessness prior to the hernia repair?	14/229	6.1 (3.0-9.2)	6/110	5.5 (1.2-9.7)	Not applicable	
5. Have you made any attempts to have children after the hernia repair?	58/230	25.2 (19.6-30.8)	31/112	27.7 (19.4-36.0)	Not applicable	
6. Have you had a period of at least one year of involuntary childlessness after the hernia repair?	14/89	15.7 (8.2-23.3)	11/48	22.9 (11.0-34.8)	Not applicable	
7. Have you undergone investigation for infertility after the hernia repair?	3/89	3.4 (0.0-7.1)	4/48	8.3 (0.5-16.2)	Not applicable	
	Total number of responders	Mean number of children ± standard deviation	Total number of responders	Mean number of children ± standard deviation		
8. How many children have you had after the last hernia repair?	91	0.9 ± 0.9	46	0.8 ± 0.7	Not applicable	

References

1. Lichtenstein IL, Shulman AG, Amid PK, Montllor MM. The tension-free hernioplasty. Am J Surg 1990; 157(2): 188-93.

2. Maciel LC, Glina S, Palma PC, Nascimento LF, Netto NR Jr. Histopathological alterations of the vas deferens in rats exposed to polypropylene mesh. BJU Int. 2007; 100(1): 187-90.

3. Junge K, Binnebösel M, Rosch R, Ottinger A, Stumpf M, Mühlenbruch G, Schumpelick V, Klinge U. Influence of mesh materials on the integrity of the vas deferens following Lichtenstein hernioplasty: an experimental model. Hernia. 2008; 12(6): 621-6.

4. Peiper C, Junge K, Klinge U, Strehlau E, Ottinger A, Schumpelick V. Is there a risk of infertility after inguinal mesh repair? Experimental studies in the pig and the rabbit. Hernia 2006; 10(1): 7-12.

5. Peiper C, Junge K, Klinge U, Strehlau E, Krones C, Ottinger A, Schumpelick V. The influence of inguinal mesh repair on the spermatic cord: a pilot study in the rabbit. J Invest Surg. 2005; 18(5): 273-8.

6. Uzzo RG, Lemack GE, Morrisey KP, Goldstein M. The effect of mesh bioprosthesis on the spermatic cord structures: a preliminary report in a canine model. J Urol. 1999; 161(4):1344-9.

7. Ayede H, Erhan Y, Sakarya A, Kara E, Ilkgul O, Can M. Effect of mesh and its location on testicular flow and spermatogenesis in patients with groin hernia. Acta Chir Belg. 2003; 103(6): 607-10.

8. Berndsen FH, Bjursten LM, Simanaitis M, Montgomery A. Does mesh implantation affect the spermatic cord structures after inguinal hernia surgery? An experimental study in rats. Eur Surg Res. 2004; 36(5):318-22.

9. Yamaguchi K, Ishikawa T, Nakano Y, Kondo Y, Shiotani M, Fujisawa M.Rapidly progressing, late-onset obstructive azoospermia linked to herniorrhaphy with mesh. Fertil Steril. 2008; 90(5): 2018.e5-7.

10. Shin D, Lipshultz LI, Goldstein M, Barmé GA, Fuchs EF, Nagler HM, McCallum SW, Niederberger CS, Schoor RA, Brugh VM 3rd, Honig SC. Herniorrhaphy with polypropylene mesh causing inguinal vasal obstruction: a preventable cause of obstructive azoospermia. Ann Surg. 2005; 241(4): 553-8.

11. Fitzgibbons RJ Jr. Can we be sure polypropylene mesh causes infertility? Ann Surg. 2005; 241(4): 559-61.

12 Jenkins JT, O'Dwyer PJ. Inguinal hernias. BMJ. 2008; 336(7638): 269-72.

13. Valenti G, Baldassarre E. Vasal obstruction after hernioplasty: the importance of surgical strategy in preventing azoospermia. Ann Surg. 2006; 244(1): 160.

14. Nagler. H, Belletete B, Gerber E, Dinlenc C. Laparoscopic retrieval of retroperitoneal vas deferens in vasovasostomy for postinguinal herniorraphy obstructive azoospermia. Fertil Steril 2005; 83(6):1842-4.

15. Agarwal BB, Sinha BK, Mahajan KC. The risk of communicating TEP-related infertility risk is an opportunity and not a “Cinderella concern” any more. Surg Endosc. 2008; 22:1557-58.