ORIGINAL ARTICLE

Microsurgical vasoepididymostomy for obstructive azoospermia

KL Ho 何嶌崙
MH Wong 王明皓
PC Tam 談寶雛

Objectives To evaluate the efficacy of microsurgical vasoepididymostomy for patients with obstructive azoospermia attending our institutions.

Design Retrospective study.

Setting Division of Urology, Department of Surgery, Queen Mary and Tung Wah hospitals, Hong Kong.

Patients All patients with obstructive azoospermia due to epididymal obstruction who had undergone microsurgical vasoepididymostomy in the study hospitals from July 2001 to November 2007.

Main outcome measures Causes of epididymal obstruction, operative techniques, patency rates, and pregnancy outcomes of their female partners.

Results Twenty-two patients with obstructive azoospermia due to epididymal obstruction had undergone 23 microsurgical vasoepididymostomy procedures. The mean age of patients and their female partners was 36 and 30 years, respectively. Six procedures were performed by the Berger's triangulation intussusception technique and 17 by Marmar or Chan's two-suture intussusception techniques. The mean operating time of unilateral and bilateral procedures was 164 and 203 minutes, respectively. The median follow-up duration was 15 months. The overall patency rate was 57%; being 50% and 64% for unilateral and bilateral procedures, respectively. The patency rate of patients with epididymal fluid positive for sperm was 71%. The mean best sperm count was 23.1 million/mL, with forward motility of 19% and normal morphology of 7%. The overall paternity rate was 32%. Natural pregnancy was achieved in three cases and assisted reproduction was used in four.

Conclusions Microsurgical intussusception vasoepididymostomy is a viable option for couples with male factor infertility due to obstructive azoospermia. Reasonable patency outcomes were achieved in the present series of cases. Individualised counselling, with expectations based on anticipated surgical outcomes, should be offered to couples before resorting to assisted reproduction.

Introduction

Infertility is defined as the inability to conceive after 1 year of regular unprotected sexual intercourse. About 15% of couples are affected. Male factors account for about 50% of couples with infertility.[1] Approximately 10 to 15% of infertile men suffer from azoospermia—complete absence of sperms in the ejaculate. Among these azoospermic patients, approximately 40% have complete obstruction in the ductal system and hence suffer from obstructive azoospermia.[2]

In this era of rapid development of reproductive medicine, many couples with male factor infertility have pursued assisted reproduction. With advances in sperm retrieval techniques and the introduction of intracytoplasmic sperm injection (ICSI[3,4]) in the 1990s, the live delivery rates of assisted reproduction have improved significantly. However, assisted reproduction subjects the female partner to increased risks, and the cost of in-vitro fertilisation (IVF) cycles must also be considered.[1] The offspring resulting from assisted reproduction may also have increased perinatal morbidities due to the increased risk of multiple pregnancy.

In western literature, the commonest cause of obstructive azoospermia is

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Division of Urology, Department of Surgery, The University of Hong Kong, Queen Mary Hospital and Tung Wah Hospital, Hong Kong
KL Ho, FRCS (Urology) (Edin), FHKAM (Surgery)
MH Wong, MB, BS, MRCS (Ed)
PC Tam, FRCS (Urology) (Edin), FHKAM (Surgery)

Correspondence to: Dr PC Tam
E-mail: tampc@ha.org.hk

vasectomy.[2,5] Other causes include congenital absence of vas deferens and ejaculatory duct obstruction, and acquired diseases (eg epididymal obstruction secondary to infection, vasal injury due to previous inguino-scrotal surgery). Treatment options of epididymal obstruction include scrotal exploration with microsurgical vasoepididymostomy or sperm retrieval with ICSI.

Due to the small luminal diameters of the vas (0.3 mm) and epididymal tubule (0.2 mm), vasoepididymostomy has been considered among the most technically challenging procedures performed on the male reproductive system,[5] and has been evolving rapidly in recent years.[6-10] The objective of the present study was to review the efficacy of microsurgical vasoepididymostomy for patients with obstructive azoospermia due to epididymal obstruction performed in our institution. Success in terms of patency was defined by the return of sperm to the ejaculate. In this study, the causes of epididymal obstruction, the operative techniques used, the patency rates, and pregnancy outcomes were evaluated.

顯微外科附睾輸精管吻合術治療梗阻性無精子症

目的 探討顯微外科附睾輸精管吻合術對於本院梗阻性無精子症患者的治療成效。

設計 回顧研究。

安排 香港瑪麗醫院及東華醫院的外科部泌尿科。

患者 2001年7月至2007年11月期間，因有梗阻性無精子症而接受顯微外科附睾輸精管吻合術的所有病人。

主要結果測量 梗阻性無精子症的病因、手術技巧、通暢率、及妊娠結果。

結果 共22位梗阻性無精子症患者接受23次顯微外科附睾輸精管吻合術。病人平均年齡36歲，他們伴侶的平均年齡30歲。有6次手術使用Berger三角狀三針式套疊吻合術，另17次使用Marmar或Chan兩針式套疊吻合術。單側手術平均時間164分鐘，雙側手術203分鐘。隨訪期中位數15個月。總通暢率57%；其中單側50%，雙側64%。帶精子附睾液的通暢率為71%。最佳精子數目為每毫升2千310萬，其中19%精子有前向運動，7%有正常外型。總妊娠率為32%。有3個自然妊娠的案例，另4個透過輔助生育法成功懷孕。

結論 顯微外科附睾輸精管套疊吻合術對於因梗阻性無精子症而引致不育的男性是一個可取的方法。此技術所得的通暢率合理。夫婦在接受輔助生育法前，應為他們進行個別輔導，讓他們知道手術的預期結果，以致有合理的期望。

Methods

From July 2001 to November 2007, 22 consecutive patients with obstructive azoospermia due to suspected epididymal obstruction who underwent 23 microsurgical vasoepididymostomy procedures were included in the present study. All procedures were performed by a single surgeon in a university teaching hospital. The inclusion criteria were: documented azoospermia in at least two consecutive semen samples collected 6 weeks apart, with normal volume ejaculate and pH. All patients had normal-sized testes, normal or marginally elevated follicle-stimulating hormone levels. No patient had recorded a history of paternity and hence all had had testicular biopsies to confirm active spermatogenesis. Each patient and his partner were evaluated in the male infertility clinic, which involved obtaining a comprehensive history and physical examination. Treatment options including scrotal exploration with microsurgical vasoepididymostomy and sperm retrieval with ICSI were thoroughly discussed with each couple. Patients who had scrotal exploration with non-reconstructable pathology were excluded.

Surgical techniques

Scrotal exploration was performed under general anaesthesia. After the testis and epididymis were exposed, hemi-transection of vas was performed just distal to the convoluted portion. Diluted methylene blue solution was used for a vasogram and the bladder catheterized to confirm the patency of the abdominal vas. The contralateral vasogram was performed with normal saline. Vas transection was completed and the abdominal vas mobilised. To assist tension-free anastomosis, the abdominal vas adventitia was sutured to the epididymal tunica covering the distended tubules. Distended epididymal tubules were exposed and subsequent vasoepididymostomy was carried out using a microscope with 12x magnification. From July 2001 to August 2003, the triangulation intussusception technique as described by Berger[6] was employed for vasoepididymostomy. Three double-armed 10-zero nylon needles were placed on a distended epididymal tubule. The epididymal tubule was then punctured and intussuscepted into the vasal lumen with 6-point fixation. Epididymal fluid was collected and analysed for the presence of sperm. Sometimes, the epididymal tubules were not big enough to accommodate three 10-zero nylon needles. After August 2003, we adopted the two-suture intussusception technique as described by Marmar and by Chan et al.[7,10] Two double-armed 10-zero nylon needles were placed on a distended epididymal tubule either transversely (Marmar[7]) or longitudinally (Chan et al[10]), depending on the tubule configuration. The epididymal tubule was then punctured and intussuscepted into the vasal lumen with 4-point fixation. Water-tightness was enhanced by the intussusception technique and to reinforce the anastomosis, the epididymal tunica was sutured to the vasal adventitia with 9-zero nylon.

TABLE 1. Perioperative variables

Variable	Data*
Mean age (years)	
Patients	36
Female partners	30
Causes of epididymal obstruction	
Infection	14
Idiopathic	8
Microsurgical vasoepididymostomy	
Unilateral	12
Bilateral	11
Techniques	
Berger's triangulation intussusception	6
Marmar/Chan's two-suture intussusception	17
Mean operating time (minutes)	
Triangulation unilateral procedures	186
Two-suture intussusception	
Unilateral procedures	142
Bilateral procedures	203
Median (range) follow-up (months)	15 (4-32)

* Data are shown as No. of patients, unless otherwise stated

TABLE 2. Patency and paternity outcomes

Outcome	Data*	P value
Patency rate		
Overall	13/23 (57%)	-
Triangulation unilateral procedures	4/6 (67%)	-
Two-suture intussusception (overall)	9/17 (53%)	0.66
Unilateral procedures	2/6 (33%)	-
Bilateral procedures	7/11 (64%)	
Infectious cause	9/15 (60%)	-
Idiopathic cause†	4/8 (50%)	0.69
Group 1	12/17 (71%)	<0.05
Group 2	1/6 (17%)	
Mean (range) best		
Sperm count (million/mL)	23.1 (0.5-71.0)	-
Forward motility (%)	19 (0-60)	-
Normal morphology (%)	7 (0-14)	-
Median (range) time to patency (months)	4 (1-20)	-
Overall paternity	7/22 (32%)	
Natural pregnancy	3/22 (14%)	-
IVF/ICSI‡	4/22 (18%)	-

* Data are shown as No. (%) of patients, unless otherwise stated

† 22 patients had undergone 23 microsurgical vasoepididymostomy: group 1=presence of sperm in epididymal fluid (n=17); group 2=absence of sperm in epididymal fluid (n=6)

‡ IVF denotes in-vitro fertilisation, and ICSI intracytoplasmic sperm injection

In the early study period from 2001 to 2005, most of the vasoepididymostomy procedures performed were unilateral due to the learning curve effect and long duration of the operation. As experience in intussusception vasoepididymostomy accumulated, most of the procedures performed from 2006 to 2007 were bilateral. Occasionally, a unilateral procedure was undertaken because of unilateral partial agenesis of the vas or absent epididymal sperm on scrotal exploration.

Routinely patients were discharged on postoperative day 1 and asked to withhold ejaculation for 4 weeks. Semen samples obtained at 1, 3, and 6 months after the surgery were analysed, and as clinically indicated thereafter. Patency was defined by the return of intact whole sperm into the ejaculate in any one semen analysis. The demographics, causes of epididymal obstruction, operative techniques, patency rates, and pregnancy outcomes of their female partners were also collected.

Results

During the study period, 22 patients with obstructive azoospermia had undergone 23 microsurgical vasoepididymostomy procedures. One patient had a right-sided vasoepididymostomy which failed and subsequently had left-sided vasoepididymostomy 1 year later. The mean age of the men was 36 years and 30 years for their female partners. The cause of epididymal obstruction was previous infection in 14 patients and the remaining 8 were idiopathic. None of the patients had had vasectomies or inguinal hernia surgery. The median duration of follow-up was 15 (range, 4-32) months (Table 1). Overall, 12 had unilateral and 11 had bilateral procedures. Six procedures were performed by the triangulation intussusception technique (Berger[6]) and 17 by the two-suture intussusception technique (Marmar[7] and Chan et al[10]). The mean operating time was 164 minutes for unilateral procedures and 203 minutes when they were bilateral.

The overall patency rate was 57%. The patency rate of the triangulation and two-suture intussusception techniques were 67% and 53%, respectively (P=0.66). The patency rates of unilateral (triangulation and two-suture unilateral procedures) and bilateral procedures were 50 and 64%, respectively (Table 2). The mean best sperm count was 23.1 (range, 0.5-71.0) million/mL, with a forward motility rate of 19% (range, 0-60%) and a normal morphology of 7% (range, 0-14%). The median time to patency after surgery was 4 (range, 1-20) months.

Following our 23 procedures, epididymal fluid analysis showed presence of sperm (group 1) in 17 subjects, but not in the remaining six (group 2). The patency rate was 71% (12/17) in group 1 and 17% (1/6) in group 2 (P<0.05). When the operative record of the single patient with 'absent epididymal sperm' and

positive patency result was reviewed, it was noted that the epididymal tubule was dry after puncture during surgery and hence no epididymal fluid analysis could be performed.

In our group of study patients, the overall paternity rate was 32%. Natural pregnancies were achieved in three cases with a mean sperm count of 28.1 million/mL. Assisted reproduction was performed in four cases, two by fresh ejaculated semen and two with epididymal sperm collection. One patient had a right-sided vasoepididymostomy, which failed and had a left-sided vasoepididymostomy a year later. That patient had epididymal sperm collection for assisted reproduction during the second scrotal exploration.

Discussion

According to studies published in western literature, infertility is likely to continue increasing in the next 20 years.[1] This phenomenon is multi-factorial and one of the frequently quoted reasons is the increase in maternal age. Delayed childbearing may be explained by increasing emphasis on educational and career goals, advanced age at first marriage, and effective birth control methods that decrease unplanned pregnancies.[4] On the other hand, male factors contribute to about 50% of couples with infertility. In the general population, less than 1% of men are azoospermic. Among infertile men, the incidence of azoospermia is about 10 to 15%, of which 40% is due to obstructive azoospermia.[2]

The causes of obstructive azoospermia are multiple. Among Caucasians, the commonest cause is vasectomy for contraception.[5] In patients with vasectomy performed more than 15 years earlier, the outcome of vasectomy reversal progressively deteriorates with time[2]; epididymal blow-out and subsequent obstruction is one of the explanations. Other causes of obstructive azoospermia include: congenital absence of the vas deferens, infection causing epididymal obstruction, inguinal surgery with iatrogenic injury to the vas deferens and ejaculatory duct obstruction. In our series of cases, 61% had had a previous identifiable infection, eg epididymitis, gonococcal or non-gonococcal urethritis. Eight patients had no identifiable cause. Infection is associated with adhesions, as noted during scrotal exploration. They also increase the difficulty of subsequent reconstructive procedures. However, Schiff et al[11] showed that previous infection was not associated with worse outcomes after microsurgical vasoepididymostomy. In our case series, the patency outcomes of patients with infectious versus idiopathic causes were also similar (Table 2).

When couples with male factor infertility secondary to obstructive azoospermia were interviewed, they were counselled on the following options: remaining childless, adoption, donor insemination, scrotal exploration with the intention of undertaking a reconstructive procedure, and assisted reproduction with sperm retrieval for IVF/ICSI. For couples with non-reconstructable obstruction (eg congenital absence of vas deferens) or advanced female age (≥35 years), assisted reproduction was usually recommended. Most of the other couples finally faced the choice between reconstructive surgery and assisted reproduction. Following the successful introduction of IVF in 1978, in the last three decades IVF cycles performed per year have been increasing worldwide. In developed countries, at least 1% of births are estimated to result from assisted reproduction.[3] In most centres, IVF/ICSI can achieve clinical pregnancy rates between 30% and 40% and delivery rates between 25% and 30%.[2] However, IVF/ICSI also predisposes the female partner to increased risk of ovarian hyperstimulation syndrome, complications of oocyte retrieval and multiple pregnancies (up to 16 to 32%).[2-4,12-16] Multiple pregnancies are associated with prematurity, preterm labour, and increased infant morbidity and mortality. Debates have continued for years on whether assisted reproduction is associated with an increased incidence of congenital malformations. Though not universally agreed, it seems that there is an increase in urogenital malformations in boys, even in singleton births from IVF/ICSI.[3] While most of the increased morbidities associated with assisted reproduction focus on the female partner, those associated with sperm retrieval procedures are small but not negligible. Bleeding, infection, and testicular atrophy may ensue after about 0.3 to 2% of such procedures.[1]

In contrast to the success of IVF since 1978 and ICSI since the early 1990s, the development of reconstructive surgery for epididymal obstructive azoospermia has lagged behind. Early attempts at end-to-end and conventional end-to-side vasoepididymostomy[17-19] produced reasonable patency outcomes. However, the technical difficulty of such complex microsurgical anastomoses limited their developments to a small number of highly specialised centres. Berger[6] revolutionised the development of intussusception vasoepididymostomy with the triangulation technique. The number of sutures required to maintain the water-tight seal of the anastomosis decreased dramatically. In a randomised controlled study on Wistar rats, McCallum et al[8] demonstrated that intussusception vasoepididymostomy was superior to conventional end-to-side vasoepididymostomy with respect to patency (92 vs 54%; P=0.004) and postoperative sperm granuloma rates (21 vs 58%; P=0.035). Marmar[7] and Chan et al[9,10] further decreased the number of sutures required and the modified techniques were especially applicable to less-distended epididymal tubules. Chan et al[9] showed that the longitudinal

two-suture technique produced patency outcomes similar to that of the triangulation technique. In terms of patency and sperm granuloma rates, in an animal study, the longitudinal two-suture technique produced better outcomes than triangulation and transverse two-suture techniques. In a retrospective review by Schiff et al,[11] among 153 consecutive vasoepididymostomies by Marc Goldstein, intussusception techniques produced better or comparable outcomes compared to conventional end-to-end and end-to-side techniques. The former techniques also entailed fewer sutures and hence simpler procedures, and lower late failure rates.

In our case series of 23 consecutive vasoepididymostomy procedures, the overall patency rate was 57%; there being no statistically significant difference in patency outcomes between patients having triangulation and the two-suture intussusception techniques. However, in future studies more patients need to be recruited to confirm that the two-suture intussusception technique produces patency outcomes equivalent to the triangulation technique. As experience in intussusception vasoepididymostomy accumulates, we were able to perform more bilateral procedures. The patency rate of unilateral and bilateral procedure was 50% and 64%, respectively. With an increase in the number of bilateral procedures, we hope that higher patency rates will be achieved in the future.

Despite careful selection of patients with normal testicular biopsy and obstructive azoospermia for scrotal exploration, six of 23 patients had absent epididymal sperm intra-operatively. For the benefit of doubt, vasoepididymostomy was nevertheless performed in these patients. The patency outcome in this group of patients was disappointing. In retrospect, we postulate that they might have had non-obstructive azoospermia to start with. If only patients positive for epididymal sperm were analysed, a patency rate of 71% was achieved. In the absence of epididymal sperm, it is logical to proceed to sperm retrieval. Some authorities have even advocated routine cryopreservation of epididymal sperm during vasoepididymostomy procedures, for potential use in future assisted reproduction. Further collaborative efforts with experts in reproductive medicine are needed to sort out the logistic problems involved in sperm retrieval and cryopreservation during scrotal exploration.

In our case series, the natural pregnancy rate achieved with vasoepididymostomy was relatively low compared to the pregnancy outcomes of IVF/ICSI in major assisted reproduction centres elsewhere. However, various studies had shown that microsurgical reconstruction was more cost-effective than sperm retrieval and IVF/ICSI,[1,2,20] particularly for couples who wanted to conceive more than one child. For patients with obstructive azoospermia, the direct costs and complications of sperm retrieval/IVF, coupled with the indirect costs of multiple pregnancies and the resulting health problems in such offspring,[1] highlight the cost-effectiveness of microsurgical reconstruction. For patients who had low sperm counts after vasoepididymostomy, assisted reproduction could be performed with fresh ejaculated semen, avoiding the additional costs and morbidity of sperm retrieval. However, IVF/ICSI may be more appropriate for couples with additional female factors, such as tubal disease or advanced maternal age. The final choice between microsurgical reconstruction and sperm retrieval/ICSI should be individualised for each couple after thorough counselling.

Further studies are needed to identify patients with normal testicular biopsy but absent epididymal sperm on scrotal exploration. Cryopreservation of epididymal sperm during vasoepididymostomy should be considered for potential assisted reproduction in the future. Longer follow-up is required to ascertain long-term patency, pregnancy outcomes, and late failures.

Conclusions

Microsurgical vasoepididymostomy is a technically challenging procedure. With the introduction of intussusception techniques, the procedure has been simplified and become a viable option for patients with obstructive azoospermia due to epididymal obstruction. Reasonable patency outcomes were achieved in the present series of cases. For couples with male factor infertility due to obstructive azoospermia, careful counselling and individualised decisions on microsurgical reconstruction versus assisted reproduction are necessary.

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