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Clinical effectiveness of unilateral single-armed vasoepididymostomy in obstructive azoospermia: a single-center experience

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Abstract

Background Vasoepididymostomy (VE) is an important surgical treatment to achieve natural conception for patients with obstructive azoospermia (OA), and only unilateral VE can be performed under certain conditions, such as OA patients with congenital unilateral absence of the vas deferens (CUAVD) and some acquired OA. There is a lack of relevant reports assessing the clinical outcomes of unilateral VE in OA patients with different causes. This study is aimed to describe the clinical features and evaluate treatments and outcomes of unilateral single-armed VE in OA patients.

Methods From December 2015 to June 2021, 46 OA patients (including 13 CUAVD-associated OA and 33 acquired OA) underwent unilateral single-armed VE in Shanghai General Hospital (Shanghai, China). Patient information, semen analysis, hormone profiles, and treatment information were collected, and the clinical outcomes were evaluated.

Results Obstruction in distal of unilateral vas deferens (16/46) was the most common cause for OA patients underwent unilateral VE, and CUAVD accounts for 28.4% (13/46). The overall patency rate was 50.0% (23/46), with 38.5% (5/13) for the CUAVD group and 54.5% (18/33) for the acquired group ($p > 0.05$). The natural pregnancy rates in CUAVD group and acquired group were 20.0% and 33.3%, respectively ($p > 0.05$).

Conclusions These findings suggest unilateral single-armed VE can achieve high patency and pregnancy rates in OA patients, whether for CUAVD or acquired OA patients.

Highlight Box

Key findings

- Unilateral single-armed vasoepididymostomy (VE) can achieve high patency and pregnancy rates in obstructive azoospermia (OA) patients, whether for congenital unilateral absence of the vas deferens (CUAVD) or acquired OA patients.

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What is known and what is new?

- Bilateral VE exhibited higher risk ratio of patency rate than unilateral VE, however only unilateral VE can be performed under certain conditions, such as OA patients with CUAVD and some acquired OA.
- Unilateral VE can achieve high patency and pregnancy rates in both CUAVD and acquired OA patients.

What is the implication, and what should change now?

- Unilateral single-armed VE is a feasible option for OA patients with different causes.

Keywords Unilateral vasoepididymostomy, Obstructive azoospermia, Patency, Pregnancy

Introduction

15% of the infertile population is identified as azoospermia, and can be classified into two general categories: obstructive azoospermia (OA) and nonobstructive azoospermia (NOA). Obstructive azoospermia is the result of blockage or loss of any segments of the male reproductive tract, and accounts for 40% of all azoospermia cases (1). Etiologically, OA may be acquired or congenital (2,3). Post-vasectomy obstruction, infection, iatrogenic injury or trauma are the main causes of acquired OA. While congenital OA is mainly caused by congenital absence of the vas deferens (CAVD).

Though with obstruction of any location, from the rete testis to the ejaculatory ducts, patients with OA are characterized by normal spermatogenesis. Thus, those patients can get their own offspring through surgical reconstruction or retrieval of sperm. Vasoepididymostomy (VE) is an important surgical treatment for epididymal obstructive azoospermia, with satisfactory patency and pregnancy rates (4,5). A recent systematic review and meta-analysis of microsurgical VE outcomes showed the overall patency and pregnancy rates of 64.1% and 31.1%, respectively (6). When compared with unilateral VE, the patency rate of bilateral VE exhibited higher risk ratio of 1.38% (6). However, only unilateral VE can be performed under certain conditions, such as OA patients with congenital unilateral absence of the vas deferens (CUAVD) and some acquired OA.

So far, although some successful microsurgical reconstruction of unilateral VE have been reported in case reports, large-sample and long-term follow-up cases have rarely been reported. The present study is aimed to summarize the clinical outcomes of unilateral single-armed VE, analyze the reasons to undergo unilateral single-armed VE and assess the potential application and value of unilateral VE in OA patients. This manuscript is written following STROBE checklist.

Methods**Patients**

This study was approved by the Ethics Committee of Shanghai General Hospital (approval No. 2017KY020-2), and written informed consent was obtained from all the patients. Patients who underwent unilateral VE between

December 2015 and June 2021 were included in this study. All the patients had normal karyotypes, and no Y chromosomal microdeletions were found. Their female partners had a normal fertility profile. Men with aspermia due to ejaculatory disorders such as anejaculation or retrograde ejaculation were not included in this study. Patient information and laboratory data were collected from the patient records.

Unilateral vasoepididymostomy

Unilateral single-armed VE was performed according to the procedures as described previously (6,7). Briefly, scrotal exploration and testicular biopsy was performed to confirm normal spermatogenesis. Then the saline or trypan blue was injected to the vas deferens using a 24-gauge angio catheter sheath to confirm the patency of the seminal vesicle side. According to intraoperative findings, a unilateral VE was finally underwent using the modified single-armed 2-suture longitudinal vasoepididymostomy (SA-LIVE) technique (7,8). Briefly, under a Carl Zeiss operating microscope, two single-armed 10–0 nylon sutures were sequentially placed outside-in through the mucosal layer of the vas deferens, parallelly through the epididymal tubule, then placed inside-out through the mucosal layer of the vas deferens. Then all the sutures were tied together, and the epididymal tubule was gently intussuscepted into the lumen of the vas deferens.

Follow-up

All the patients were followed up every 3–6 months. Semen analysis was performed at four weeks after surgery, and then at 2-month intervals until pregnancy was achieved. Patency was defined as the sperm concentration more than 1 million per milliliter in at least one post-operative ejaculate sample. Pregnancy was defined as an identified gestational sac by ultrasound examination.

Statistical analysis

Parameters are described as the mean \pm standard deviation (SD). The patency and pregnancy rates were calculated. The statistical analysis was conducted using SPSS software, version 19.0 (SPSS Inc., Chicago, IL, USA). P value < 0.05 was considered to be statistically significant.

Table 1 Characteristics of patients underwent unilateral vasoepididymostomy

Characteristics	Total	CUAVD group	Acquired group	p value
Patients, n	46	13	33	
Age (year), Mean ± SD	30.1 ± 5.4	28.2 ± 3.0	30.8 ± 5.9	0.060
Patients	26.9 ± 2.8	26.1 ± 1.8	27.3 ± 3.1	0.116
Female partners				
Infertility duration (month), Mean ± SD	34.2 ± 32.1	32.2 ± 22.1	35.0 ± 35.5	0.788
Testicular size, ml				
Left	14.3 ± 5.8	15.1 ± 4.2	14.0 ± 6.4	0.594
Right	15.0 ± 6.8	13.1 ± 5.5	15.7 ± 7.2	0.234
Semen Volume, ml	2.2 ± 1.1	1.7 ± 0.9	2.5 ± 1.1	0.028
Semen pH	7.2 ± 0.2	7.1 ± 0.3	7.3 ± 0.1	0.032
Semen fructose				0.075
Negative	2	2	0	
Positive	44	11	33	
FSH, IU/L	5.0 ± 2.4	4.7 ± 1.8	5.1 ± 2.7	0.597
LH, IU/L	4.8 ± 1.8	4.9 ± 1.4	4.8 ± 2.0	0.951
T, ng/ml	4.4 ± 3.0	3.5 ± 2.1	4.7 ± 3.3	0.218

FSH normal range: 1.27–19.26 IU/L; LH normal range: 1.24–8.62 IU/L; T normal range: 1.75–7.81 µg/L. CUAVD: congenital unilateral absence of the vas deferens; FSH: follicle-stimulating hormone; LH: luteinizing hormone; SD: standard deviation; T: testosterone

Table 2 Causes for performing unilateral single-armed VE

Causes	n (%)
Obstruction in distal of unilateral vas deferens	16 (34.8)
Unilateral testicular atrophy caused by cryptorchidism	6 (13.0)
Unilateral epididymal dysplasia	4 (8.7)
Idiopathic	3 (6.5)
Unilateral testicular atrophy caused by epididymo-orchitis	2 (4.3)
Unilateral intratesticular obstruction	2 (4.3)
CUAVD	13 (28.4)

CUAVD: congenital unilateral absence of the vas deferens; VE: vasoepididymostomy

Results

Demographics

A total of 46 OA patients underwent unilateral VE between December 2015 and June 2021, including 13 patients with CUAVD and 33 patients with acquired OA. The ages (mean ± SD) of the male patients and their female partners in the CUAVD group and acquired group were 28.2 ± 3.0, 26.1 ± 1.8 and 30.8 ± 5.9, 27.3 ± 3.1 years, respectively. The volume and pH of the semen sample in CUAVD group were lower than those of acquired group (1.7 ± 0.9 vs. 2.5 ± 1.1 ml, 7.1 ± 0.3 vs. 7.3 ± 0.1, respectively). While there were no significant differences in infertility duration, testicular size and hormone levels between the two groups (Table 1).

Intraoperative findings and treatments

Unilateral single-armed VE was performed in all the 46 patients. The causes for performing unilateral single-armed VE in acquired group were as follows: obstruction in distal of unilateral vas deferens ($n=16$), unilateral testicular atrophy caused by cryptorchidism ($n=6$), unilateral epididymal dysplasia ($n=4$), idiopathic ($n=3$), unilateral testicular atrophy caused by epididymo-orchitis

($n=2$) and unilateral intratesticular obstruction ($n=2$) (Table 2). Three patients in the CUAVD group underwent unilateral cross VE due to obstruction in contralateral caput of epididymis, and one patient in the acquired group underwent unilateral cross VE due to obstruction in distal of unilateral vas deferens and contralateral testicular atrophy. There were no significant differences in the side and site of anastomosis between the two groups (Table 3).

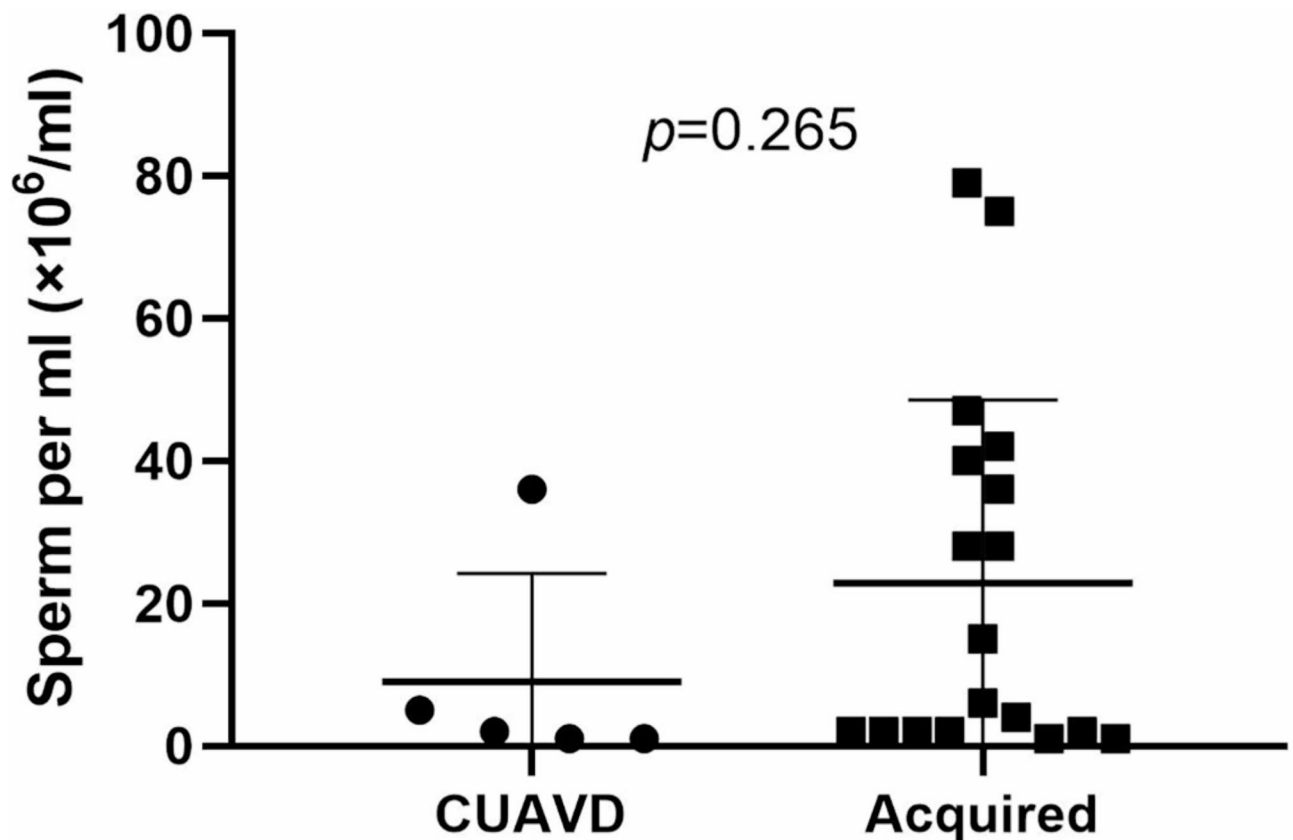
Patency and pregnancy

Sperm was detected in the ejaculate between 1 and 6 months after surgery. The overall patency rate was 50.0% (23/46), with 38.5% (5/13) for the CUAVD group and 54.5% (18/33) for the acquired group. There was no statistical significance of the sperm concentration after recanalization in CUAVD group and acquired group ($p=0.265$) (Fig. 1). Five patients underwent assisted reproductive technology (ART) after surgery in CUAVD group, and 8 patients in acquired group. Notably, there was 1 couple in each group achieved pregnancy through intracytoplasmic sperm injection (ICSI) using the sperm in the fresh ejaculate. The natural pregnancy rate was 20.0% (1/5)

Table 3 Clinical outcomes of patients underwent unilateral VE in CUAVD-associated or acquired OA group

Variables	CUAVD group	Acquired group	p value
Side of anastomosis, n (%)			0.161
Left	10 (76.9%)	18 (55.5%)	
Right	3 (23.1%)	15 (44.5%)	
Site of anastomosis, n (%)			1.000
Caput	4 (30.7%)	9 (27.3%)	
Corpus or caudal	9 (69.3%)	24 (72.7%)	
Patency, n (%)	5/13 (38.5%)	18/33 (54.5%)	0.326
Pregnancy, n (%)	6/13 (46.2%)	11/33 (33.3%)	0.637
Natural Pregnancy, n (%)	1/5 (20%)	6/18 (33.3%)	1.000

CUAVD: congenital unilateral absence of the vas deferens; OA: obstructive azoospermia

**Fig. 1** Sperm concentration after recanalization in CUAVD group and acquired group

for CUAVD group and 33.3% (6/18) for acquired group ($p=1.000$) (Table 3).

Discussion

Vasoe epididymostomy (VE) is one of representative methods of vasal repair to get natural conception for patients with obstructive azoospermia (OA). The surgical procedures and techniques of VE are constantly innovated and improved. Several modified single-armed VE techniques with high patency and pregnancy rates have been reported (8–11). In our center, we also attempted to

explore modified surgical techniques to improve the rate of spontaneous pregnancy rate (7,8,12).

Epididymal obstruction is considered as a common cause of OA, and quite a large part of these patients have an epididymitis history. In a cohort of 110 patients underwent VE, 42% of the patients had a history of epididymitis (13). What's worse, Binsaleh reported that 83.3% (10/12) of the patients could only underwent unilateral VE due to genitourinary infection (14). With surgical techniques modified and improved, high patency can be also achieved in patients underwent unilateral VE. Recently, multiple reports have showed a patency rate

of 45.8–66.7% in unilateral VE (10,13,15). In the present study, an overall patency rate of 50.0% (23/46) was achieved, which was consistent with previous studies.

To date, most studies upon unilateral VE have been conducted with small samples. And seldom studies focused on intraoperative findings for unilateral VE. In 2017, Peng et al. reported a retrospective study including 51 patients underwent unilateral VE. Contralateral intratesticular obstruction ($n=26$) was the main cause of unilateral reconstruction, followed by distal vas deferens obstruction ($n=14$), contralateral absent vas deferens ($n=6$) and cryptorchidism ($n=5$) (16). Different from their research, the current study showed that obstruction in distal of unilateral vas deferens (16/46) was the most common cause, while unilateral intratesticular obstruction was found in only two patients. Notably, 28.4% (13/46) of the OA patients performing unilateral single-armed VE presented with CUAVD, suggesting that CUAVD patients with OA seeking for natural conception is not a small population.

Several studies have compared the clinical outcomes between unilateral VE and bilateral VE (13,17,18), however no studies have focused on the efficacy of unilateral VE in OA of different causes. To the best of our knowledge, this is the first study reporting the clinical outcomes of unilateral VE between congenital and acquired OA patients. Our results showed the patency and natural pregnancy rates in CUAVD group and acquired group were 38.5% and 54.5%, 20.0% and 33.3%, respectively. There was no statistical significance of patency and pregnancy rates between the two groups ($p>0.05$). These findings suggest unilateral single-armed VE is a feasible option for OA patients with different causes.

Apart from high rates of patency and natural pregnancy, VE has potential benefits over assisted reproductive technology (ART), including low costs, no additional risks to the female partner and fetus and can achieve multiple pregnancies (13,19). It is suggested that VE should be the first option for epididymal obstruction, not an alternative treatment after ART failure (16). Our results showed unilateral VE could also achieve a satisfactory result, whether in patients with CUAVD-associated or acquired OA. However, ART should be taken into account when making intraoperative and postoperative decisions. In the current study, the epididymal and testicular sperms were cryopreserved during VE as a backup of the procedure. And 13 patients underwent ART after surgery, including 2 couples achieved pregnancy through ICSI using the sperm in the fresh ejaculate. Thus, ART can be a remedy after unilateral single-armed VE for patients.

Our study has several limitations. Given the retrospective design, potential information bias is possible. We failed to collect some important surgical variables,

such as operation and patency time. The short follow-up period is also a limitation. A prolonged observation period is beneficial in the comparison of patency and natural pregnancy. Due to the low incidence of CUAVD, this study contained a small number of patients in CUAVD group. Thus, a prospective, multicenter, and large sample cohort study is needed.

Conclusions

In summary, unilateral single-armed VE can achieve high patency and pregnancy rates in OA patients, whether for CUAVD or acquired OA patients. When considering the treatments, unilateral single-armed VE is a feasible option to OA patients with different causes.

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Not applicable.

Author contributions

(I) Conception and design: YZ, PL and ZE. (II) Administrative support: JD, CY and LZ. (III) Provision of study materials or patients: YH, TR. (IV) Collection and assembly of data: YZ and EZ. (V) Data analysis and interpretation: YD, YT and FZ. (VI) Manuscript writing: All authors. (VII) Final approval of manuscript: All authors.

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Data availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study obtained approval from the Ethics Committee of Shanghai General Hospital (No.: 2017KY020-2) and informed consent was obtained from all individual participants.

Consent for publication

All authors have completed the ICMJE uniform disclosure form. The authors have no conflicts of interest to declare.

Competing interests

The authors declare no competing interests.

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