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ORIGINAL ARTICLE

Bilateral endoscopic totally extraperitoneal (TEP) inguinal hernia repair does not impair male fertility

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Abstract
Purpose Endoscopic totally extraperitoneal (TEP) hernia repair with polypropylene mesh has become a well-established technique. However, since the mesh is placed in close contact with the spermatic cord, mesh-induced inflammation may affect its structures, possibly resulting in impaired fertility. The aim of this observational prospective cohort study was to assess fertility after bilateral endoscopic TEP inguinal hernia repair in male patients.
Methods Fifty-seven male patients (22–60 years old) with primary, reducible, bilateral inguinal hernias underwent elective bilateral endoscopic TEP hernia repair with use of polypropylene mesh. The primary outcome was testicular perfusion; secondary outcomes were testicular volume, endocrinological status, and semen quality. All patients were assessed preoperatively and 6 months postoperatively.
Results Follow-up was completed in 44 patients. No statistically significant differences in measurements of testicular blood flow parameters or testicular volume were found. Postoperative LH levels were significantly higher [preoperative median 4.3 IU/L (IQR 3.4–5.3) versus postoperative median 5.0 IU/L (IQR 3.6–6.5), $p = 0.03$]. Levels of inhibin B were significantly lower postoperatively [preoperative median 139.0 ng/L (IQR 106.5–183.0) versus postoperative median 27.0 ng/L (IQR 88.3–170.9), $p = 0.01$]. No significant changes in FSH or testosterone levels were observed. There were no differences in semen quality.
Conclusions Our data suggest that bilateral endoscopic TEP hernia repair with polypropylene mesh does not impair fertility, as no differences in testicular blood flow, testicular volume, or semen quality were observed. Postoperative levels of LH and inhibin B differed significantly from preoperative measurements, yet no clinical relevance could be ascribed to these findings.

Keywords Inguinal hernia · Bilateral · Endoscopic · TEP · Fertility

Introduction

Inguinal hernia repair is the most commonly performed general surgical procedure worldwide, with a lifetime risk of developing an inguinal hernia of 27% for men and 3% for women [1]. There has been a considerable reduction in recurrence rates since the introduction of tension-free mesh repair, which has now become standard practice [2]. Endoscopic totally extraperitoneal (TEP) hernia repair, based on the concept of strengthening the weak inguinal floor by reducing the sac and placing preperitoneal mesh, has become increasingly popular, since this approach provides faster recovery and a lower incidence of postoperative (chronic) pain compared to open techniques [3–5]. Hypothetically, mesh-induced fibrosis or direct iatrogenic damage may affect the structures of the spermatic cord and impair testicular function and fertility. Rare but potentially harmful complications that may occur after hernia surgery include ischemic orchitis, testicular atrophy, or obstructive

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azoospermia [6]. Several experimental animal studies and case reports have described patients with these complications after open hernia repair with implantation of polypropylene mesh [7–10]. A systematic review on male infertility following inguinal hernia repair was recently conducted; however, the majority of procedures were open (99.5%) and unilateral (>80%) [11]. Men undergoing bilateral mesh hernia repair or unilateral hernia repair with pre-existing impairment of the contralateral testis are considered to be at greatest risk of fertility impairment, but relevant large and prospective clinical trials on endoscopic bilateral hernia repair are lacking. The objective of this study was to evaluate the effect of endoscopic bilateral TEP inguinal hernia repair on male fertility by analyzing testicular perfusion and volume, semen analysis, and endocrinological status.

Patients and methods

Patients

This observational, prospective study was conducted on male patients (22–60 years old) with primary bilateral inguinal hernias at the Department of Surgery in a high-volume hospital in the Netherlands specialized in the TEP technique for inguinal hernia repair (Diakonessenhuis Utrecht/Zeist). The aim of this study was to evaluate male fertility preoperatively and 6 months after bilateral TEP inguinal hernia surgery. The study was approved by the regional Medical Ethics Committee (VCMO, Nieuwegein, The Netherlands) and the hospital's Ethics Board, and it was registered in the Netherlands National Trial Registry (NTR2208). Written informed consent was obtained from all participants. Patients eligible for inclusion were men of fertile age (18–60 years old) with primary, bilateral inguinal hernias who were scheduled for elective endoscopic totally extraperitoneal (TEP) hernia repair. Patients with an ASA classification >III, recurrent and/or femoral/scrotal hernias, a medical history of testicular pathology, pelvic surgery or radiotherapy, known fertility problems, co-morbidity associated with possible fertility problems, and use of medication that might impair fertility were excluded from participation (Table 1). Participants were recruited at their first visit to the outpatient clinic and enrolled after signing informed consent. Preoperative patient data [age, medical history, smoking habit, and body mass index (BMI)] were obtained through measurements and a general questionnaire.

Surgical procedure

Patients underwent simultaneous bilateral endoscopic TEP inguinal hernia repair with use of a double-mesh implantation technique. The procedure was performed under general anesthesia. Two identical polypropylene meshes (Prolene®, 10 × 15 cm) were positioned in a tension-free manner in the preperitoneal space. The mesh graft was not fixed to avoid possible entrapment neuralgia. Nyhus classification, operative time, and intraoperative complications were recorded during surgery. Surgeons with extensive expertise in this procedure (>500 procedures per surgeon) performed all

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Male gender	Female gender
Age ≥18 and ≤60 years	Age ≥60 years
Primary, reducible inguinal hernias	Period of high fever prior to semen analysis
Bilateral hernias	Recurrent inguinal hernias
Eligible for TEP (and therefore for general anesthesia)	Unilateral hernias
	Hydrocele and/or varicocele
	Femoral or scrotal hernia
	Incarcerated hernia
	ASA classification ≥III
	Previous medical history of:
	Testicular infarction
	Testicular torsion
	Cryptorchidism
	Inguinal, scrotal, testicular or prostate surgery
	Vasectomy
	Radiotherapy of pelvic region
	Diabetes mellitus
	Cystic fibrosis
	Fertility problems and/or treatment, erection disorders or (other) problems in sexual function
	Use of gonadotropins
	Use of anabolic steroids

TEP totally extraperitoneal, *ASA* american society of anesthesiologists operations. The operation and perioperative care did not differ from those of patients not participating in the study.

Postoperative management and follow-up

Patients were discharged on the day of surgery, unless complications prohibited early discharge. Duration of hospital stay and postoperative complications were recorded. Patients were advised to take pain medication as needed (paracetamol, and if necessary, diclofenac) and to avoid strenuous physical activity (such as lifting and sports) during the first postoperative week. The routine follow-up schedule after TEP hernia repair in our center was followed: patients were followed-up by telephone 6 weeks after surgery and were scheduled for an additional visit to the outpatient clinic in case of complaints. Six months postoperatively, all participants visited the outpatient clinic for assessment of fertility parameters.

Outcome measures

Male fertility parameters were assessed preoperatively on the day of surgery and 6 months postoperatively by means of bilateral scrotal ultrasonography, semen analysis, and biochemical analysis. The primary outcome of this study was testicular perfusion, and secondary outcome measures were testicular volume, semen quality, and serum endocrinological status.

Testicular perfusion and volume

Bilateral testicular perfusion and volume were determined by measuring the blood flow velocity (cm/s) by color Doppler ultrasonography (CDUS) and gray-scale ultrasonography, respectively. Measurements were performed by experienced ultrasound technicians, who received specific instructions for the purpose of this study. The patient was placed in the supine position and the penis was held suprapubically. For testicular perfusion, blood flow was measured at four different points: the inguinal and extratesticular–intrascrotal level of the testicular artery, the capsular arteries, and the intratesticular arteries. The parameters assessed were peak systolic velocity (PSV), end diastolic velocity (EDV), resistive index (RI), pulsatility index (PI), and acceleration time (ATA). To improve intraobserver reliability, each parameter was measured three different times and the mean value was calculated. Possible signs of distension of the epididymis and/or vas deferens, as well as formation of a thrombus in the pampiniform plexus, were also assessed.

To determine testicular volume, length, width, and height were measured separately, and the ultrasonography device performed a volume calculation with these dimensions.

Semen analysis

For semen analysis, seminal volume (mL), sperm concentration (10^6 cells/mL), motility (% progression), VCM (volume × concentration × progressive motility), and pH were analyzed. Semen was obtained in our hospital by means of masturbation after which the sample was analyzed within an hour. Patients were instructed to remain abstinent for 48 h so that reliable semen samples could be obtained.

Biochemical analysis

Endocrinological status was assessed by determining serum levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone. Inhibin B serum level was also collected. Blood samples were obtained and analyzed in our hospital.

Statistical analysis

Statistical analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). Differences in preoperative and postoperative fertility parameters were analyzed by means of the paired sample t-test (parametric data) or the Wilcoxon signed-rank test (non-parametric data). Comparison of preoperative and postoperative measurements of testicular perfusion and volume was done separately for the left and right testes. In case of a statistically significant difference in blood hormone levels, an additional calculation with the reference change value (RCV) formula was performed. The RCV formula incorporates analytical variation and intraindividual biological variation, and the difference in hormone level must exceed the RCV to be clinically significant [12]. A p value <0.05 was considered statistically significant.

Results

Fifty-seven consecutive patients were recruited and operated on between March 2010 and March 2016 (Table 2). The median age of the study population was 51 years (range 22–60 years). One patient with a history of appendicitis complicated by abscess formation had multiple adhesions, leading to bladder perforation intraoperatively, which was managed conservatively with an indwelling catheter. Two patients were clinically diagnosed with a recurrent hernia and underwent an additional operation: one patient developed an early recurrence 5 days after surgery, the other recurrence was diagnosed 4 months after surgery. Two patients required an additional visit to the outpatient clinic due to pain. Ultrasonography showed postoperative hematomas in both patients, and the pain subsided with conservative

Table 2 Patient and treatment characteristics ($n = 57$)

Age (years)	51.0 (42.0–56.2)
BMI (kg/m^2)	24.7 (23.0–27.3)
ASA classification (%)	
I	77
II	23
Smoking (%)	
No	82
Yes	18
Type of hernia (%)	
Left, medial	54
Left, lateral	46
Right, medial	49
Right, lateral	51
Operation time (min)	28.0 (24.5–31.5)
Intraoperative complications (%)	
Bladder injury	2
Conversion rate (%)	0
Postoperative complications (%)	
Hematoma	4
Recurrence	4

Continuous data are presented as median (IQR)

BMI body mass index, *ASA* american society of anesthesiologists

treatment. No readmissions after discharge from the hospital were reported.

In total, 44 patients (78.6%) completed the follow-up period of 6 months. One patient was excluded since he was not able to obtain semen preoperatively. One patient who was only experiencing symptoms in the right inguinal region requested a change to unilateral intervention hours before surgery. Eight of the patients withdrew their consent, and 3 of the patients could not be reached for follow-up, despite multiple attempts by telephone and e-mail.

Testicular perfusion and volume

There were no significant changes in PSV, EDV, RI, PI, and AT between pre- and postoperative measurements of testicular perfusion at all levels of both sides (Table 3). There was an increase in the PSV and EDV of the left intratesticular arteries from preoperative to postoperative assessment that trended towards significance. A thrombus in the right-sided pampiniform plexus was observed in 1 patient preoperatively and 3 patients postoperatively. None of the patients had a thrombus in the left pampiniform plexus on preoperative assessment; postoperatively, this finding was present in 3 patients.

Analysis of bilateral testicular volume showed no significant differences between pre- and postoperative measurements.

Endocrinological status

Comparison of blood hormone values revealed higher LH levels postoperatively with a median value of 5.0 IU/L (IQR 3.6–6.5) compared to 4.3 IU/L (IQR 3.4–5.3) (Table 4). Both measurements were within the LH reference range of 1.3–13.0 IU/L. There were no significant differences in FSH or testosterone levels. Levels of inhibin B were significantly lower postoperatively with a preoperative median of 139.0 ng/L (IQR 106.5–183.0) versus a postoperative median of 127.0 ng/L (IQR 88.3–170.9); both measurements were within the inhibin B reference range (<400 ng/L).

Semen quality

No statistically significant differences in semen volume, concentration, motility, VCM, or pH after bilateral TEP inguinal hernia repair were found (Table 4).

Discussion

The present study shows no impairment of fertility 6 months after bilateral endoscopic TEP inguinal hernia repair. Polypropylene, the biomaterial most commonly used in mesh hernia repair, has good mechanical stability and induces an acute inflammatory reaction followed by a chronic foreign body fibroblastic reaction, which is essential for optimal fixation and incorporation of the biomaterial in the abdominal wall [13]. During the TEP procedure, the mesh is placed in close contact with the vas deferens, testicular vessels, autonomic nerves, and fascia. Injuries to the vas deferens and/or spermatic vessels may be a result of direct iatrogenic injury by dissection of the preperitoneal space, or delayed obstruction caused by scar tissue from the mesh-induced inflammatory tissue response, which is part of the normal healing process [9, 14].

No significant differences in testicular perfusion or volume 6 months after bilateral mesh hernia repair were observed. Blood supply through the spermatic vessels was assessed in this study using CDUS, a well-documented procedure for investigating testicular vascularization and perfusion [15]. Due to interdependence of flow within an arterial network, the blood flow was measured on testicular, intracapsular, and intratesticular levels to avoid false normal results from partial measurements. On CDUS measurements, the RI and PI are used for interpretation of vascular resistance and tissue perfusion. When testicular perfusion is disrupted, a decrease in end diastolic pressure and an increase in RI and PI can be seen, with an elevated RI suggestive of ischemia [16]. While we did not find significant changes in blood flow parameters for left and right testicular perfusion, we did observe a trend

Table 3 Testicular perfusion and volume ($n = 44$)

	Preoperative		Postoperative		*p* value	
	Left	Right	Left	Right	Left	Right
Perfusion testicular artery (inguinal)						
PSV (cm/s)	15.5 (10.1–22.4)	15.9 (11.1–24.8)	15.5 (10.1–21.4)	14.4 (9.8–19.9)	0.80	0.52
EDV (cm/s)	2.3 (1.8–3.0)	2.4 (1.7–3.4)	2.0 (2.0–3.7)	2.5 (1.6–3.4)	0.12	0.51
RI	0.8 (0.7–0.9)	0.8 (0.8–0.9)	0.8 (0.8–0.9)	0.8 (0.7–0.9)	0.09	0.52
PI	2.2 (1.5–2.8)	2.6 (2.0–3.3)	2.4 (1.9–2.8)	2.5 (1.8–3.1)	0.97	0.78
AT (ms)	131.1 (76.3–248.7)	162.0 (6.3–238.8)	150.0 (83.0–217.0)	140.0 (80.0–213.0)	0.83	0.85
Perfusion testicular artery (scrotal)						
PSV (cm/s)	12.2 (9.0–14.5)	10.6 (8.7–14.7)	11.1 (8.6–16.3)	11.8 (8.3–14.4)	0.68	0.89
EDV (cm/s)	2.5 (1.8–3.5)	2.3 (1.7–3.4)	2.4 (1.7–3.6)	2.6 (2.0–3.7)	0.76	0.36
RI	0.8 (0.7–0.8)	0.8 (0.7–0.8)	0.8 (0.7–0.8)	0.8 (0.7–0.8)	0.67	0.62
PI	1.9 (1.6–2.2)	1.8 (1.4–2.2)	1.8 (1.5–2.6)	1.9(1.4–2.5)	0.88	0.34
AT (ms)	79.0 (57.0–123.6)	80.0 (48.0–122.0)	86.0 (56.4–137.0)	76.3 (49.8–123.2)	0.93	0.23
Perfusion intracapsular arteries						
PSV (cm/s)	9.4 (7.5–13.0)	9.2 (6.6–10.7)	9.1 (6.8–11.2)	10.0 (7.0–12.6)	0.28	0.51
EDV (cm/s)	3.1 (1.9–4.1)	3.0 (1.9–3.5)	2.9 (1.9–4.0)	3.0 (1.9–3.9)	0.87	0.38
RI	0.7 (0.6–0.7)	0.7 (0.6–0.7)	0.7 (0.6–0.7)	0.7 (0.6–0.7)	0.68	0.84
PI	1.4 (1.0–1.7)	1.4 (1.1–1.8)	1.4 (1.1–1.6)	1.3 (1.1–1.8)	0.31	0.39
AT (ms)	53.0 (36.2–78.0)	47.3 (29.3–71.4)	49.1 (36.5–72.7)	52.3 (32.7–88.6)	0.26	0.73
Perfusion intratesticular arteries						
PSV (cm/s)	6.7 (5.0–8.8)	5.6 (4.0–8.0)	7.7 (4.8–11.3)	6.1 (4.6–10.2)	0.07	0.11
EDV (cm/s)	2.5 (1.8–3.4)	2.4 (1.3–3.0)	3.1 (2.1–4.2)	2.4 (1.8–3.3)	0.05	0.28
RI	0.6 (0.5–0.7)	0.6 (0.5–0.7)	0.6 (0.5–0.7)	0.6 (0.5–0.7)	0.86	0.49
PI	1.0 (0.8–1.4)	1.1 (0.8–1.5)	1.1 (0.9–1.3)	1.1 (0.8–1.3)	0.62	0.37
AT (ms)	31.1 (17.7–43.1)	24.0 (14.0–31.3)	34.5(25.1–52.0)	25.9 (19.3–45.0)	0.12	0.44
Testicular volume (mL)	15.5 (11.8–18.8)	16.5 (12.8–19.8)	15.4 (11.9–18.6)	17.4 (12.9–20.3)	0.14	0.95

Data are presented as median (IQR)

PSV peak systolic velocity, *EDV* end diastolic velocity, *RI* resistive index, *PI* pulsatility index, *AT* acceleration time

Table 4 Endocrinological status and semen analysis ($n = 44$)

	Preoperative	Postoperative	*p* value
Endocrinological status			
LH (IU/L)	4.3 (3.4–5.3)	5.0 (3.6–6.5)	0.03
FSH (IU/L)	5.0 (3.5–7.1)	5.0 (3.3–7.0)	0.99
Testosterone (nmol/L)	15.1 (11.9–19.9)	14.7 (10.4–19.4)	0.14
Inhibin B (pg/mL)	139.0 (106.5–183.0)	127.0 (88.3–170.9)	0.01
Semen quality			
Volume (mL)	3.0 (2.0–3.5)	3.0 (1.7–4.0)	0.74
Concentration (10^6 cells/mL)	49.0 (22.3–90.3)	39.0 (11.8–82.3)	0.21
Motility (% progression)	41.5 (24.5–58.0)	42.0 (26.3–59.3)	0.86
VCM (10^6)	51.5 (20.0–133.0)	28.5 (14.3–121.3)	0.29
pH (mol/L)	7.7 (7.5–8.0)	7.7 (7.5–7.7)	0.87

Data are presented as median (IQR)

LH luteinizing hormone, *FSH* follicle-stimulating hormone, *VCM* volume × concentration × progressive motility towards significance in higher PSV and EDV values of the left intratesticular arteries. However, RI and PI ratios calculated from the PSV and EDV were not significantly different, so we did not regard these differences as clinically relevant. Since the start of this study, several other studies have investigated the effect of endoscopic mesh hernia repair on testicular perfusion and volume [17–23]. Results of these studies may be divided into early postoperative (1–7 days after surgery) and late postoperative (3 months–3 years after surgery) categories. With respect to early postoperative results of testicular perfusion, Stula et al. demonstrated an increase in PSV at the testicular, capsular, and intratesticular level, and higher RI and PI ratios of the intratesticular artery 2 days after laparoscopic TAPP hernia repair, which normalized in the late postoperative period after 5 months [17]. While not statistically significant, Lal et al. demonstrated a trend of increased RI of testicular, capsular, and intratesticular arteries 1 day after laparoscopic TEP repair, which then decreased to preoperative values 7 days after surgery [18]. Ersin et al. noticed a significant decrease in RI of capsular and intratesticular arteries and an increase in PSV and EDV of the capsular artery on the first day postoperative that normalized 1 week after the operation [19]. In summary, the findings of these studies suggest only a transient change in testicular perfusion in the early postoperative period. The results might be influenced by hypervascularity and edema of the testes and epididymes, as these are known to occur in the early postoperative period. Thus, the short-term effects on perfusion appear to be a result of the operation itself rather than the fibroblastic tissue response, which would be expected to have more long-term effects. In concordance with our study, the studies that assessed testicular perfusion between 3 months and 3 years after mesh hernia repair did not find clinically relevant changes in the testicular blood supply [20–23].

Since interruption of the testicular blood supply may result in testicular atrophy, testicular volume was also taken into account. No significant differences in testicular volume were found in our study population. Akbulut et al. found a significant decrease in testicular volume after TEP hernia repair; however, postoperative testicular volume remained within normal limits, and this finding was not considered as testicular atrophy [24]. This study did not assess testicular perfusion.

Thrombosis of the pampiniform plexus may result from overzealous dissection of the cord or excessive use of cauterization intraoperatively, or from pressure exerted by a large hematoma in the groin postoperatively [25]. Pampiniform plexus thrombosis may cause venous outflow obstruction and testicular infarction. Although a few patients had plexus pampiniformis thrombi on scrotal ultrasound, no testicular infarction was observed in our study population. In our opinion, it is more likely that these thrombi are the result of postoperative hematoma or are not even related to the surgical intervention.

Six months postoperatively, significantly higher blood levels of LH and lower blood levels of Inhibin B were found. LH, also called interstitial cell-stimulating hormone in males, stimulates secretion of the steroid hormone testosterone by Leydig cells [24]. High levels of LH could indicate testicular dysfunction due to decreased testosterone production. In the case of low testosterone, hypothalamic secretion of GnRH and hypophysic secretion of LH and FSH would be stimulated to increase spermatogenesis. However, FSH was not increased in our study. Furthermore, when applying the reference change value (RCV) for LH, which takes biological and analytic variations between separate measurements into account, LH levels did not increase significantly. Inhibin B, secreted by the Sertoli cells, inhibits production of FSH, thereby leading to decreased spermatogenesis. However, levels of FSH did not differ significantly, and the RCV formula showed that the decrease in inhibin B was not significant. Taking these factors into consideration, we did not regard the isolated higher levels of LH and decreased levels of inhibin B as clinically relevant. Our findings on LH, FSH, and testosterone levels are in line with other studies that analyzed blood hormone levels after endoscopic inguinal hernia repair and did not find significant changes in endocrinological parameters in the early postoperative to 6 months postoperative period [18, 22, 24]. Inhibin B has, to our knowledge, not been investigated in this context before.

Semen analysis can be used as a parameter for seminal tract patency or obstruction. No significant differences in semen volume, concentration, motility, or pH were found after TEP hernia repair. Several other studies performed semen analysis after endoscopic inguinal hernia repair [17, 21, 22, 26]. Only the study conducted by Peeters et al. found a significant decrease in one of the parameters assessed in semen [21]. In this trial, where quality of life and fertility analysis after laparoscopic inguinal hernia repair were compared between patients who received a lightweight (Vypro II, TiMesh) versus a heavyweight (Marlex) mesh, sperm motility was decreased at 1-year follow-up in the lightweight group. This decrease in sperm motility could not be confirmed in a long-term follow-up of 3 years [23]. The clinical relevance of this isolated decreased sperm motility is not entirely clear, as fertility depends on several factors and all other sperm parameters remained within normal limits.

To our knowledge, this study represents the first clinical prospective trial assessing testicular perfusion and volume, semen quality, and endocrinological status after endoscopic TEP inguinal hernia repair in a human patient population comprised solely of bilateral hernia repairs. This study design ensured that a healthy contralateral side did not positively influence our results. More than 80% of studies that have been performed on male fertility after inguinal hernia repair consisted of unilateral repairs [11]. Studies involving bilateral inguinal hernia repairs often had mixed populations of uni- and bilateral hernias, did not involve TEP hernia repair, had relatively small numbers of patients, or measured different outcome parameters. Since we are an expertise TEP hernia center, our patient population involved only bilateral TEP hernia repairs, making our results not applicable to other frequently performed preperitoneal techniques. However, since clinical outcomes of laparoendoscopic techniques are similar, we do not expect differences in fertility outcomes between TEP and TAPP. In open preperitoneal operations such as TIPP and TREPP mesh placement and possible damage to the vas are theoretically comparable with laparoendoscopic techniques. However, long-term outcomes of these techniques have not been studied thoroughly and there is insufficient evidence to recommend these techniques for primary (bilateral) inguinal hernia repair. With regard to frequently performed open techniques with anterior mesh placement (Lichtenstein), we would like to recommend performing a study similar to ours. Even though studies evaluating fertility after Lichtenstein repair demonstrated good results with low rates of infertility-related complications, no prospective study had a patient population consisting of bilateral inguinal hernia repairs only [11].

A limitation of this study is the relatively small sample size and the high percentage of loss to follow-up. Participant enrollment was slow due to the fact that many patients had been previously sterilized or were not willing to participate due to the study needs (two times scrotal ultrasonography and collection of semen, additional visit to the hospital after surgery), therefore we closed the study prematurely after 6 years. However, the sample size that we initially calculated (76 patients) was based on 2 studies with very small patient numbers [27]. Also, the size of our patient population is comparable to the previously mentioned studies that assessed fertility.

In this study, we did not assess early postoperative effects on fertility, therefore we may have missed significant changes in early testicular perfusion, semen quality, or endocrinological status that have been shown in other studies. However, we regard the long-term outcomes as clinically relevant, since the early postoperative effects can be attributed to the impact of the surgical intervention itself and its natural postoperative course.

Since it is assumed that the mesh-related inflammatory reaction subsides after 6 months, we deliberately chose our follow-up period at this time point [28]. After this time interval it is not likely to expect any decrease of perfusion or other late-delayed complications impairing fertility. This is in accordance with the long-term follow-up study of Peeters et al., where no significant changes in testicular volume or flow and no other fertility-related complications were reported until 3 years after TEP inguinal hernia repair [23].

In conclusion, the available data suggest that there are no clinically relevant long-term effects of endoscopic bilateral TEP hernia repair on fertility. Based on our current results, we think bilateral TEP inguinal hernia repair can be safely performed in men of fertile age.

Author contributions MR: data collection, analysis and interpretation of data, drafting of manuscript. GJC: study conception and design, critical revision, EJV: study conception and design, critical revision. PD: study conception and design, critical revision. CW: study conception and design (clinical chemistry), interpretation of data (clinical chemistry), critical revision. RS: study conception and design (urology), interpretation of data (urology), critical revision. LSM: study conception and design (radiology), interpretation of data (radiology), critical revision. IB: study conception and design, drafting of manuscript, critical revision.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interests.

Ethical approval Ethical approval was obtained by the Regional Medical Ethics Committee and the hospitals EthicsBoard.

Human and animal rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent All subjects signed informed consent.

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