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Clinical application of cross microsurgical vasovasostomy in scrotum for atypical obstructive azoospermia*

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Seminal duct obstruction may result in obstructive azoospermia (OA) and severe oligoasthenoteratozoospermia (OAT) (<0.5 million/mL) (Nordhoff et al., 2015). Cases of partial OA and OAT can be treated effectively by microsurgical anastomosis (Goldstein and Kim, 2013) to obtain successful surgical reversal. However, microsurgical vasovasostomy (VV) (Dickey et al., 2015) and vasoepididymostomy (VE) (Peng et al., 2017) are not suitable for patients with atypical OA and poor epididymis conditions or unpredictable obstruction of the distal vas deferens. For those patients, cross anastomosis may be applied instead of routine VE or VV. A single-center, retrospective, comparison study was conducted, which assessed the usefulness of the cross VV (CVV) in the scrotum for indication and efficacy. A total of 77 cases with OA or OAT were included, and 20 cases implemented cross anastomosis, including unilateral CVV (UCVV) in 4 cases, unilateral VE plus CVV (UVE+CVV) in 11 cases, and unilateral VV-based CVV (UVV+CVV) in 5 cases. The other 57 cases received no cross-matching anastomosis. The patency and natural pregnancy rates in one year were 75.0% and 50.0%, respectively, in the UCVV group; 54.5% and 27.3%, respectively, in the UVE+CVV group; and 60.0% and 40.0%, respectively, in the UVV+CVV group. The CVV in the scrotum in the selected patients with OA and severe OAT could yield good results. We regard the CVV in the scrotum as an efficacious operation with a lower risk of injury in cases of atypical OA.

The prevalence of azoospermia is less than 1% of the male population and about 10%–15% among infertile males. Furthermore, 40% of azoospermia cases involve OA resulting from seminal duct obstruction (Jarow et al., 1989). Both microsurgical VV and VE can yield successful surgical reversal and allow infertile couples to have babies naturally in cases of OA. Such operations are not universally suitable for all cases. Those with poor epididymis conditions or unpredictable obstruction of the distal vas deferens could be referred to as atypical OA, and cross anastomosis might be applied instead of routine VE or VV. However, the efficacy of the cross methods has been only mentioned in a few previous reports (Chen et al., 2014; Li et al., 2016), and whether additional cross anastomosis can improve patency and pregnancy rates was unclear.

Seventy-seven patients with clinically OA (67/77) and severe OAT (10/77) who sought treatment in our center were analyzed in this study from January 2012 to June 2016. Our center implemented cross anastomosis in 20 cases, and no-cross-matching cases in 57 cases. This retrospective comparison study was carried out in Zhejiang Women's Hospital (Zhejiang, China). The Ethics Committee of Zhejiang Women's Hospital, School of Medicine, Zhejiang University,

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approved the study protocol. All patients provided written informed consent to be in the study with guarantees of confidentiality. OA was confirmed by at least two consecutive semen analyses without sperm, and severe OAT by semen concentration less than 0.5 million/mL. For all patients, the following criteria were met: (1) azoospermia or severe OAT, (2) epididymis and/or vas deferens obstruction via scrotal ultrasonography and transrectal ultrasound (TRUS) (Lotti and Maggi, 2015) for at least one side, (3) no history of acute urogenital infection, and (4) normal follicle-stimulating hormone levels and no chromosome abnormality.

Cross anastomosis was performed with the steps as described below. A 24-gauge angiocatheter was cannulated into the lumen of the vas deferens, and diluted methylene blue was injected. After confirming the vas deferens patency and epididymal obstruction, we performed a microsurgical longitudinal 2-stuture intussusceptive VE (Hong et al., 2016). For patients who underwent inguinal herniorrhaphy before adolescence, we could identify and dissociate the proximal obstruction site of the vas deferens with the guidance of a catheter in the vas deferens. The routine VV was performed in cases where the distal remnants were present. The microsurgical two-layer technique under operative microscopy was mandatorily required for VV according to literature (Silber, 1976). However, because of sharply reduced wall thickness of the distal vasal remnants in some cases, one layer anastomosis was applied (Fig. 1a).

The microscopic examination of liquid in the vas deferens was critical (Ramasamy et al., 2015). The identification of sperm and predominately sperm heads demonstrated an obstruction of the vas deferens instead of the epididymis. Cross anastomosis was applied with the following conditions. (1) For the UVV+CVV group: ipsilateral VV was accomplished in situ, absence of the contralateral distal vas deferens, and patency of epididymis. The additional CVV in the scrotum based on the UVV was performed in situ (Fig. 1b). (2) For the UVE+CVV group: ipsilateral VE was performed, contralateral distal vas deferens obstruction, and patency of epididymis. The additional CVV in the scrotum plus UVE was applied (Fig. 1c). (3) UCVV group: ipsilateral patency of the vas deference and poor conditions of the epididymis or testis, contralateral obstruction of the distal vas deferens, and patency of epididymis. The UCVV in the scrotum was performed (Fig. 1d). For the CVV, we dissociated the vas deferens (obstruction side) for approximately 3 cm distal to the epididymis and resected it, then pulled it through the scrotal septum. A longitudinal incision with a diameter identical to the vas deferens was made in the contralateral vas deferens. The procedure was similar to the routine VV mentioned above. For all CVV cases, we implemented an end-to-side anastomosis instead of an end-to-end procedure (Figs. 2 and 3).

All surgical approaches mentioned above were conducted under spinal anesthesia and under a surgical microscope (Carl Zeiss, S88, Germany). The sperm parameters were evaluated by semen analysis separately during the follow-ups at 3, 6, and 12 months. The couples' pregnancy rates were recorded. The elevated sperm concentration at least 1.5 times after surgery demonstrated successful reversal for patients with OAT.

All the patients' characteristics are listed in Table 1. Twenty patients underwent various types of CVV: 11/20 (55.0%) underwent UVE+CVV, 4/20 (20.0%) underwent UCVV, and 5/20 (25.0%) underwent UVV+CVV. The other 57 patients did not have cross anastomosis, including 35/57 (61.4%) for UVE group, 9/57 (15.8%) for UVV group, and 13/57 (22.8%) for

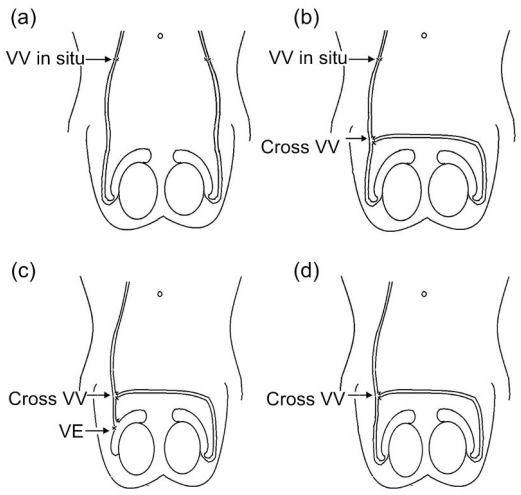

Fig. 1 Three types of cross vasovasostomy (CVV) in the scrotum

(a) VV in situ (inguinal region); (b) CVV on the basis of unilateral VV in situ (UVV+CVV); (c) CVV plus unilateral vasoepididymostomy (UVE+CVV); (d) unilateral cross VV (UCVV)

bilateral VV (BVV group) with 9 patients in the scrotum (BVV-S group) and 4 patients in the inguen (BVV-I group) (Table 2). We achieved a 44.2% patency rate and 23.4% nature pregnancy rate separately (Table 1). The patency and nature pregnancy rates in each group with different methods are listed in Table 2. The highest patency and natural pregnancy rates were in the BVV-S group (77.8% and 66.7%, respectively). We observed comparatively higher patency and natural pregnancy rates in the UCVV group (75.0% and 50.0%, respectively) compared with those of the UVE+CVV group (54.5% and 27.3%, respectively) and the UVE group (31.4% and 11.4%, respectively). The Pearson chi-square test or Fisher's exact test was used to compare the patency and pregnancy rates among the different groups. One-way analysis of variance was used to compare the ages of men and women, and volume of surgical testis (Table 3). A *P*-value of <0.05 was considered to be statistically significant. The mean patency rate of the BVV group was significantly higher than that of the UVV group (76.9% vs. 11.1%, $P<0.05$), as well as that of the CVV group compared to the UVV group (60.0% vs. 11.1%, $P<0.05$). There was no significant difference in the mean patency rate between the CVV and BVV groups (60.0% vs. 76.9%, $P>0.05$). The mean natural pregnancy rate of the BVV group was higher than that of the UVV group (53.8% vs. 0%, $P<0.05$), and no significant differences were observed between the CVV and BVV groups (35.0% vs. 53.8%, $P>0.05$), as well as that between the CVV and UVV groups (35.0% vs. 0%, $P>0.05$). Regarding the volume of average surgical testis, there were no significant differences between all the groups ($P>0.05$).

Table 1 Baseline characteristics of obstructive azoospermia and oligoathernotetrazoospermia with all anastomosis cases

Parameter	Value
Age, male (year)	32.6±6.5
Age, female (year)	28.9±4.5
Primary infertility	60 (77.9%)
Secondary infertility	17 (22.1%)
Obstructive azoospermia	68 (88.3%)
Oligoathernotetrazoospermia	9 (11.7%)
Infertility interval (year)	3.5±3.2
Etiology	
Childhood inguinal herniorrhaphy (sides)	31 (20.1%)
Inflammatory (sides)	79 (51.3%)
Absences of vas (sides)	4 (2.6%)
Atrophy (sides)	10 (6.5%)
Suspected epididymal dysplasia (sides)	6 (3.9%)
Vasectomy (sides)	24 (15.6%)
Average volume of surgical testis (mL)	15.5±3.6
Dilated vas deferens in ultrasound	35 (45.5%)
Total patency	34 (44.2%)
Total nature pregnancy	18 (23.4%)

Data are expressed as mean±standard deviation (SD) or number (percentage)

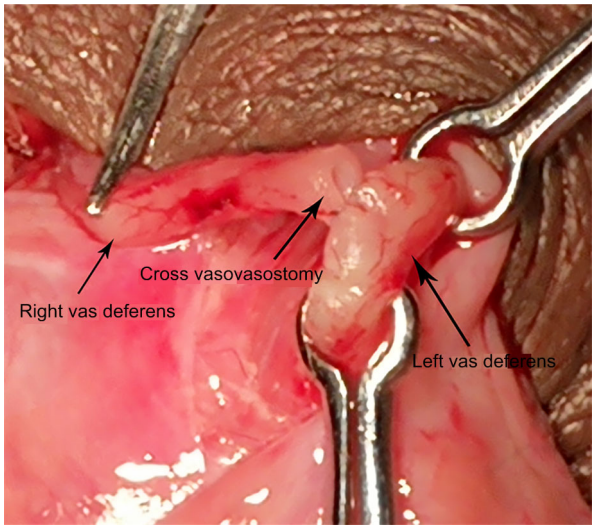

Fig. 2 Cross vasovasostomy in the scrotum
The end of right vas deferens anastomoses the side of the left vas deferens

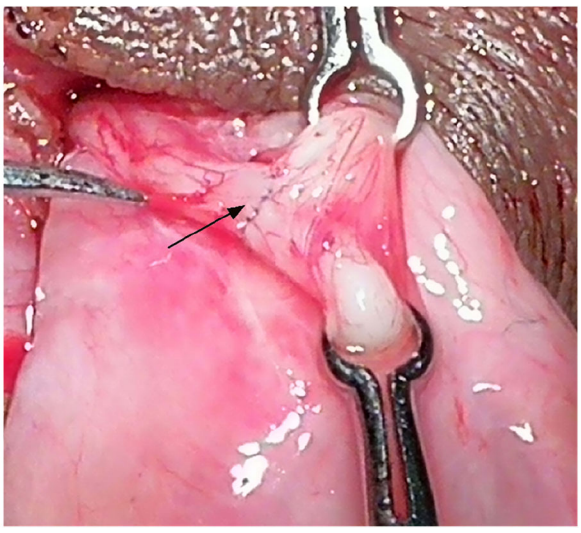

Fig. 3 Cross vasovasostomy in the scrotum
The arrow refers to the anastomosis site

We found a significant difference in the patency rate between the CVV and UVV groups, and no significant difference between the CVV and BVV groups (Table 3), which implied that any kind of CVV may provide good supplementation to the unilateral anastomosis in situ. The higher rates in the UVE+CVV group compared to the UVE group suggest that additional CVV may be a better alternative than UVE. Similar results of the UVV+CVV group compared to the UVV group corroborate the conclusion (Table 2). It was interesting that UCVV in the scrotum has comparatively higher patency and pregnancy rates. This may have been because: (1) Compared with the inguinal area, the CVV area in the scrotum was well exposed and under less anastomotic tension. Microsurgery techniques are more difficult for surgeons to perform in the deep inguinal region. Furthermore, the internal diameter and wall thickness of the vas deferens are inconsistent. (2) According to the literature, the patency and natural pregnancy rates of VV were higher than those of VE (Chan, 2013; Dickey et al., 2015). (3) The additional manipulation on the ipsilateral vas deferens might lead to insufficient blood supply or unpredictable scar formation.

However, the implementation of additional cross anastomosis might affect blood supply to the vas deferens, and whether additional anastomosis increases scar formation and decreases the patency remains unknown. This study was a nonrandomized study that only included a small sample size, and a randomized study with longer follow-up would be necessary to confirm our results.

Table 2 Post-operative patency and nature pregnancy rates in each group with cross anastomosis and comparative anastomosis

Group	Case	Patency*	Nature pregnancy*
UVV+CVV	5	3 (60.0%)	2 (40.0%)
BVV-S	9	7 (77.8%)	6 (66.7%)
BVV-I	4	3 (75.0%)	1 (25.0%)
UVV	9	1 (11.1%)	0 (0%)
UCVV	4	3 (75.0%)	2 (50.0%)
UVE+CVV	11	6 (54.5%)	3 (27.3%)
UVE	35	11 (31.4%)	4 (11.4%)

UVV: unilateral vasovasostomy; CVV: cross vasovasostomy; BVV-S: bilateral vasovasostomy in the scrotum; BVV-I: bilateral vasovasostomy in the inguen; UCVV: unilateral cross vasovasostomy; UVE: unilateral vasoepididymostomy. * Data are expressed as number (percentage)

Contributors

Zhong-yan LIANG performed the research and data analysis, wrote and edited the manuscript. Feng-bin ZHANG guided the surgery. Feng-bin ZHANG, Zhong-yan LIANG, Le-jun LI, Jing-ping LI, and Jing-gen WU performed the surgery. Yi-min ZHU contributed to the study design, data analysis, writing and editing of the manuscript. Chong CHEN performed the ultrasound examination. All authors read and approved the final manuscript and, therefore, had full access to all the data in the study and take responsibility for the integrity and security of the data.

Compliance with ethics guidelines

Zhong-yan LIANG, Feng-bin ZHANG, Le-jun LI, Jing-ping LI, Jing-gen WU, Chong CHEN, and Yi-min ZHU declare that they have no conflict of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from all patients for being included in the study.

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Table 3 Comparison of each parameter between the cross anastomosis (CVV) and comparative anastomosis groups (UVV, BVV)

Group	Case	Age (year)[1]		Volume of surgical testis (mL)[1]	Patency[2]	Natural pregnancy[2]
		Male	Female			
CVV	20	31.4±4.4*	28.3±3.7*	14.9±2.5	12 (60.0)*	7 (35.0)
UVV	9	30.8±6.1#	28.2±5.2	16.2±4.6	1 (11.1)	0 (0)
BVV	13	37.3±10.6	32.0±5.9	15.4±4.8	10 (76.9)*	7 (53.8)*
P-value		0.05	0.08	0.68	0.01	0.01

CVV: cross vasovasostomy (including unilateral vasovasostomy (UVV)+CVV, unilateral cross vasovasostomy (UCVV), unilateral vasoepididymostomy (UVE)+CVV). BVV: bilateral vasovasostomy. Male age: * P=0.027 vs. BVV; # P=0.043 vs. BVV. Female age: * P=0.034 vs. BVV. Patency: * P<0.05 vs. UVV. Natural pregnancy: * P<0.05 vs. UVV. [1] Data are expressed as mean±standard deviation (SD); [2] Data are expressed as number (percentage)

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中文概要

题　目：阴囊内输精管交叉显微吻合手术在不典型梗阻性无精子症患者中的临床应用

目　的：探讨在不典型梗阻性无精子症患者中施行不同方式阴囊内输精管交叉显微吻合手术的指征及有效性。

创新点：分析不同方式阴囊内输精管交叉显微吻合手术的指征及有效性，建议使用损伤小且成功率较高的阴囊内单纯输精管交叉显微吻合手术方式。

方　法：收集 2012 年 1 月至 2016 年 6 月浙江大学医学院附属妇产科医院 68 例不典型梗阻性无精子症和 9 例重度少弱精子症患者的临床资料，对施行不同手术方式的患者的特征、术后精子参数和配偶自然妊娠率结果等相关数据进行分析。

结　论：不典型梗阻性无精子症患者中施行各种类型的输精管交叉吻合手术均是对传统原位吻合手术有益的补充，阴囊内单纯输精管交叉显微吻合手术损伤小且成功率较高。

关键词：输精管吻合；无精子症；显微手术