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Microsurgical seminal reconstruction; our experiences in a single institute

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ABSTRACT

We assessed the contribution of microsurgical seminal reconstruction to achieving natural conception in conjunction with advanced assisted reproductive technologies. Ninety obstructive azoospermic subjects who underwent microsurgical seminal reconstruction were evaluated. Vasovasostomy (VV) was undertaken in 45 subjects whereas vasoepididymostomy (VE) in 45, respectively. VV was performed by employing a two microlayer anastomotic technique, whilst VE was undertaken using double needle longitudinal vaspepididymostomy (LIVE). Patency was achieved in 41 VV (91.1%), and 25 VE (55.6%) cases. In cases where patency was achieved, pregnancy and healthy delivery were recorded following natural intercourse in 7/41 (17.0%) VV, and in 7/25 (28.0%) VE cases. Where patency was not achieved, the use of cryopreserved sperm for intracytoplasmic sperm injection (ICSI), resulted in a healthy delivery in 4/4 (100%) VV and 14/21 (66.6%) in VE subjects. Although natural pregnancy was achieved only in a limited number of subjects treated (14/90; 15.6%), sperm harvested during surgery and cryopreserved for future ICSI use proved valuable, doubling the overall delivery rate (32/90; 36.6%). Surgical intervention is considered to be a useful technique in order to allow the possibility of a natural conception and by harvesting sperm at the same time contributes to the cost-effectiveness.

Keywords: obstructive azoospermia (OA), vasovasostomy, longitudinal intussusception vasoepididymostomy (LIVE), cryopreservation, ICSI

INTRODUCTION

Obstructive azoospermia (OA) can be caused by vasectomy, congenital bilateral absence of the vas deferens (CBAVD), scarring from past epididymal infections, inguinal hernia, and hydrocelectomy. However, most previous papers regarding to OA are vasectomy reversal. It has been estimated that 175,000–354,000 vasectomies are undergone each year in the United States.[1] Thus, vasectomy is a major cause of OA.

Optimal management of vasal or epididymal obstruction includes microsurgical vasovasostomy (VV) or vasoepididymostomy (VE). However, this is not always possible in cases of CBAVD,

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and additionally, the microsurgical skill required for reconstruction may not be available. Varying surgical sperm retrieval methods are utilized for intracytoplasmic sperm injection (ICSI). Testicular sperm extraction (TESE) for non-obstructive azoospermia (NOA), and also for OA, is widely performed by probably as less surgical skill is required. On the other hand, OA patients are good candidates for seminal reconstruction or microscopic epididymal sperm aspiration (MEA). We previously emphasized superior pregnancy and clinical delivery rates were observed in MESA following ICSI without testicular surgical damage.[2] In order to further document pregnancy and live birth outcomes we have reviewed 90 consecutive microsurgical seminal reconstruction performed in the Department of Urology, Kyoritsu General Hospital and by a single surgeon (H. H.) between 2002 June to 2018.

MATERIALS AND METHODS

Patients

1920 subjects were referred to our male infertility clinic between July 2002 and December 2018. Of the 442 was diagnosed as having OA, 90 subjects who underwent microsurgical seminal reconstruction were fully evaluated. Of these, VV was performed in 45 and VE in 45, respectively. During the same period, 171 subjects underwent MESA due to CBAVD, failed seminal reconstruction, and in those not desiring surgical reconstruction.

The etiology of vasal obstruction was inguinal herniorrhaphy (3) and previous vasectomy in 42 subjects. Of these, one subject had previous history of failed vasovasostomy, and another had 5 TESE attempts. In those who had VE, epididymal obstruction was caused by orchidopexy (4), Young's syndrome (3), epididymitis (2), and unknown cause in 36 subjects. In cases of unknown etiology of epididymal obstruction, three subjects had a live birth following natural intercourse. Sperm harvest and cryopreservation during surgery was performed when requested by the patient. Post-operative follow-up consisted of serial semen analysis from 3 weeks to up to 3 years.

Surgery

The surgical procedure was undertaken using an operative microscope under general anesthesia. VV was performed by the two microlayer anastomotic technique under an operative microscope, whereas VE was carried out using a double needle longitudinal intussusception technique (LIVE).[3] In cases where sperm were requested to be harvested during surgery for cryopreservation, the samples were transferred to an in vitro fertilization (IVF) laboratory. The patient was required to rest in bed overnight and to stay in hospital for two days after surgery. Scrotal support was maintained for three weeks.

Surgical technique for vasovasostomy (VV group)

Scrotal skin was incised longitudinally just above to the vas deference in cases of vasectomy, whereas in cases of inguinal vasal obstruction, skin incision was made on the previous operative scar. The vas deferens was dissected carefully to avoid vascular injury. If adequate vasal length was obtained without any tension for the anastomosis, vasotomy was made. Two to three mL of indigo carmine solution was gently injected to the distal vas. Distal patency was confirmed with drainage of blue-colored-urine through a Foley's catheter inserted to the bladder during surgery. Proximal vasal fluid was then examined. Although no sperm was obtained from bilateral vas deferens anastomoses performed, TESE was carried out and sperm cryopreserved in cases where patient had consented. Mucosal anastomosis was done using six sutures using10-0 double armed nylon inside to outside fashion to ensure the mucosal adhesion. Additional eight sutures

by 9-0 nylon were used for adventitial anastomosis to complete VV. No drain was necessary.

Surgical technique for vasoepididymostomy (VE-group)

Vasotomy and confirmation of distal vasal patency were made by same maneuver as VV. Then the epididymis was inspected under the operating microscope to pick a convenient point above the site of suspected obstruction. The epididymal tunic was cut and trimmed to expose the dilated epididymal tubule with a micro-scissors. Two 10-0 double armed nylon sutures were parallelly placed to the epididymal tubule longitudinally. The tubulotomy was made and epididymal fluid was examined and collected. If spermatozoa were present, anastomosis and harvest of epididymal sperm for cryopreservation was carried out. The needles were pulled through and placed through the 4 microdots on the vasal ends in an inside-out fashion. (Figure-1a,b) To ligate these sutures, the epididymal tubule intussuscepted into the vas lumen. (Figure-1c) Then, the outer layer of 9-0 nylon sutures completed the anastomosis. (Figure-1d) If no sperm was found in the epididymis, the procedure was repeated more proximally. If no sperm were observed in the whole epididymis, anastomosis was not carried out. No drain was left.

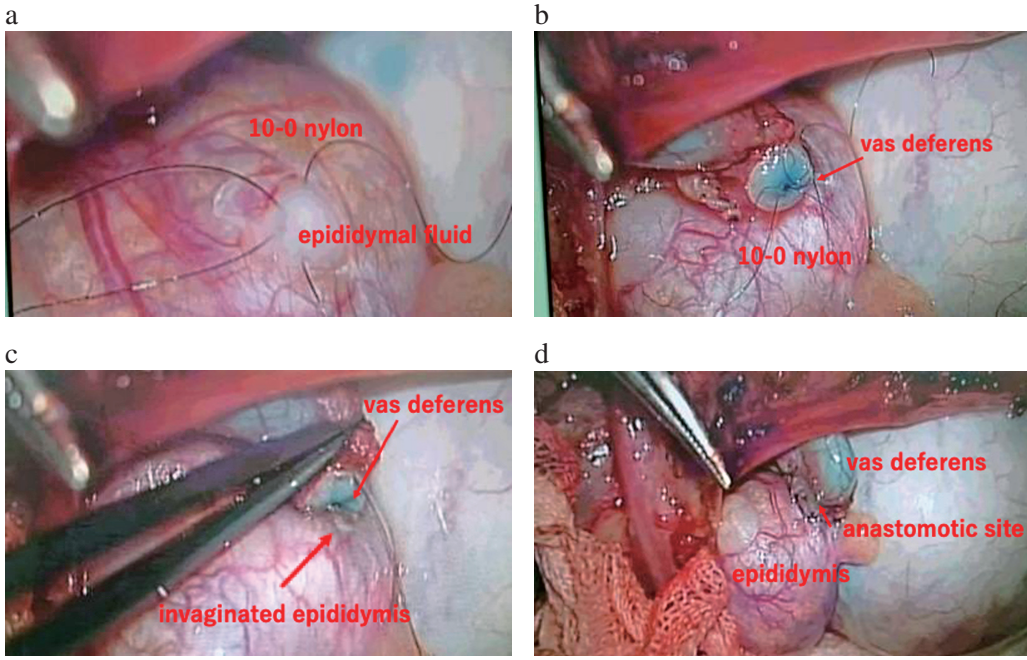

Fig. 1 A surgical technique for vasoepididymostomy

Fig. 1a: Two 10-0 nylon sutures were placed to the epididymal tubule and tubulotomy was made. White epididymal fluid exuded up.

Fig. 1b: The 10-0 nylon needles were pulled through and placed through the 4 microdots on the vasal ends in an inside-out fashion.

Fig. 1c: Epididymal tubule was invaginated into the vasal lumen.

Fig. 1d: The outer layer of 9-0 nylon sutures completed the anastomosis.

RESULTS

VV group

Patient characteristics are shown in table. The mean age was 41.1 (range: 27 to 61) years, and the mean age of the spouses was 32.2 (range: 20 to 45) years. The mean duration of vasal obstruction was 12 years (range; 0.5 to 30). One patient had a history of the left nephrectomy and extended cholecystectomy due to kidney and gall bladder cancer. Sperm granuloma were observed in only 21 subjects. Bilateral anastomosis was done in 44, and unilateral in 1 subject due to unilateral vasal absence with ipsilateral renal agenesis. The mean duration of operation was 283 minutes (range; 210–350). Overall patency was achieved in 41(91.1%). Cryopreservation of sperm harvested during surgery was done in 16 cases. Correlation of patency and obstructive duration are shown in Figure-2. Patency was 17/17 (100%) subjects at 0–9.9 years of obstruction interval, 19/20 (95%) subjects at 10–19.9 years, and 5/8 (62.5%) subjects at over 20 years, respectively. Semen volume was 1.2–4.8mL (median 2.3), sperm count 13–10^6×10^6/mL (median 65.1), and sperm motility 16–80% (median 46.4%), respectively. Duration of sperm appearance was 0.7–6 (median 2.1) months. No patients showed patency for after inguinal herniorrhaphy and with a previous history of 5 attempts at TESE. Thirteen subjects showed no sperm in vasal fluid. Of these, ten subjects achieved patency, whereas three did not get patency. However, two subjects had cryopreserved sperm after TESE. Seven subject (15.6%) achieved natural pregnancy and delivery. On the other hand, four pregnancies and delivery (8.9%) were obtained by ICSI using frozen thawed sperm. Overall pregnancy and delivery were achieved in 11 (24.4%) subjects. Due to lack of regular checks at our hospital, pregnancy could not be evaluated in other subjects.

Table Patients characteristics

	VV (n=45)	VE (n=45)	*P value*
Mean age (y)	41 (27–61)	33 (25–44)	*P*=0.0159
Spouse age (y)	32 (20–45)	31 (26–39)	*NS*
Duration of obstruction (y)	12 (0.5–30)	unknown	–
Testicular volume (R/L) (mL)	20 (12–30) / 18 (10–26)	22 (8–30) / 19 (8–28)	*NS*
LH (mIU/mL)	3.4 (1.2–6.4)	2.6 (1.2–4.6)	*NS*
FSH (mIU/mL)	5.1 (2.1–16.1)	3.6 (1.8–11.7)	*NS*
Testosterone (ng/mL)	4.48 (1.84–9.94)	5.33 (3.04–9.25)	*NS*
Free-testosterone (pg/mL)	10.3 (4.3–19.6)	12.1 (6.6–25.3)	*NS*
E2 (pg/mL)	23.5 (14.2–25.5)	29.2 (14.0–30.4)	*NS*
BMI	23.9 (17.8–29.7)	23.1 (18.8–32.1)	*NS*

VE-group

The mean age was 33.2 (range: 25 to 44) years, and the spouses mean age was 31.1 (range: 26 to 39) years. Although spouses age was same as VV group, patient's age was younger. (*P*=0.0159) Cryopreservation of sperm harvested during surgery was done in all cases. Bilateral anastomosis was carried out in 37 and unilateral in 8 cases. Of the unilateral anastomoses, six subjects had no sperm recovery from the epididymis and two showed contralateral vasal absence. One of the two latter subjects had a cross-over VE, following contralateral orchiectomy and using the vas deferens which had tiny seminoma. The mean duration of operation was 254 minutes

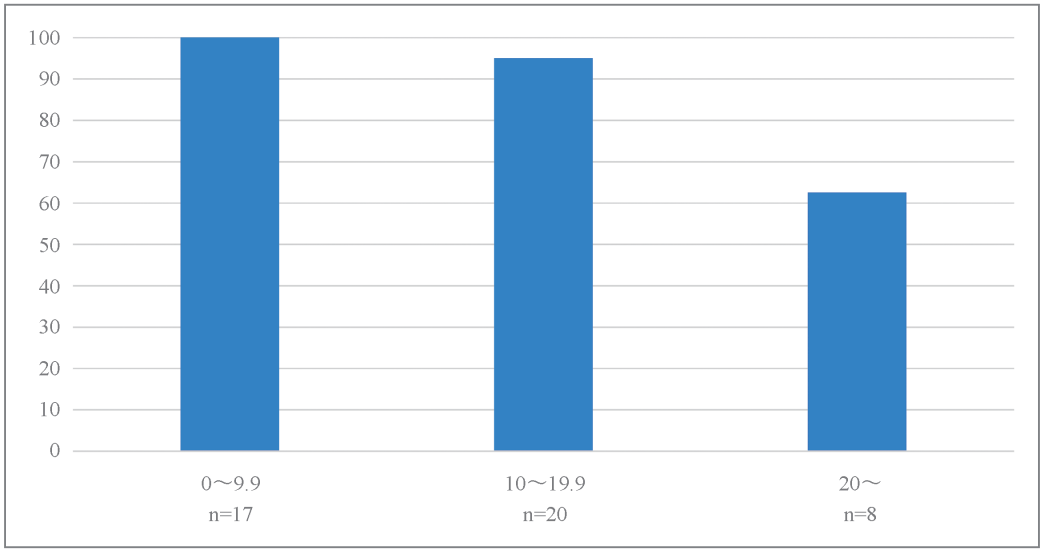

Fig. 2 Duration of vasal obstruction and patency rate

(range; 135–334). Overall patency was achieved in 25 (55.6%). Anastomotic site was in the caput in 4 subjects, to corpus in 3, and to cauda in 18, respectively. Semen volume was 1.0–6.5 mL (median 2.3), sperm count 0.1–45.0×10^6/mL (median 12.5), and sperm motility 0–70% (median 33.2%), respectively. Duration of sperm appearance was 0.7–15 (median 6.5) months. In seven subject (15.6%) achieved natural pregnancy and delivery. Twenty subjects who did not have patency received ICSI by using frozen-thawed sperm and 14 pregnancies (31.1%) and deliveries were obtained. Overall pregnancy and delivery were achieved in 21 (46.7%) subjects.

DISCUSSION

Azoospermia is classified as either OA or NOA, according mainly to the FSH value, testicular volume, chromosomal evaluation, and past history. OA cases brought on by vasectomy, CBAVD, scarring from past epididymal infections, inguinal hernia, and hydrocelectomy are a very different condition from NOA. Initial therapy for OA is classically microsurgical seminal reconstruction except in cases of CBAVD or obstruction of rete testis. Seminal tract reconstruction can lead to natural pregnancy without invasive in vitro fertilization (IVF) procedure for spouse, and considered to be cost-effectiveness. Microsurgical VE for epididymal obstruction caused by unknown etiology is considered to be a challenging surgery due to the low patency achieved and low pregnancy rates. A nationwide Japanese survey for microsurgical seminal reconstruction, reported the % appearance of sperm in the postoperative ejaculate for vasectomy, epididymal obstruction, herniorrhaphy, unknown etiology and other etiology groups as 73.6%, 38.9%, 38.9%, 34.0%, and 70.0%, respectively.[4] In that study, although these patency rates for each procedures were almost equal to previous nationwide Japanese survey (2000), frequency of vasal obstruction caused by herniorrhaphy declined from 23% to 9%.[4,5] In the present study, vasal obstruction by herniorrhaphy was found in only three cases, moreover, no case occurred during the last decade.

Microsurgical seminal reconstruction is possible only in a limited number of facilities, and requires rigorous microsurgical skill. Furthermore, the patient requires hospitalization over 2 days

following surgery. Sperm retrieval surgery such as MESA and TESE have become the standard treatment for OA. In general, return of sperm rates (52% to 92%) and pregnancy rates (11% to 56%) by microsurgical seminal reconstruction are similar to IVF/ICSI. If an experienced surgeon performs the microsurgical procedure, the results maybe further improved. More importantly, the actual overall cost per live baby should be considered. Hospital cost of the vasovasostomy is almost 605,000 yen, whereas vasoepididymostomy is 160,000 yen when covered by Japanese insurance system in our hospital. Nevertheless, there are advantages and disadvantages to each approach, and the choice of treatment is depended on the patient's desire and potential fertility of each partner, as well as the cost. Surgical patency rates of VV ranged from 65–90%, however, the natural pregnancy rates are lower.[6] Thus, sperm harvest and cryopreservation during surgery is advantageous and previously we emphasized the importance of sperm harvest and cryopreservation during VE to subsequently reduce patient's burden.[7] On the other hand, Boyle et al concluded in a multi-center analysis that sperm harvesting during vasectomy reversal was not cost effective.[8] Glazier et al reported that when couples were offered the sperm cryopreservation during reversal surgery, only 64% of couples elected to do so. Furthermore, 21% of these couples requested destruction of the sperm within 4 months after the surgery because they changed their minds about ICSI.[9] In the present study, only 16 subjects (35.6%) in VV group desired cryopreservation. Although the necessity of sperm harvest and cryopreservation during surgery is controversial, we believe these procedures can be beneficial because it can enhance the chance of a healthy delivery for a couple.

We performed VV even when no sperm were observed from proximal vasal fluid. Should we do only VV at the first reversal, or if there is no sperm in the vasal fluid, should we perform VE? There are certainly a number of controversies on this subject. Silber and Grotjan reported from a large dataset, patients with no sperm in the vasal fluid underwent VE instead of VV.[10] Only 22% of their vasectomy reversals involved bilateral VV, and 78% required VE on either one or both sides. Using this approach, performing VV when there is sperm in the vasal fluid and VE when there is no sperm in the vasal fluid, an overall patency rate of 96.2% was achieved.[10] Similarly, Schrepferman et al reported in vasectomy reversals that the patency rate after bilateral VV, unilateral VV with contralateral VE, and unilateral or bilateral VE was 96%, 83%, and 57%, respectively.[11] In the present dataset, 13 subjects (28.9%) of the VV group presented no sperm in the vasal fluid. Of these, 10 subjects (76.9%) achieved patency, and two of three who did not achieve patency had sperm cryopreservation by TESE. Although overall patency in VV group was good (91.1%), the result of failed cases for the history of herniorrhaphy was poor with the obstructive duration being 20, 25, 26 years, respectively.

Previous reported VE were mainly post-vasectomy cases.[10] The outcome of microsurgical seminal reconstruction in men with OA unrelated to vasectomy is dependent on the obstructive etiology. While the prognosis is good for men with epididymal obstruction due to vasectomy, men with idiopathic epididymal obstruction have a poorer outcome.[12] Matsuda et al also reported that patients with epididymitis or vasectomy patients with an obstruction for ≤ 15 years had the best prognosis following patients who underwent VE.[13] Microsurgical VE for epididymal obstruction caused by unknown etiology is considered to be a challenging surgery with limited patency and pregnancy rates.

In 1978, Silber initially reported microscopic VE,[14] the success rate of this procedure dramatically improved results. A novel VE technique involving epididymal tubular intussusception called triangulation for human application has been documented to simplify the procedure by Berger.[15] We reported early patency and good outcome using this triangulation technique.[16] The concept of tubular intussusception VE was originally described in a rat model by Stefanovic et al in 1993.[17] Patency was confirmed at 97%; moreover, a histological examination revealed

resorption of the intussuscepted portion of the epididymal tubule. Thus, intussusception of the epididymal tubule into the vas deferens may help prevent sperm leakage and subsequent scarring at the site. Marmar developed more simplified VE with simultaneous double needle placement, tubulotomy and epididymal tubular intussusception,[18] and Chan et al modified this technique to longitudinal intussusception VE (LIVE).[3,9] The late failure rate is lower with the use of the intussusception technique (4%), compared with the non-intussusception technique (37%).[20] Thus, LIVE has become as a standard technique for VE.[21] We previously reported that if end-to-side two layers VE was employed for the patients with no previous history of vasectomy, and the patency rate was 54%.[7] Our present study was similar to between end-to-side anastomosis and intussusception technique.

Predictors of patency include intraoperative vasal or tubular fluid quality, presence of granuloma, duration of obstruction, and surgeon's experience.[10] Among factors predicting success, the presence of motile sperm was found to be significant in VE cases.[22,23] Although the presence of granuloma is considered as a good success predictor in VV, granuloma was observed in only 21 subjects in present study. Ten of 13 who did have no sperm in vasal fluid achieved patency. Thus, vasal granuloma seems to have no relation with the outcome. On the other hand, among the VE group, no sperm in the epididymal fluid, anastomosis was not done. Since 6 cases (13.3%) showed no sperm unilaterally, anastomosis was terminated. Of the six cases, only two achieved patency. Anastomotic site is considered as a good predictor of patency among VE cases. While Kim et al reported 100% patency rate after anastomosis to epididymal caput, and 73% after anastomosis to corpus.[24] Although anastomotic sites were varied, most studies show higher pregnancy rate after distal anastomosis.[25,26] There was a similar tendency in the present series, patency achieved at caput in 4, at corpus in 3, and at cauda in 18, respectively. Silber et al reported that several factors may influence pregnancy rate, the greatest impact is the age of the wife.[10] Distal anastomosis in VE seems to be as a good predictor. The patency rate between using end-side anastomosis and intussusception technique was not different in our previous and present study (54.2% versus 55.6%).[7] Although natural pregnancy rate was similar (16.7% versus 15.6%), overall pregnancy was superior (25.0% versus 46.7%). It is reversely related with the spouse age (mean 26.9 versus 31.1).

Belker et al reported that VV resulted in 85–90% of patency and 50–70% in US Vasovasostomy Study Group.[6] Comparing with the Japanese nationwide survey, patency of VV was 73.6%, and pregnancy was 27.5%. Taniguchi hypothesized this difference was insufficient follow-up due to high rate of such patients (56%).4) In respect to our VV group, only 11 (24.4%) subjects achieved fatherhood, the others were dropped-out from follow-up. Fuch and Burt also reported that 48 cases out of 173 (27.7%) were lost because of lack of inability to contact the patients, and 9 because apparently the patients were not attempting to achieve pregnancy.[26] Silber SJ and Grotjan emphasized that an intensive telephone campaign should be done to validate the outcome and update data.[10] However, this may not be a feasible solution in routine clinical practice.

In conclusion, overall pregnancy was achieved 11 (24.4%) in VV group, and 21 (46.7%) in VE group. Natural pregnancy may be obtained as a consecutive treatment for OA instead of sperm retrieval surgery. It can reduce costs and avoid invasive procedures for the spouse. We believe that sperm harvest and cryopreservation during surgery may enhance the chance of pregnancy. Moreover, we should present and discuss the most appropriate treatment with patient and spouse depending on their life time ambitions.

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STATEMENT OF ETHICS

Human rights and informed consent statements: All procedures completed were dome in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national), and with the Helsinki Declaration of 1964 and its later amendments. Informed consent was obtained from patients for the purpose of inclusion in this study. The protocol for this research project, including its use of human subjects, was approved by a suitably constituted Ethics Committee.

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