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A novel experience of deferential vessel-sparing microsurgical vasoepididymostomy

Kun-Long Lyu[1,2,*], Jin-Tao Zhuang[1,*], Philip S Li[3], Yong Gao[4], Liang Zhao[1], Ya-Dong Zhang[1], Ming-Kuan Zhou[1], Jing-Wei Yu[1], Xin Feng[1], Xiang-Zhou Sun[1], Chun-Hua Deng[1], Xiang-An Tu[1]

Microsurgical longitudinal intussusception vasoepididymostomy (LIVE) has been widely used to treat epididymal obstructive azoospermia since 2004. Although the deferential vasculature plays an important role in supplying blood to the testis and epididymis, little attention has been paid to the potential benefits of sparing the deferential vessels during the anastomosis in LIVE. This study aimed to evaluate the efficacy and safety of deferential vessel-sparing LIVE in humans. From December 2013 to December 2015, 69 azoospermic men with epididymal obstruction due to a genital infection, trauma, or idiopathic factors underwent deferential vessel-sparing LIVE in the First Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China. The outcomes of these patients were analyzed retrospectively. The mean age was 31.1 years for men and 28.3 years for their partners. Fifty-nine (85.5%, 59/69) men were followed up after surgery for approximately 16 months. Patency was noted and confirmed by semen analysis (>10 000 sperm/ml) in 83.1% (49/59) of men. The natural pregnancy rate was 40.7% (24/59) by the end of the study, with 87.5% (21/24) of these natural pregnancies achieved within 12 months after surgery. No severe adverse events or complications were observed. In this study, we present a novel technique for sparing the deferential vessels during LIVE. The preliminary outcomes show this technique to be safe with favorable patency and pregnancy rates.

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INTRODUCTION

Epididymal obstruction is the most common cause of obstructive azoospermia and can be corrected by microsurgical reconstruction with vasoepididymostomy.[1] Microsurgical reconstruction is considered to be a more cost-effective treatment option than assisted reproductive technologies, such as *in vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI).[2,3] Microsurgical vasoepididymostomy (MVE) is generally regarded as the most technically challenging male infertility microsurgery. Although various MVE techniques have been described previously, longitudinal intussusception vasoepididymostomy (LIVE) has been recognized as the gold standard to achieve a superior patency rate because it provides a wider opening in the epididymal tubule and stronger epididymal back-wall support.[4] Monoski *et al.*[5] from Weill Cornell Medicine of Cornell University (New York, NY, USA) first reported the single-armed suture LIVE technique in a rat model, while our group first pioneered a modified single-armed suture human LIVE technique and achieved an early 6-month patency rate of 61.5%.[6,7] This novel single-armed suture LIVE technique is especially suitable for surgeons in areas without specialized double-armed sutures.

In the spermatic cord, each testicular artery (internal spermatic artery) lies with the ipsilateral deferential artery and cremasteric artery (external spermatic artery). Although there are anastomoses between these vessels, the testicular artery primarily supplies the testis, the deferential artery primarily supplies the epididymis and vas deferens, and the cremasteric artery primarily supplies blood to peritesticular tissues and the scrotal wall.[8–10] Homonymic veins accompany the arteries and are responsible for the venous return.[11]

The deferential vessels are typically ligated to facilitate a good MVE anastomosis, even though preserving the deferential vessels during MVE would better simulate the normal physiological structure.[4,12] However, whether preservation of the deferential vessels during MVE could improve the MVE outcomes, such as patency or the pregnancy rate, remains unknown. In this study, we performed single-armed deferential-vessel sparing LIVE in 69 men and carefully evaluated the efficacy and safety outcomes.

PATIENTS AND METHODS

Patients

We conducted a retrospective review of 69 men with the mean age of 31.1 (s.d.: 5.2, range: 18–42) years who underwent deferential vessel-sparing LIVE in the First Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China, between December 2013 and December 2015. The study procedure complied with the guidelines provided by the Declaration of Helsinki, and informed consent was provided by every patient.

[1]Department of Urology and Andrology, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou 510000, China; [2]Department of Urology and Andrology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou 450000, China; [3]Center for Male Reproductive Medicine and Microsurgery, Department of Urology, Weill Cornell Medicine of Cornell University, New York, NY 10065, USA; [4]Center for Reproductive Medicine, Guangdong Provincial Key Laboratory of Reproductive Medicine, The First Affiliated Hospital of Sun Yat-Sen University, Guangzhou 510000, China.
*These authors contributed equally to this work.
Correspondence: Dr. CH Deng (dch0313@163.com) or Dr. XA Tu (txabs9988@163.com)
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Our inclusion criteria were as follows: azoospermia that was confirmed twice using routine semen analysis at least 6 weeks apart;[13] normal semen pH, semen volume, and seminal plasma fructose; decreased seminal plasma neutral α-glucosidase; normal serum total testosterone (T) and follicle-stimulating hormone (FSH) levels; normal karyotype; normal ultrasound findings of the testes, prostate, seminal vesicles, and ejaculatory ducts; normal female partner fertility workups; and no history of vasectomy.

Preparation

A Leica operating microscope (Model M520 MC-1, Leica Microsystems Schweiz AG, Heerbrugg, Switzerland) was used to perform the microsurgical procedure. The deferential vessels were spared (**Figure 1a**) and the modified single-armed suture LIVE technique was used (**Figure 1b**). All procedures were performed by the same microsurgical team.

Surgical approaches

The testis was accessed through a 3–4 cm vertical scrotal incision, and the vas was exposed at the junction of the straight and convoluted portions. Under the operating microscope, the deferential vessels were visible and easy to identify along the vas deferens. A vascular sling was passed through the gap between the vas deferens and deferential vessels. The vas was lifted, and the small vertical branches of the deferential vessels supplying the vas were bluntly separated and cauterized by low-power microsurgical cautery. Then, the deferential vessels were carefully separated from the vas deferens for 1–3 cm (**Figure 2**). A microvascular Doppler ultrasound (VTI 20 MHz, Vascular Technology, Inc., Nashua, NH, USA) was used to identify the deferential artery and ensure that no inadvertent injuries to the deferential artery occurred during microsurgical dissection and anastomosis. After vasal hemisection, epididymal obstruction was confirmed by the absence of sperm in the fluid collected from the testicular end, while distal patency was confirmed by infusing diluted methylene blue through the abdominal vas and detecting dye in the urine. A suitable site for anastomosis on the epididymis was chosen by examining the dilated epididymal tubules under the operating microscope. The vas deferens was fully transected, and the isolated segment of the vas deferens was passed through a small window in the parietal tunica vaginalis to reach the anastomotic site. If the length of the vas deferens was insufficient to achieve a tension-free anastomosis, the distal vas with its vessels was further mobilized toward the external ring.

Our modified single-armed suture technique for LIVE was performed using two single-armed nonabsorbable monofilament polypropylene blue 10-0 sutures (W2790, 13 cm length, 3.8 mm 3/8 circle taper point, BV 75-3; Ethicon, New Brunswick, NJ, USA). Each suture was trimmed to a length of 4–5 cm prior to LIVE. Two sutures were then passed in an outside-in fashion through the mucosal layer of the vas deferens at points "a1" and "b1" (**Figure 3a**). Then, the two needles (a1 and b1) were placed in parallel with each other longitudinally on a single exposed epididymal tubule (**Figure 3b**). After carefully opening the epididymal tubule between the two needles, the exuded epididymal fluid was examined under the microscope for the presence of motile sperm. When motile sperm were found, the epididymal fluid was aspirated for cryopreservation. The needles were then pulled out and placed inside-out through the mucosal layer of the vas at positions "a2" and "b2" (**Figure 3c**). The opening of the epididymal tubule was intussuscepted into the vasal lumen when the sutures were carefully tied together (**Figure 3d**). Then, the epididymal tunic was secured to the muscularis edge of the vas deferens with 8 to 10 interrupted monofilament polypropylene 9-0 sutures (Ethicon, W2783, 13 cm length, 5 mm 3/8 circle taper point, BV 100-4) to ensure a tension-free anastomosis.

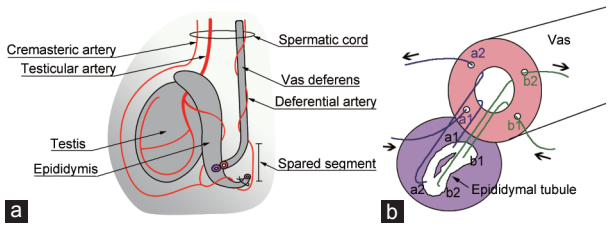

Figure 1: Schematic illustration of the deferential vessel-sparing technique for LIVE. (**a**) Blood supply of the vasoepididymostomy with the spared segment of the deferential artery. The spared deferential artery was carefully isolated for 1-3 cm from the vas deferens. (**b**) Suture placement of the modified single-armed suture LIVE technique. LIVE: longitudinal intussusception vasoepididymostomy.

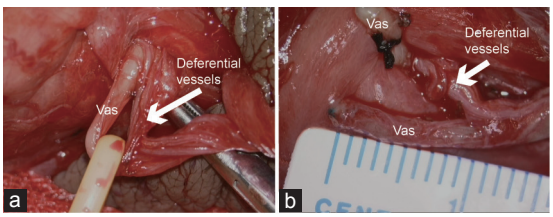

Figure 2: Deferential vessel-sparing technique. (**a**) The deferential vessels were dissected from the vas deferens. (**b**) The 1–3 cm isolated segment of the vas deferens.

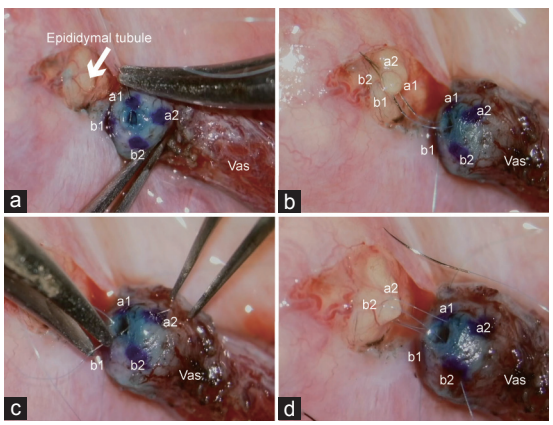

Figure 3: Modified single-armed suture LIVE technique. (**a**) The needles were sequentially placed outside-in (a1 and b1) through the mucosal layer of the vas deferens. (**b**) Two needles were placed longitudinally (a1 and b1) in parallel with each other on a single exposed epididymal tubule. (**c**) The needles were sequentially placed inside-out (a2 and b2) through the mucosal layer of the vas deferens. (**d**) The opening of the epididymal tubule was intussuscepted into the vasal lumen. LIVE: longitudinal intussusception vasoepididymostomy.

Postoperative care and follow-up

Patients were advised to wear a scrotal supporter or tight underpants and to minimize physical activity for the first several days after surgery. Sexual intercourse was prohibited for at least 6 weeks after surgery. Follow-up instructions were provided, and arrangements for a follow-up visit or telephone call were made prior to discharge. The first two semen analyses were performed at 6 weeks and 12 weeks and then at 3-month intervals until pregnancy was achieved. Normally,

IVF/ICSI was recommended to the couples if no sperm was found in semen analyses after 12 months following surgery, especially if the female partner was more than 34 years old. Patency was defined as the presence of sperm (>10 000 per ml) in the semen sample. All adverse effects or complications were documented at each follow-up visit or contact.

Statistical analysis

The associations between the patency rate and predictors (age, the etiology of the epididymal obstruction, bilateral or unilateral anastomosis, anastomotic site, and presence of motile sperm in the epididymal fluid) were analyzed using the Chi-square test. Data were analyzed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA). Statistical significance was considered if $P < 0.05$.

RESULTS

A total of 69 patients underwent deferential vessel-sparing LIVE for azoospermia secondary to epididymal obstruction during the study. The causes of epididymal obstruction were infection (56.5%, 39/69), idiopathic (36.2%, 25/69), and trauma (7.2%, 5/69) (**Table 1**). Fifty-nine (85.5%) patients underwent bilateral LIVE, while 10 (14.5%) patients underwent a unilateral anastomosis because of the absence of testis (30.0%, 3/10), vas deferens dysplasia (20.0%, 2/10), or an abdominal vas deferens obstruction (50.0%, 5/10). The average operating time for each deferential vessel-sparing LIVE was 2.1 h per LIVE anastomosis.

Follow-up data from 59 (85.5%, 59/69) patients were included in the final statistical analysis. The mean follow-up time was 15.6 (range: 3–33) months. The patency rate was 83.1% (49/59) (**Table 2**). Semen analyses were performed, and the mean sperm concentration was 25.8×10^6 (range 0.8×10^6–100×10^6) ml^{-1} with a forward motility rate of 25.0% (range: 0–80.0%). Sperm concentrations $>15 \times 10^6$ ml^{-1} were found in 16 men. To predict the patency rate, many factors (age, the etiology of the epididymal obstruction, bilateral or unilateral anastomosis, anastomotic site, and presence of motile sperm in the epididymal fluid) had been explored. However, in this study, no statistically significant associations were found between the patency rate and various predictors ($P > 0.05$; **Table 3**).

The overall pregnancy rate was 45.8% (27/59) (**Table 2**). Among the pregnancies, three were achieved with IVF/ICSI, including one pregnancy using freshly ejaculated sperm. These three couples stopped waiting for a natural pregnancy because of the pressure from their surrounding social environment. The other 24 patients' partners got natural pregnancies and 87.5% (21/24) of the natural pregnancies occurred within 12 months after surgery. This result also suggested that most natural pregnancies came up early after the operation. Twenty patients' partners delivered healthy babies during this study.

No severe adverse effects or surgical complications were reported. One 22-year-old man suffered mild scrotal edema for 1 month after surgery that subsequently settled after taking Aescuven Forte (Cesra Arzneimittel GmbH and CO. KG, Baden, Germany) orally.

Table 1: Preoperative characteristics and intraoperative findings in all the 69 men

Items	*Value*
Age (year), mean (range)	
Patients	31.1 (18–42)
Female partners	28.3 (20–39)
Causes of epididymal obstruction, *n* (%)	
Infection	39 (56.5)
Idiopathic	25 (36.2)
Trauma	5 (7.2)
Serum FSH (IU l^{-1}), mean (range)	4.7 (2.0–18.0)
Serum total testosterone (μg l^{-1}), mean (range)	5.8 (1.1–11.3)
Seminal neutral α-glucosidase (mU per ejaculate), mean (range)	6.3 (0.9–14.0)
Surgery, *n* (%)	
Bilateral LIVE	59 (85.5)
Unilateral LIVE	10 (14.5)
Anastomotic site, *n* (%)	
Caput	3 (4.3)
Corpus	5 (7.2)
Cauda	61 (88.4)
Patients with motile spermatozoa at anastomotic site (%)	49 (71.0)

FSH: follicle-stimulating hormone; LIVE: longitudinal intussusception vasoepididymostomy

Table 2: Surgical outcomes in 59 (85.5%) follow-up men

Items	*Value*
Follow-up (month), mean (range)	15.6 (3–33)
Patency rate, *n* (%)	49 (83.1)
Overall pregnancy rate, *n* (%)	27 (45.8)
Natural pregnancy rate, *n* (%)	24 (40.7)
Rate of pregnancy by IVF/ICSI, *n* (%)	3 (5.1)
Time of natural pregnancy (month), mean (range)	8.5 (3–20)
Natural pregnancy rate at 1 year, *n* (%)	21 (35.6)

IVF: *in vitro* fertilization; ICSI: intracytoplasmic sperm injection

Table 3: Comparative data of 59 follow-up men

Parameter	*Patency rate (%)*	*P*
Age (year)		
≤30	89.3 (25/28)	0.225
>30	77.4 (24/31)	
History of genital infection		
Yes	83.3 (30/36)	0.942
No	82.6 (19/23)	
Surgery anastomosis (LIVE)		
Bilateral	86.0 (43/50)	0.155
Unilateral	66.7 (6/9)	
Level of anastomotic site		
Caput or corpus	71.4 (5/7)	0.383
Cauda	84.6 (44/52)	
Motile sperm found at anastomotic site		
Yes	87.5 (35/40)	0.186
No	73.7 (14/19)	

LIVE: longitudinal intussusception vasoepididymostomy

DISCUSSION

Obstructive azoospermia accounts for 40.0% of azoospermia and is commonly caused by epididymal obstruction.[14] The etiologies of epididymal obstruction include vasectomy, infection, trauma, and congenital abnormalities. In Western countries, most epididymal obstructions are secondary to vasectomy, whereas epididymal obstructions in China are more often caused by infection or idiopathic factors.[4,5,15,16] In our series, 56.5% (39/69) of patients had a previous identifiable infection, including 38 patients with a history of epididymitis and one patient with a history of urethritis.

MVE techniques have continued to evolve and improve since 1998, with LIVE becoming the gold standard.[4–7,15–19] In our previous studies,

we described a modified single-armed suture technique for LIVE and achieved a patency rate of 61.5% in men with epididymal obstructive azoospermia.[5,6]

Successful MVE is highly dependent on the skill and experience of the surgeon. Close attention should be paid to every detail during the operation. A tension-free anastomosis is critical to achieving a successful outcome after MVE. It has always been taken for granted that the deferential vessels should be divided during surgery to help mobilize the vas deferens. However, few published studies have investigated the effect of deferential vessel division in humans.[20] The advantages and disadvantages of deferential vessel-sparing for MVE have not been previously assessed in the literature.

The normal human testis is supplied by three arteries: the testicular artery, which arises from the abdominal aorta; the deferential artery, which emerges from the superior or inferior vesical artery; and the cremasteric artery, which originates from the inferior epigastric artery (**Figure 1a**).[8,9,11] Although the testicular artery provides most of the blood flow to the human testis, the deferential and cremasteric arteries also make a significant contribution to the testicular blood supply.[9,21] The deferential artery also contributes to the blood supply of the epididymis. The caput epididymis receives blood from branches of the testicular artery, whereas the corpus and cauda epididymes receive blood from the testicular, deferential, and cremasteric arteries (**Figure 1a**).[22] With its larger diameter, the deferential artery (1.1 mm) likely provides more collateral blood flow than the cremasteric artery (0.5 mm).[23]

It is of vital importance to maintain the vasal vasculature in patients who have previously undergone varicocelectomy. Because of the anastomotic channels among these arteries, the deferential and cremasteric arteries potentially compensate the testicular blood supply and maintain normal testicular function if the testicular artery is inadvertently ligated.[23–25] This collateralization is demonstrated by studies in which ligation of the testicular artery during varicocelectomy does not result in testicular atrophy.[26,27] Moreover, when the testicular veins, cremasteric veins, and gubernacular veins are ligated during varicocelectomy, the venous return of the testis will heavily depend on the deferential veins.[11]

Although the functional significance of deferential vessel-sparing during MVE is still uncertain, preservation of the deferential vessels can ensure the normal blood supply of the testis. As a result, if the length of the vas deferens allows a tension-free anastomosis, we believe that it is more beneficial to spare the deferential vessels.

In our experience, it is easy to complete a tension-free anastomosis without having to divide the deferential vessels if the anastomotic site is at the level of the cauda or corpus epididymis (**Figure 3**). When anastomosing on the caput, the distal vas deferens may require additional mobilization to ensure a good tension-free anastomosis. The distal vas can be mobilized with its vessels all the way to the level of the inguinal canal, affording several additional centimeters of length. Care should be taken to ensure that the deferential vessels remain intact. Microvascular Doppler ultrasound, which has been used to improve the precise identification and preservation of testicular blood supply during varicocelectomy, was used in this study to help identify and protect the deferential artery.[28]

In this study, deferential-vessel sparing during our modified LIVE resulted in a favorable patency rate of 83.1% (49/59) (**Table 2**). Some factors, such as the etiology of the epididymal obstruction, anastomotic site, and presence of motile sperm in the epididymal fluid, have been shown to be related to the patency rate.[5,16] However, in this study, there were no significant associations between the patency rate and these predictors ($P > 0.05$; **Table 3**).

In our study, we were only able to follow up 59 of the 69 patients. The "late failure" or "shut-down" rate was defined as having a return of sperm to the ejaculate after vasoepididymostomy and then becoming azoospermic on at least two times of semen analyses. Although the "late failure" rate was reported to be lower with the use of the intussusception technique compared to nonintussusception techniques,[29,30] two of our patients experienced late failures 1 year after the operation. A repeat surgical reconstruction was considered for these late failure patients because MVE remains an effective treatment option for patients with a previous failed surgical reconstruction.[31] In addition, IVF/ICSI was recommended to the late failure patients as a potential next step.

Although patency was confirmed in many patients after surgery, more than one-half of the couples could not achieve natural pregnancies.[5,30] A natural pregnancy rate of 40.7% (24/59) was achieved in our study. The mean time to natural pregnancy was 8.5 months. Inadequate quantity and quality of sperm, presence of anti-sperm antibodies, and coexisting female factors are potential reasons that impede a natural pregnancy.[30]

The limitations of this retrospective study are the small sample size and lack of a comparator group not undergoing deferential vessel-sparing LIVE. Compared with a patency rate of 61.5% (24/39) and natural pregnancy rate of 35.9% (14/39) for those undergoing nondeferential vessel-sparing LIVE in our previous study,[5] the deferential vessel-sparing LIVE carried out by the same surgeons over various periods resulted in a favorable patency rate of 83.1% (49/59) and a natural pregnancy rate of 40.7% (24/59). Although the data are encouraging, a well-designed prospectively randomized controlled clinical trial with a larger sample size to further explore the efficacy of sparing deferential vessels in LIVE is required.

CONCLUSION

Our results suggest that deferential vessel-sparing LIVE is safe and effective and has favorable patency and pregnancy rates. Assisting in protecting the testicular artery supply and venous return, deferential vessel-sparing LIVE is recommended for men with epididymal obstructive azoospermia, especially when the site of anastomosis is in the corpus or cauda epididymis and a tension-free anastomosis is feasible.

AUTHOR CONTRIBUTIONS

XAT and CHD were responsible for the conception and design of the study; XAT, CHD, and LZ carried out the microsurgical procedure; KLL and JTZ participated in the design and coordination of the study and carried it out and they followed the patients and drafted the manuscript; YG and XZS revised the manuscript; YDZ and MKZ analyzed the data; JWY and XF analyzed the epididymal fluid and semen samples; and PSL provided critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

COMPETING INTERESTS

All authors declared no competing interests.

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