Surgical Management of Male Infertility

Sandro C Esteves, Alaa Hamada, Ashok Agarwal

INTRODUCTION

Infertility is a common problem in the urologic practice. Approximately, 8% of men in reproductive age may ask for medical consultation for fertility problems. Of these, 1–10% carries conditions that compromise the reproductive potential.1 The essential roles of the urologist in this context are to diagnose, to counsel, to provide medical or surgical treatment whenever possible or to correctly refer the male patient for assisted conception. The urologist can also be part of the multiprofessional reproductive team in the assisted reproduction unit, being responsible for the above-cited tasks as well as for surgical sperm retrieval.

Surgical management can be offered to more than 50% of our patient population in daily practice. In a group of 2,875 infertile couples attending one of the authors (Sandro C Esteves) tertiary center for male reproduction, potentially surgical correctable conditions were identified in 34.4% of the male partners. Azoospermia is identified in about one-third of the individuals. Despite the feasibility of reconstructive surgery in only about 30% of the azoospermic subgroup, most of the remaining would be candidates for sperm retrieval techniques, if enrolled in assisted reproduction programs. These figures are clearly shown in Table 1.

Two major advances have recently occurred in the surgical management of male infertility. The first was the implementation of microsurgery which increased success rates for reconstruction of the reproductive tract. The second was the development of intracytoplasmic sperm injection (ICSI) and the demonstration that spermatozoa retrieved from either the epididymis or the testis were capable of fertilization and pregnancy.2,3 Thereafter, several sperm retrieval methods have been developed to collect epididymal and testicular sperm for ICSI in azoospermic men. Microsurgery was incorporated to this armamentarium, either for collection of sperm from the epididymis in men with obstructive azoospermia or from the testicle in those with nonobstructive azoospermia (NOA).2,4

Surgeries for male infertility can be classified into three major categories:
1. Surgeries to improve sperm production
2. Reconstructive surgeries to correct the sperm transport pathways
3. Surgeries to retrieve spermatozoa from the gonads to be used in assisted conception.
This chapter describes the most common surgical options in the management of male infertility. It includes not only the reconstructive interventions for the male reproductive system but also the sperm retrieval techniques to be used in cases of obstructive azoospermia (OA) and NOA.

**SURGICAL TREATMENT TO IMPROVE SPERM PRODUCTION**

**Varicocele Repair**

Varicocele is believed to be the cause or a contributing factor of male infertility/subfertility in up to 35% of the cases. Several hypotheses try to explain the mechanisms underlying the negative impact of varicocele on male fertility. Proposed mechanisms include hypoxia and stasis, testicular venous hypertension, elevated testicular temperature, increase in spermatic vein catecholamine leading to testicular underperfusion and increased oxidative stress. Nevertheless, none of them fully elucidates the unpredictable effect of varicocele on human spermatogenesis and male fertility. The association between varicocele and infertility is still a matter of debate. However, there is an unquestionable increased incidence of this condition among infertile men. Moreover, an association of varicocele with reduced semen parameters and testicular size exists, and improvement in semen quality and pregnancy rates after varicocelectomy constitute strong evidence for a cause-effect relationship. Despite these facts, it is still unclear why most men with varicocele retain fertility and why fertility status is not always improved after treatment.

**Preoperative Planning**

**Assessment and Patient Selection**

The aim of varicocelectomy in infertile men is to restore or improve testicular function. Current recommendations suggest that treatment should be offered for couples with documented infertility whose male partner has a clinically palpable varicocele and abnormal semen analysis. The diagnosis of such condition is mainly clinical. Therefore, a detailed medical history must be taken and prognostic factors identified. Physical examination, with the patient standing in a warm room, is the preferred diagnostic method. Varicoceles diagnosed by physical examination are termed ‘clinical’ and may be graded according to the size. Large varicoceles (grade III) are varicose veins seen through the scrotal skin. Moderate (grade II) and small-sized varicoceles (grade I) are dilated veins palpable without and with the aid of the Valsalva maneuver, respectively. In the presence of bilateral palpable varicocele, it is recommended to perform surgery on both sides at the same operative time. However, physical examination may be inconclusive or equivocal in cases of low grade varicocele and, in men with a history of previous scrotal surgery, concomitant hydrocele or obesity. Therefore, imaging studies may be recommended when assessing infertile men for varicocele when physical examination is inconclusive. When a varicocele is not palpable but a retrograde blood flow is detected by other diagnostic methods, such as venography, Doppler examination, ultrasonography, scintigraphy or thermography, the varicocele is termed subclinical. The role of subclinical varicocele as a cause of male infertility remains debatable, and current evidence does not recommend surgical intervention for treating infertile men with subclinical varicocele. It is our routine, however, to examine the contralateral cord with a pencil-probe Doppler (9 MHz) stethoscope to determine if a subclinical varicocele exists when a clinically palpable varicocele is only identified at one side. In such cases, the subclinical varicocele is treated at the same time as the coexistent clinical varicocele. Preoperative workup should include hormone profile testing particularly, follicle-stimulating hormone (FSH) and testosterone level. Testicular volume should be assessed using a measurement instrument such as the
Section 2  Male Factor Infertility

Prader orchidometer or a pachometer. At least two semen analyses must be obtained and evaluated according to the World Health Organization guidelines.22

Infertile men either with higher preoperative semen parameters or undergoing varicocele repair for large varicoceles are more likely to show postoperative semen parameters improvement.23 On the other hand, reduced preoperative testicular volume, elevated serum FSH levels, diminished testosterone concentrations and subclinical varicocele are negative predictors for fertility improvement after surgery.9,24-29

Men with clinical varicoceles presenting with azoospermia may be candidates for surgical repair. In such cases, genetic evaluation including Giemsa karyotyping and polymerase chain Yq microdeletion screening for AZFa, AZFb and AZFc regions are recommended. A testis biopsy (open or percutaneous) may be obtained to assess testicular histology, which has been shown to be the only valid prognostic factor for restoration of spermatogenesis.30,31 The benefit of varicocelectomy in azoospermic men with genetic abnormalities is doubtful and should be carefully balanced. The same caution is valid for patients with atrophic testes and/or history of cryptorchidism, testicular trauma, orchitis, systemic or hormonal dysfunction due to the fact that varicocele in such cases may not be the cause of infertility but merely coincidental.32

As for all restorative surgical procedures in male infertility, the evaluation of the female partner’s reproductive potential is recommended before an intervention is indicated, and the alternatives to varicocele repair discussed.

Operative Procedure

Overview

The aim of surgical treatment of varicocele in infertile men is to achieve the highest improvement in the male fertility status with lower complication rates. Increase in the likelihood of spontaneous pregnancy after treatment is difficult to ascertain due to a variety of factors that includes the lack of a uniform post-treatment follow-up interval and the female factor parameters such as age and reproductive health. The ultimate treatment goal is to improve the male fertility status regardless of the method to be used for conception (unassisted or assisted). The ideal surgical technique should aim for ligation of all internal and external spermatic and cremasteric veins, with preservation of spermatic arteries and lymphatics.

Anesthesia

Anesthesia for varicocelectomy may be carried out using local, regional or general type, according solely with the surgeon and patient’s preferences. The authors routinely perform microsurgical subinguinal varicocele repair using short-acting propofol intravenous anesthesia associated with the blockage of the spermatic cord using 10 ml of a 2% lidocaine hydrochloride in an outpatient basis.30

Techniques

Varicoceles are surgically treated either by open (with or without magnification) or laparoscopic approaches. The principle of the surgery is the occlusion of the dilated veins of the pampiniform plexus. The high retroperitoneal and laparoscopic approaches are performed for internal spermatic vein ligation, while the inguinal and subinguinal approaches allow the ligation of the internal and external spermatic and cremasteric veins that may contribute to the varicocele.

Retroperitoneal technique: High open retroperitoneal varicocele ligation involves incision medial to the anterior superior iliac spine at the level of the internal inguinal ring (Figure 1). The external oblique muscle is split, the internal oblique muscle is retracted and the peritoneum is teased away. Exposure of the internal spermatic artery and vein is carried out retroperitoneally near the ureter. At this level, only one or two internal spermatic veins are present, but the internal spermatic artery may not be easy to identify. The veins are ligated near to the point of drainage into the left renal vein. Neither the parallel inguinal and retroperitoneal collateral veins that may exit the testis and bypass the retroperitoneal area of ligation nor the cremasteric veins can be identified in the retroperitoneal approach. It is believed that these collaterals cause the high recurrence rate seen in high retroperitoneal varicocelectomy. The surgical approach on the right side may be more difficult because the right gonadal vein drains into the inferior vena cava. Laparoscopic varicocelectomy is a retroperitoneal approach using high magnification. The spermatic artery and the lymphatics are easily identified and spared; collateral veins can also be clipped or coagulated. However, external spermatic veins, the second cause of varicocele recurrence, cannot be treated, leading to a recurrence rate of approximately 5%.33 Laparoscopy varicocele repair is more invasive, costly and associated with higher complication rates than open procedures.33-35

Inguinal and subinguinal technique: The classic approach to the inguinal varicocelectomy involves a 5–10 cm incision over the inguinal canal, opening of the external oblique aponeurosis and isolation of the spermatic cord (Figure 1). The internal spermatic veins are dissected and ligated. An attempt is made to positively identify and
Chapter 6  Surgical Management of Male Infertility

spare the testicular artery and the lymphatics. External spermatic veins running parallel to the spermatic cord or perforating the floor of the inguinal canal can be identified and ligated. Although internal and external spermatic veins can be identified macroscopically, the use of magnification facilitates identification and preservation of internal spermatic artery and lymphatics, which may prevent testicular atrophy and hydrocele formation respectively.36

The urologist who opts to treat varicocele using microsurgery should obtain appropriate training. It is also important to have adequate microsurgical instruments and a binocular operating microscope with foot-control zoom magnification. Loupe magnification is insufficient for identification of testicular arteries and lymphatics. Microsurgical varicocelectomy, either using inguinal or subinguinal approaches, requires more skill as compared to other surgical modalities because a higher number of internal spermatic vein channels and smaller diameter artery are seen at the level of the inguinal canal. However, the routine use of microsurgery during varicocele repair may help the urologist to master his/her microsurgical skills, which will be of great benefit when performing more demanding reconstructive procedures.

Microsurgical varicocelectomy can be performed via an inguinal or subinguinal approach. The main advantage of the subinguinal over the inguinal approach is that the former obviates the need to open the aponeurosis of the external oblique, which usually results in more postoperative pain and a longer time before the patient can return to work. The authors treat varicocele with a testicular artery and lymphatic-sparing subinguinal microsurgical repair12,30 (Figures 2A to D). Briefly, a 2.5 cm skin incision is made over the external inguinal ring. The subcutaneous tissue is separated until the spermatic cord is exposed. The cord is elevated with a Babcock clamp and the posterior cremasteric veins are ligated and transected. A Penrose drain is placed behind the cord without tension. The cremasteric fascia is then opened to expose the cord structures and the dissection proceeds using the operating microscope with magnification ranging from 6X to 16X. Dilated cremasteric veins within the fascia are ligated and transected. Lymphatics and arteries are visually identified and preserved. Whenever needed, the cord structures are sprayed with papaverine hydrochloride to increase the arterial beat. All dilated veins of the spermatic cord are identified, tagged with vessel loops, then ligated using nonabsorbable sutures and transected. Vasal veins are ligated only if they exceed 2 mm in diameter. Sclerosis of small veins is not used.

Postoperative Care

Postoperative care includes local dressing and scrotal supporter for 48–72 hours and 1 week respectively. Scrotal ice packing is always recommended to control local edema for the first 48 hours postoperatively. Patients are counseled to restrain from physical activity and sexual intercourse for 2–3 weeks. Oral analgesics usually suffice to control postoperative pain.

Postoperative follow-up aims to evaluate improvement in semen parameters, complications and spontaneous or assisted conception. Semen analysis should be performed every 3 months until the semen parameters stabilize or pregnancy occurs.

In a recent systematic review comparing different surgical modalities to treat varicocele for male infertility,33 it was concluded that open microsurgical inguinal or subinguinal varicocelectomy techniques resulted in higher spontaneous pregnancy rates and fewer recurrences, and postoperative complications than laparoscopic, radiologic embolization and macroscopic inguinal or retroperitoneal varicocelectomy techniques. Postoperative complications vary with surgical techniques. Hydrocele formation is the most common complication of varicocelectomy, with the incidence ranging from 0% to 10% (Table 2). The lowest and highest reported hydrocele formation rates are seen in the microsurgical and in the high retroperitoneal series.

Figure 1 Schematic illustration of the incision sites commonly used for retroperitoneal, inguinal and subinguinal varicocele repair (from top to bottom)
Section 2  Male Factor Infertility

respectively. Recurrences are reported in the range of 0–35%, varying with varicocelectomy techniques. Overall recurrence rates are low for microsurgical varicocelectomy and high for retroperitoneal and macrosurgical inguinal approaches. Accidental testicular artery ligation during microsurgical varicocelectomy has been reported to be about 1%, and it may cause testicular atrophy. It has been recently demonstrated that the concomitant use of intraoperative vascular Doppler during microsurgical varicocelectomy allows more arterial branches to be preserved, and more internal spermatic veins are likely to be ligated.

Varicocelectomy studies report significant improvements in one or more semen parameters in approximately 65% of men. The meantime for semen improvement and spontaneous pregnancy after surgery is approximately 5 months and 7 months respectively. Overall, sperm concentration, motility and morphology are increased by 9.7 million/ml, 10% and 3% respectively after varicocelectomy. Sperm DNA integrity is also increased after varicocele repair. Spontaneous pregnancy rates are higher in men with treated varicoceles (33–36%) as compared to untreated varicoceles (15–20%). Our group has recently demonstrated that treatment of clinical varicoceles may improve the outcomes of ICSI in couples with varicocele-related infertility. In our study, the chances of live birth were significantly increased by 1.9-fold while the chance of miscarriage were reduced by 2.3-fold, if the varicocele had been treated before assisted conception. However, it is still unknown why fertility potential is not always improved after varicocelectomy. Studies evaluating predictors for successful varicocele repair indicate that infertile men either with higher preoperative semen parameters or undergoing varicocele repair for large varicoceles are more likely to show postoperative semen parameters improvement. It was also shown that men who achieved a postoperative total motile sperm count greater than 20 millions and decreased sperm DNA fragmentation after surgical varicocelectomy were more likely to initiate a pregnancy either spontaneously or via assisted conception. The individual response after varicocele repair may be related to the different profile of antioxidant enzymes genes genotype in infertile men with varicocele. It has been suggested that genetic polymorphisms in the glutathione S-transferase T1 gene may affect individual response to varicocelectomy. Conversely, reduced preoperative testicular volume, elevated serum FSH levels, diminished testosterone concentrations, subclinical varicocele, as well as the presence of Y
A choice between the two must be based not only on the needs and preferences of the individual couple but also on the couple’s clinical profile taking into account the cause of azoospermia and any coexisting factors in the female partner. Consequently, both partners should be evaluated thoroughly before making a specific treatment recommendation. Cost issues also play a role in the decision-making process since assisted reproductive technology (ART) is seldom reimbursed by health insurance companies in most countries. Most importantly, infertility clinics and doctors should not limit couple’s options for treatment based on their own technical limitations, but always provide all treatment options available for that particular case scenario.

**Vasovasostomy and vasoepididymostomy** are surgical procedures designed to bypass an obstruction in the male genital tract. While the vast majority of vasovasostomy and vasoepididymostomy procedures are to reverse intentional obstructions, other indications include correction of epididymal or vasal obstructions due to genital infections, iatrogenic injuries related to inguinal or scrotal surgery, especially during the early childhood years, and postvasectomy pain syndrome. Currently, several programs offer microsurgical training for urology residents. Short-term microsurgery courses are of limited value; however, they can help urologists acquire the initial skills needed to use microsurgery in a routine basis. It is important to emphasize that microsurgical procedures for male infertility may be very demanding; therefore, one should only embark on performing either vasovasostomies or vasoepididymostomies after mastering microsurgical skills in the microsurgery laboratory using animals or synthetic models. Among several predictors for a successful microsurgical reconstruction of the male reproductive system, surgeon’s skills are the most relevant for treatment outcomes. Surgeon’s skills are crucial when vasoepididymostomies are needed, which frequently cannot be anticipated. Therefore, mastering both vasovasostomy and vasoepididymostomy techniques allows for real-time decision making without compromising clinical results.

### Table 2

<table>
<thead>
<tr>
<th>Technique</th>
<th>Recurrence rate</th>
<th>Hydrocele formation rate</th>
<th>Spontaneous pregnancy rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retroperitoneal high-ligation</td>
<td>7-35%</td>
<td>6-10%</td>
<td>25-55%</td>
</tr>
<tr>
<td>Laparoscopic</td>
<td>2.7%</td>
<td>0-9%</td>
<td>14-42%</td>
</tr>
<tr>
<td>Macroscopic inguinal</td>
<td>0-37%</td>
<td>7%</td>
<td>34-39%</td>
</tr>
<tr>
<td>Microscopic inguinal or subinguinal</td>
<td>0-0.3%</td>
<td>0-1.6%</td>
<td>33-56%</td>
</tr>
</tbody>
</table>

*Note: Values are expressed as range*
**Section 2  Male Factor Infertility**

**Preoperative Planning**

**Patient Assessment**

Some historical and prognostic factors must be taken in consideration in preoperative workup. Obstruction intervals from vasectomy to reversal are believed to play a major role in determining surgery outcomes. Obstruction intervals longer than 15 years are associated with lower patency and pregnancy rates. Long-interval obstructions are associated with higher incidence of epididymal obstruction and as a result, vasoepididymostomy is likely to be required. A computer model based on obstructive interval and patient age was created to determine the need for vasoepididymostomy. The model was designed to be 100% sensitive in detecting patients requiring vasoepididymostomy. In the test group, the model was 100% sensitive in predicting vasoepididymostomy with a specificity of 58.8%.

A history of a previous vasectomy reversal attempt does not preclude a new one. Satisfactory results are reported for repeated reversals, and the history of conception with the current partner seems to be the only significant predictor for a successful pregnancy. History of genital/inguinal surgery should raise the concern about the possibility of iatrogenic inadvertent surgical obstruction. Repair of obstruction in the inguinal canal or retroperitoneum can be technically challenging.

There are important physical signs that can also predict the success of vasovasostomy. Small and soft testes may indicate impaired spermatogenesis. Indurate, irregular epididymis and the presence of hydrocele are often associated with epididymal obstruction and may suggest the need for vasoepididymostomy. Palpation of a granuloma in the vas deferens should be interpreted as a favorable prognostic sign. Its presence means that sperm has leaked at the vasectomy site preventing from overpressure within the epididymis tubules and rupture. If a vasal gap is detected, the patient should be advised that a larger incision into the inguinal region may be needed in order to allow a tension-free anastomosis to be performed. Specific laboratory tests are not necessary before reconstructive surgeries. Serum FSH testing is indicated as a marker of testicular reserve only if testicular damage is suspected on physical examination. The usefulness of antibody testing remains controversial and evidence suggests that late failures following reversals are likely to be technical rather than immunological. Besides, overall conception rates are acceptably high and the presence of antisperm antibodies does not correlate closely with postsurgical fecundability.

The female partner fertility has to be carefully assessed before indicating reconstruction procedures and alternatives to vasectomy reversal should be discussed. It has been shown that reversal outcomes in men with the same partners are significantly better than those with new partners. The proven fecundity as a couple, shorter obstructive interval and stronger emotional dedication to achieving conception may act as possible factors for the higher success rate. Female age greater than 40 years is a negative predictor for pregnancy achievement.

**Operative Procedure**

**Overview**

There are several techniques described to perform restoration of the vas integrity. The standard method involves suturing of the vasal segments or the vas to the epididymis tubule. The operating microscope and adequate microsurgical instruments are crucial to facilitate reconstruction. It is not advisable to perform varicocele repair at the same time of vasectomy reversal. In vasectomized men, varicose veins are often compromised which would jeopardize venous return after ligation of internal and external spermatic veins. If necessary, varicocelectomy may be performed 6 months later, when new venous and arterial channels are formed around the anastomosis. Although reconstructive surgery can be performed after percutaneous epididymal sperm aspiration (PESA), the likelihoods for sperm appearance in the semen and pregnancy are decreased.

**Anesthesia**

Vasovasostomy and vasoepididymostomy may be safely performed using local, regional or general anesthesia. The authors carry out procedures in an outpatient basis. Continuous propofol intravenous anesthesia coupled with the blockage of the spermatic cord using 10–20 ml of a 1% lidocaine hydrochloride solution is our preferred anesthetic method.

**Incision**

Two centimeters longitudinal scrotal incisions are placed in the anterior aspect of the scrotum on each side. The incision is made onto the palpable granuloma or onto the identified vasal gap. Only the vas ends are delivered through the skin incision. The incision may be extended to the inguinal region when the vasectomy was performed high in the scrotum or a large segment was removed or in repeat reconstructions with difficult vasal mobilization. The testis is delivered only if a vasoepididymostomy or a robotic-assisted anastomosis is to be performed.
**Approaching the Vas**

Microsurgical dissection is carried out onto the region of the prior vasectomy site to free the vas and its vascular pedicle from surrounding scar tissue. Hemostasis is obtained with great care using either bipolar or hand-held thermal cautery units. After the vas has been mobilized and its scarred ends excised, patency of the abdominal vas end is confirmed with the introduction of a 24-gauge blunt tipped angiocatheter into the lumen and the injection of 20 ml sterile saline through the catheter. The ends of the vas must be adequately mobilized in order to allow a complete tension-free anastomosis. Either a microsurgical clamp or holding sutures can be used according to the surgeon’s preference.

**Vasal Fluid Examination**

Intraoperative factors affecting the success rates of reconstructive procedures include the gross appearance of vas fluid, the presence and quality of sperm in the fluid, the length of the remaining segment adjacent to the epididymis. Fluid emanating from the testicular vas end is examined both macroscopically and under the optical microscope for the presence of sperm. The presence of copious, clear, watery or cloudy fluid and motile sperm is associated with excellent patency rates of 94%, opposed to only 60% when no sperm is found in the vasal fluid. Thick toothpaste-like vasal fluid is suggestive of epididymal obstruction. The quality of sperm found in the intravasal fluid and the surgeon’s microsurgical skills are the most important factors to determine the type of reconstructive technique. Typically, the presence of sperm or sperm parts, and even a ‘dry’ vas, are associated with adequate patency rates of about 70–80% following vasovasostomies.

**Vasovasostomy Techniques**

In general, there are four fundamental surgical principles of vasal restorative surgery. These include the accurate mucosa-to-mucosa approximation, a water-tight tension-free anastomosis, preservation of the vasal blood supply and healthy tissue (mucosa and muscularis) and an adequate microscopic atraumatic technique.

**Modified One-Layer Technique**

The modified one-layer technique was originally described by Sharlip. The anastomosis is completed by placing a total of 12 sutures. Of these, six are through the full thickness of the vas wall at 60° intervals and six are placed in the muscularis only, between the full thickness sutures. The operation is performed entirely with the surgeon located on the patient’s right side. One of the authors (Sandro C Esteves) has made some modifications to the modified one-layer technique as described above (Figure 3A). Briefly, the first suture is placed in the medial surface of the right vas (0° position). This suture is placed through the full thickness of the vas wall on the testicular side first taking a generous bite of adventitia and muscularis and a tiny portion of the mucosa. The suture is then passed into the corresponding 0° position of the abdominal side again taking a bite at the edge of the mucosa and a large portion of the muscularis/adventitia layer. This suture is tied and cut long so it is easily identified as the procedure continues. The second suture is placed 180° opposite to the first, again taking the full aspect of the vas wall, firstly on the testicular side and then on the abdominal one. This suture is also tied and cut long. A third full thickness suture is placed at the 60° position, one-third of the distance from the first to the second sutures. Before it is tied, a fourth suture is placed at the 120° position, two-thirds of the distance from the first to the second sutures. Third and fourth sutures are then tied after careful inspection of their proper placement. A fifth suture is placed between these two at the 90° position, but only superficially through the muscularis. This completes the anastomosis of the anterior portion of the vas. At this point, four full thickness stitches and one muscular suture have been placed and half of the total circumference of the vas wall is closed. The vas clamp is then rotated 180° and verification of accidental back-walling and proper position of full thickness sutures is checked. After rotation of the vas, two full thickness sutures are then placed at 240° and 300° positions. These sutures are inserted and inspected before being tied. A final suture is placed in the muscularis at 270° position. These complete the anastomosis, summing up eight sutures in total instead of twelve as first described by Sharlip. Upon anastomosis completion, the surrounding loose fibrous tissue is sutured over the anastomotic site alleviating tension. Scrotal incision is closed in the routine usual manner.

**Two-Layer Technique**

This technique, described by Belker, involves placing five to eight interrupted 10-0 nylon sutures in the inner mucosal layer and eight to ten 9-0 nylon sutures in the outer muscular and adventitial layer. The use of an approximating clamp and a holding suture are recommended to stabilize vas ends for the anastomosis. Before the suturing begins, the surgeon looks straight down into the lumen of each end of the vas situated parallel to each other. As suturing proceeds, the transected ends of the vas bend toward each other, bringing the suture together without tension. Firstly, three posterior muscular layer sutures are placed in a row so that the knots are outside. Only 90° of the circumference are approximated, leaving full access to the mucosa.
Then, after three posterior mucosal sutures have been placed and tied, the far-corner and near-corner sutures are placed and tied alternately until space remains for only two or three sutures in the anterior aspect of the anastomosis. These remaining stitches are then placed and left long and untied until back-walling can be safely ruled out. The sutures are finally tied and the closing muscular layer is sutured with caution to visualize the underlying mucosal layer sutures to prevent penetration of the lumen by the outer-layer ones. Placement of these sutures is easier to perform from the assistant side toward the surgeon’s side. Closure of scrotal incision is performed in the usual manner.

**Multilayer Microdot Technique**

This method, originally described by Goldstein, is adequate to treat markedly discrepant diameters in straight or convoluted vas. Vasal ends are prepared with a 90° right angle cut and methylene blue stain can be used to better visualize the mucosal rings. Planned needle exit points can be marked with microtip marking (Figure 3B). Polypropylene monofilament 10-0 double-armed sutures with 70 µm diameter taper-pointed needles are used for the anastomosis. Sutures are placed in an inside-out fashion eliminating the possibility for accidental back-walling. The mucosa and about one-third thickness of the muscularis should be included in each bite, symmetrically on each side of vas ends. Four initial sutures are placed in the anterior aspect of the vas and tied up (Figure 3B). Three 9-0 sutures are then placed exactly in between the previously placed mucosal sutures, just above but not through the mucosa, sealing the gap between the mucosal sutures. The vas is then rotated 180° and four additional 10-0 sutures are placed completing the mucosal part of the anastomosis. Just prior to tying the last mucosal knot, vas lumen is irrigated with heparinized saline solution to prevent formation of clots. After completion of mucosal layer, 9-0 sutures are placed between each mucosal suture again, avoiding penetrating the mucosa itself (Figure 3B). Sutures are placed but not tied until two or three more have been placed. Superficial additional adventitia 9-0 sutures should be placed only when necessary. Procedure is complete approximating vas sheath with four to six 6-0 sutures.

**Robotic-Assisted Technique**

Recent reports have shown the possibility to perform the classic above described techniques using robotic assistance. The robot can offer the benefits of enhanced imaging (up to 100X magnification) and control of physiologic tremor.}

**Vasoepididymostomy Techniques**

Vasoepididymostomy is a challenging surgical procedure that should only be attempted by experienced microsurgeons. Meticulous microsurgical technique and high magnification are required for a precise anastomosis of the vas (luminal diameter of 300–400 µm) to the epididymal tubule (150–250 µm).

The procedure starts with the placement of a longitudinal incision in the upper scrotum. The testis is delivered through the incision and the testis and epididymis are thoroughly inspected. The site of obstruction can be often grossly visible as an area where the epididymis transitions from a firm, wide caliber to a smaller, softer structure. The distal end of the vas deferens is mobilized in a similar fashion as that described for the vasovasostomy but often a longer length is required to perform an epididymal anastomosis. At this point, the microscope is brought into the operating field to perform the anastomosis. Currently, three variations of the technique have been used for precise approximation of the vas deferens lumen to a single epididymal tubule: end-to-end, end-to-side, and end-to-side intussusception techniques. Prior to the anastomosis, a dilated epididymal tubule must be identified immediately above the level of obstruction. The tubule must be opened and the fluid inspected for the presence of motile sperm. If no sperm is identified, a more proximal site of the epididymis will be required for the anastomosis. Intraoperative sperm harvesting and cryopreservation can be offered during vasoepididymostomy.

**End-to-End Technique**

First described by Silber, the end-to-end vasoepididymostomy is the most difficult anastomosis to
Surgical Management of Male Infertility

73 Perform. It involves dissection of a single epididymal tubule, complete transection and anastomosis to the vas lumen. The epididymis is dissected off the testis for 3–5 cm to provide an adequate length to achieve a tension-free anastomosis. Initially, two 9-0 nylon sutures are placed at the 5 O’clock and 7 O’clock positions of the seromuscular surface of the vas, to secure the cut end of the distal vas to the epididymal tunica. Next, four double-armed 10-0 nylon sutures mounted in double-armed 70 µm fishhook-shape taper-pointed needle are placed in a quadrant fashion between the vas mucosa and the epididymal tubule (Figure 4A). These sutures are not tied until all have been positioned. The anastomosis is completed by placing several interrupted 9-0 nylon sutures to approximate the seromuscular layer of the vas to the epididymal tunic layer.

End-to-Side Technique

The end-to-side vasoepididymostomy, popularized by Thomas, is performed by creating a small window in a loop of the epididymal tubule proximal to the obstruction and by suturing the end of the vas lumen to the open window. The advantages over the end-to-end anastomosis include less dissection and bleeding during the anastomosis because hemostasis can be secured before opening the tubule. Moreover, only one tubule is opened making the identification of the patent tubule more precise and easy. With the tubule opened and sperm presence confirmed, three or four double-armed 10-0 nylon sutures are placed in a quadrant fashion through the edge of the epididymal tubule (Figure 4B). The sutures are placed in the corresponding quadrant of the vasal mucosa and tied. The anastomosis is completed with additional 9-0 nylon sutures between the epididymal tunic and the seromuscular layer of the vas deferens. Finally, several 9-0 nylon sutures are used to anchor the vas deferens to the parietal layer of the tunica vaginalis. These final sutures are designed to prevent tension on the anastomosis and are placed well away from the vasoepididymostomy site.

Triangulation End-to-Side Vasoe epididymostomy

This technique was introduced by Berger with subsequent modifications by others. It is the simplest and fastest among the three techniques described in this chapter. The intention is to combine the precision of the conventional end-to-side anastomosis with a simplified microsuture placement. Rather than a direct approximation of the epididymal tubule to the vas, this method involves pulling the epididymal tubule into the vas lumen. An opening window is made in the epididymal tunic corresponding to the vas diameter. Two 9-0 sutures are used to secure the muscular layer of the vas to the epididymal tunic to avoid tension on the anastomosis site. Three double-armed 10-0 nylon sutures are placed equidistantly in a triangular configuration in the desired epididymal tubule (Figure 4C). Then, the epididymal tubule is carefully opened with microscissors or microknife between the positioned sutures. Once sperm is confirmed in the epididymal fluid, the needles are passed through the lumen of the vas in an inside-out fashion. The sutures are then tied, creating an invagination of the epididymal tubule into the vasal lumen (Figure 4C). Finally, additional 9-0 nylon sutures are placed to approximate the seromuscular layer of the vas to the epididymal tunic.

Recently, a modification of the triangulation end-to-side vasoe epididymostomy was described by Marmar. In this technique, a single epididymal tubule is exposed and two 10-0 nylon sutures mounted on double-armed 70 µm bicurve needles are placed on the field. A needle from each suture is mounted on a styrofoam block and positioned parallel to the other with sufficient room for passage of the tip of a microblade between them. A microneedle holder is used to grasp both needles simultaneously and move them from the block to the field while maintaining the parallel arrangement. The tips of both needles are passed through a selected tubule at once. The two sutures are retracted laterally and a tubulotomy is cut between them with a microknife. Then, all four needles from the epididymal sutures are individually placed into the mucosal lumen of the vas and out through the muscularis on the cut end. Needles
Section 2  Male Factor Infertility

are placed at the 8 O’clock and 10 O’clock positions on the left side and at the 2 O’clock and 4 O’clock positions on the right side. Sutures are tied allowing the epididymal tubule to invaginate into the vas lumen. The anastomosis is completed with three to four additional 9-0 nylon sutures through the muscularis of the vas and epididymal tunic.

Postoperative Follow-up and Results

Postoperative care involves local dressing and scrotal supporter that are kept for 48–72 hours and 2 weeks respectively. Scrotal ice-packing is always recommended to control local edema for the first 72 hours postoperatively. Patients are counseled to refrain from physical activity and sexual intercourse for 1 or 2 months in cases of vaso-vasostomy and vasoepididymostomy respectively. Oral analgesics usually suffice to control postoperative pain. Postoperative follow-up is aimed to evaluate improvement in semen parameters, complications and spontaneous or assisted conception. Semen analysis should be performed every 2 months after surgery until the semen parameters stabilize or pregnancy occurs.

Over the past two decades, treatment options for couples with reconstructible OA had a marked improvement. Despite the advances in ART, specifically sperm retrieval techniques for ICSI, microsurgical reconstruction of the vas remains a cost-effective, reliable and effective means of restoring fertility in most individuals with OA.82 Nevertheless, a comprehensive understanding of the factors that can affect outcomes, overall cost and the morbidity associated with each treatment modality, respective of the institution providing the treatment, is recommended.

Overall, patency/pregnancy rates following microsurgical vasovasostomy and vasoepididymostomy are 92%/55% and 78%/40% respectively.54,55,61,64,66,73,74,83 (Table 3). Microsurgical techniques are clearly superior compared to macrosurgical or loupe-assisted anastomoses.54,84 Most pregnancies occur within 24 months after surgery. Pregnancy rates are related to the time elapsed from vasectomy to reversal and female age. Although female partner’s age does not affect patency rates after vasectomy reversal (86–90% in female partners aged < 40 years old vs 83% in those older than 40 years), it does affect pregnancy rates (14% in women aged > 40 years vs 56% in those aged < 39 years).83 Pregnancy rates are also lower after longer duration of vasal obstruction. Approximately 30–40% of couples

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients (N)</th>
<th>Technique</th>
<th>Patency rate (%)</th>
<th>Pregnancy rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasovasostomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Belker et al.54</td>
<td>1,247</td>
<td>Modified One-layer</td>
<td>89</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Two-layer</td>
<td>86</td>
<td>51</td>
</tr>
<tr>
<td>Boorjian and Lipkin55</td>
<td>159</td>
<td>Two-layer</td>
<td>95</td>
<td>83</td>
</tr>
<tr>
<td>Chan and Goldstein61</td>
<td>1,048</td>
<td>Two-layer</td>
<td>99</td>
<td>54</td>
</tr>
<tr>
<td>Kolettis et al.66</td>
<td>34</td>
<td>Both</td>
<td>76</td>
<td>35</td>
</tr>
<tr>
<td>Vasoepididymostomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silber73</td>
<td>139</td>
<td>End-to-end</td>
<td>78</td>
<td>56</td>
</tr>
<tr>
<td>Thomas84</td>
<td>137</td>
<td>End-to-side</td>
<td>79</td>
<td>50</td>
</tr>
<tr>
<td>Berger75</td>
<td>12</td>
<td>Triangulation intussusception</td>
<td>92</td>
<td>NR</td>
</tr>
<tr>
<td>Marmar76</td>
<td>9</td>
<td>Modified intussusception</td>
<td>78</td>
<td>22</td>
</tr>
<tr>
<td>Chan et al.83</td>
<td>68</td>
<td>Triangulation intussusception</td>
<td>84</td>
<td>40</td>
</tr>
<tr>
<td>Schiff et al.84</td>
<td>153</td>
<td>End-to-end</td>
<td>73</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>End-to-side</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-suture intussusception</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-suture intussusception</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>NR: not reported</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
achieve pregnancy following surgical reconstructions performed in obstruction intervals greater than 15 years as compared to > 50% in shorter intervals.\textsuperscript{64,85} Vasectomy reversal has been shown to be feasible in patients, who failed PESA. Marmar et al. showed that PESA procedures cause limited trauma to the epididymis and up to 50% pregnancy rates may be obtained in vasectomy reversal after PESA; however, success is higher for couples whose female partners are 37 years old or less.\textsuperscript{86}

As patency and pregnancy rates yielded by the existing surgical procedures do not reach 100% and are technically demanding, efforts continue to be made in order to widen the options for reconstructive repair. Several modifications have been suggested and include intussusception vasoepididymostomy anastomotic techniques, the use of novel biomaterials/sealants, absorbable and nonabsorbable stents, and the use of robotics.\textsuperscript{64,71,83-90} In a prospective study, Chan et al. reported overall patency and pregnancy rates of 84% and 40% using the vasoepididymostomy intussusception technique.\textsuperscript{83} These findings were confirmed by Schiff et al., who reported patency and pregnancy rates of approximately 82% and 45% respectively, using simplified intussusception techniques.\textsuperscript{84} It is suggested that anastomoses are more water-tight by using intussusception techniques; therefore, granuloma formation is decreased. The rationale of using sealants around the anastomotic site is to decrease operative time and to simplify the procedure without compromising success rates. Fibrin sealant can stimulate the coagulation cascade producing a fibrin seal around the anastomosis. When mixed with thrombin and calcium, fibrinogen is converted to fibrin monomer which in turn is converted to a stable cross-linked fibrin polymer.\textsuperscript{88} Ho et al. achieved 85% patency rates and 23% pregnancy rates using three transmural 9-0 sutures and fibrin glue in a mean follow-up of 6.2 months.\textsuperscript{88} There are concerns, however, about the potential contact of the glue with the vas lumen, which may result in possible obstruction, and also about transmission of viral disease because fibrin glue is derived from pooled plasma.\textsuperscript{87} The use of nonabsorbable polymeric stent has been reported only in animal model. Preliminary results showed 100% patency rates in a follow-up of 39–47 weeks, and the total sperm count was significantly higher in the stented group.\textsuperscript{89} The use of robotics for microsurgical procedures is also a novel concept. The rationale to add this technology to the already existing armamentarium relies on the possibility of physiologic static tremor correction, visual magnification (up to 100X when using a digital microscopic camera) and ergonomics.\textsuperscript{90} Animal studies suggest that robotic assisted vasectomy reversal are easier to perform and yields better pregnancy rates than microsurgical reversal.\textsuperscript{91} In a preliminary experience in humans, Parekattil et al. reported shorter operative time and higher postoperative sperm count for robot-assisted vasectomy reversal as compared to the microsurgical technique.\textsuperscript{90} However, the advantages of the robot over an experienced microsurgeon are yet to be proven in larger series. A robotic system costs more than one million dollars and its annual maintenance surpasses one hundred thousand dollars. These cost issues will certainly represent a barrier to the widely adoption of robotics into microsurgical urologic practice.

**EJACULATORY DUCT**

Congenital obstructions may be caused either by utricular, Müllerian and Wolffian duct cysts or atresia/stenosis of the ejaculatory ducts. Acquired obstructions may be secondary to trauma or infectious/inflammatory etiologies. Traumatic damage to the ejaculatory ducts may occur after removal of seminal vesicle cysts, pull-through operations for imperforate anus and even ducts may occur after removal of seminal vesicle cysts, pull-through operations for imperforate anus and even prolonged catheterization or instrumentation. Genital or urinary infection and prostatic abscess may cause stenosis or complete obstruction of the ducts.\textsuperscript{92} Prostatic infection may also result in calculous formation and secondary obstruction, while tuberculosis produces genital devastation.

Ejaculatory duct obstruction (EDO) is a potential surgically correctable cause of male infertility.

**Preoperative Planning**

**Patient Evaluation**

Diagnostic criteria typically included history, physical examination, semen analyses and transrectal ultrasound evaluation. The clinical presentation may be highly variable and, in addition to a history of infertility. Complaints may include painful ejaculation, hemospermia, perineal and/or testicular pain, but patients may be completely asymptomatic. Typically, physical examination is normal. Occasionally, the seminal vesicles or a mass are palpable on rectal examination. Prostatic tenderness and/or epididymal enlargement may exist. Hormone profiles are usually normal.

Semen analyses may reveal oligozoospermia or azoospermia, decreased motility and decreased ejaculate volume. The presence of a low volume (< 1.5 ml) acidic (pH < 7.0) azoospermic ejaculate with absent fructose, palpable vas and epididymal thickening is virtually pathognomonic. However, the typical clinical picture may be complicated whether obstruction is unilateral, partial or functional.\textsuperscript{92} Postejaculate urinalyses are often performed to exclude retrograde ejaculation in patients with low-volume ejaculates.
Section 2  Male Factor Infertility

High-resolution transrectal ultrasound evaluation (TRUS) using a 5–7 MHz biplanar transducer is recommended in all cases of suspected EDO. The exact definition of obstruction on TRUS, however, is still a matter of debate due to marked variability in the size and shape of the vas deferens, seminal vesicles, and ejaculatory ducts in fertile and infertile men. Common ultrasound findings include dilation of the seminal vesicles (defined as a cross-sectional width of greater than 1.5 cm) or ejaculatory ducts (defined as an internal duct diameter of greater than 2.0 mm), calcifications or calculi in the region of the ejaculatory duct or verumontanum and midline or eccentrically located prostatic cysts.93–95 It has been suggested that adjunctive procedures, such as magnetic resonance imaging, chromotubation, seminal vesicle aspiration, seminal vesicle scintigraphy and ejaculatory duct manometry are more sensitive for diagnosis.96–100 Ultrasound-guided transrectal seminal vesiculography has been shown to provide excellent radiographic visualization of the ejaculatory ducts.96 TRUS-guided seminal vesicle aspiration and the presence of motile sperm in the aspirates seem to be a useful diagnostic tool, since the seminal vesicles are not sperm reservoirs.97 The proper management of azoospermic men with EDO involves the confirmation of sperm production. The presence of normal spermatogenesis can be determined by testicular biopsy or ‘wet prep’. The presence of motile sperm is highly indicative of ductal obstruction.

Operative Aspects

The standard treatment of EDO is the transurethral resection of the ejaculatory duct (TURED). Resection of the ejaculatory ducts is a technically demanding and critical procedure. The typical patient with EDO is young and has a small prostate. Therefore, TURED is carried out very close to the bladder neck, rectum and sphincter.

Anesthesia

Transurethral resection of the ejaculatory ducts is performed using regional or general anesthesia.

Technique

Our choice is to perform TURED, as originally described by Farley and Barnes,101 with minor modifications.92 First, the obstruction is documented using intraoperative vasotomy and vasography. The vas is delivered using a small scrotal incision and dissected free of the associated perivascular vessels. A mixture of injectable saline and radiographic contrast material in a 1:1 ratio is injected into the abdominal end of the vas, together with methylene blue dye, by direct vas puncture with a 30-gauge lymphangiogram needle. Vasography confirms obstruction, whereas dye injection confirms patency by visualization of the effluxing dye mixture during TURED. A 9-0 nylon suture is placed at the muscular layer of the vas to close the vasotomy site. TURED is performed with the patient in the dorsal lithotomy position. A resectoscope with 24-French loop is used to remove a strip of tissue on the floor of the prostate just proximal to and including a portion of the verumontanum (Figures 5A and B). The ducts are considered adequately opened by visualizing its dilated portion and the dye efflux. If a midline cyst is present, resection is performed to completely unroof the cyst. Resection is performed with pure cutting to avoid thermal injury to the proximal ejaculatory duct. The authors feel more comfortable placing a finger in the patient’s rectum to prevent rectal injury during resection and having methylene blue injected through the vasotomy site. Resection is completed by positive identification of free dye efflux into the urethra. An 18-French Foley catheter is left in place for 24 hours and the patient is discharged the next day.

Postoperative Follow-up and Results

An indwelling catheter is kept in place for 24–48 hours and patients are discharged the following day. Oral quinolone antibiotics and anti-inflammatory medication is prescribed for 5 days. Scrotal supporter is recommended for 1 week to avoid scrotal edema due to vasotomy. Frequent ejaculation is recommended 3–4 weeks postoperatively and patients are monitored with monthly semen analyses.

TURED results vary according to the etiology of obstruction being congenital or acquired.92 Semen quality improvement (ejaculate volume, sperm count and motility) and unassisted conception is observed in approximately 85% and 60% of individuals with congenital obstructions. Conversely, seminal improvement occurs in only about 30% of the individuals with infectious/inflammatory etiologies. Complications occur in approximately one-third of men treated by TURED and

Figures 5A and B  Transurethral resection of the ejaculatory duct. (A) Schematic representation of the ejaculatory duct entering into the prostatic urethra; (B) Resectoscope loop is used to remove a strip of tissue on the floor of the prostate just proximal to and including a portion of the verumontanum
mainly include reflux of urine to the unroofed cyst cavity with consequent impairment of the semen parameters, retrograde ejaculation and epididymitis with obstruction. Rectal injury or incontinence is rarely reported.

Modern and less invasive approaches using balloon dilation coupled or not with transurethral incision of the ejaculatory ducts have been proposed to treat EDO. Preliminary data show that such alternatives have similar results and fewer complications than TURED.102,103

**SPERM RETRIEVAL TECHNIQUES**

Azoospermia, defined as the absence of spermatozoa in the ejaculate after centrifugation, is found in 1–3% of the male population and approximately 10% of infertile males. In this scenario, two different clinical situations exist, i.e. obstructive (OA) and nonobstructive azoospermia (NOA). In OA, spermatogenesis is normal but a mechanical blockage exists in the genital tract, somewhere between the epididymis and the ejaculatory duct, or the epididymis and vas deferens are totally or partially absent. Acquired OA may be due to vasectomy, failure of vasectomy reversal, postinfectious diseases, surgical procedures in the scrotal, inguinal, pelvic or abdominal regions and trauma. Congenital cause of OA include cystic fibrosis, congenital absence of the vas deferens (CAVD), ejaculatory duct or prostatic cysts and Young’s syndrome. NOA comprises of a spectrum of testicular histopathology resulting from various causes that include environmental toxins, medications, cryptorchidism, genetic and congenital abnormalities, varicocele, trauma, viral orchitis, endocrine disorders and idiopathic. In both OA and NOA, pregnancy may be achieved through IVF associated to ICSI.

The goals of surgical sperm retrieval are threefold: (i) to retrieve an adequate number of sperm for both immediate use and for cryopreservation; (ii) to obtain the best quality sperm possible and (iii) to minimize damage to the reproductive tract so as not to jeopardize future attempts of sperm retrieval or testicular function. Several surgical methods have been developed to retrieve epididymal and testicular sperm from azoospermic men. Either percutaneous epididymal sperm aspiration (PESA) or microsurgical epididymal sperm aspiration (MESA) can be successfully used to retrieve sperm from the epididymis in men with OA. Testicular sperm aspiration (TESA) can be used to retrieve sperm from the testes either in men with OA, who fail PESA, or in those with NOA. Testicular sperm extraction (TESE) using single or multiple open biopsies and, more recently, TESE using microsurgery (micro-TESE) are indicated for men with NOA. Sperm can be easily obtained from infertile men with OA whereas individuals exhibiting NOA have historically been the most difficult to treat.

**PREOPERATIVE PLANNING**

**Patient Assessment**

It is important to distinguish whether the lack of sperm in the ejaculate is from an obstructive or nonobstructive process since the choice of the retrieval method is based on the type of azoospermia. History, physical examination and hormonal analysis (FSH, testosterone) are undertaken to define the type of azoospermia. Together, these factors provide a 90% prediction of its type (OA and NOA). Men with OA usually have normal testes and hormone profile. Occasionally, the epididymis or the seminal vesicles may be enlarged or a cyst can be palpable on rectal examination. The presence of a low volume (< 1.5 ml) acidic (pH < 7.0) azoospermic ejaculate with absent or low fructose and epididymal thickening is pathognomonic of OA due to either congenital bilateral absence of the vas deferens (CAVD) or EDO; the differential diagnosis would be the presence of the vas in the latter. Approximately two-thirds of men with CAVD have mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Failure to identify a CFTR abnormality in a man with CBAVD does not rule out the presence of a mutation, since some are undetectable by routine testing methods. In couples whose male partners have CBAVD, the female partner should be offered cystic fibrosis (CF) testing before proceeding with treatments that utilize their sperm because of the high risk of the male being a CF carrier. If a CFTR gene mutation is identified (approximately 4% of female partners are carriers), testing should be offered to the male as well, and counseling is recommended before proceeding with sperm retrieval and ICSI due to the risk of the transmission of CF to the offspring. Azoospermic men with idiopathic obstruction and men with a clinical triad of chronic sinusitis, bronchiectasis and OA (Young’s syndrome) may be at higher risk for CF gene mutations as well.

The serum FSH is a critical factor in determining whether a diagnostic testicular biopsy is needed to differentiate the type of azoospermia in men with normal semen volume. Elevated FSH and small testis are indicative of testicular failure (NOA); therefore, a testicular biopsy is not necessary for diagnostic purposes. However, if sperm retrieval with ICSI is being considered, a biopsy may be performed for prognostic purposes, to determine whether spermatozoa are likely to be retrievable by future
Section 2  Male Factor Infertility

testicular sperm aspiration or extraction. The absence of sperm in a biopsy specimen taken from a man with NOA, however, does not absolutely predict whether sperm are present elsewhere within the testicle. Conversely, men with normal levels of FSH and semen volume may have either NOA or OA. In such cases, there is no non-invasive method to differentiate OA from NOA and a testicular biopsy is usually required to provide a definitive diagnosis. Testicular biopsy can be performed by a standard open incision technique or by percutaneous methods. Histology evaluation of testicular specimens may indicate the presence of normal spermatogenesis in cases of OA while hypospermatogenesis or maturation arrest or SCO syndrome are seen in NOA ones.

All men with primary testicular failure of unknown origin should be offered karyotyping and Y-chromosome microdeletion testing. The frequency of karyotypic abnormalities is reported to be 10–15% in men with NOA, and Klinefelter’s syndrome accounts for approximately two-thirds of cases. Genetic testing may provide prognostic information for sperm retrieval. In contrast to partial and complete AZFc deletion patients, in whom sperm can be found within the testis, the chance of finding sperm in men with complete AZFa or AZFb deletions is unlikely. Genetic counseling should be offered whenever a genetic abnormality is detected in the male prior to performing ICSI with his sperm.

OPERATIVE PROCEDURE

Surgical sperm retrievals using open or percutaneous methods can be carried out in outpatient basis.

Anesthesia

Sperm retrieval techniques are safely performed using local, regional or general anesthesia. The authors perform percutaneous sperm retrievals under local anesthesia only or in association with intravenous bolus infusion of a short-acting hypnotic agent (propofol). In both cases, a 10–15 ml solution of 2% lidocaine hydrochloride is injected around the spermatic cord near the external inguinal ring. In cases where intravenous anesthesia is used, local injection of the anesthetic is performed after patient unconsciousness is achieved. The authors carry out microsurgical sperm retrievals under local anesthesia, as described above, in association with continuous infusion of propofol using a syringe-drive automated-pump device.

Techniques

Sperm retrieval from the epididymis is indicated in obstructive cases only. Testicular sperm retrieval can be performed either in OA and NOA cases. In OA, testicular retrievals are carried out after failed epididymal retrieval or as a primary retrieval procedure in cases of absent epididymis or intense epididymal fibrosis. In NOA, testicular sperm retrievals are the only viable option to collect sperm.

Percutaneous Sperm Retrieval

Typically, percutaneous sperm retrieval is performed using a needle attached to a syringe. The standard procedure is described below. Minor modifications to the methods have been added, but the main goals remain the same which are to aspirate either epididymal fluid or testicular parenchyma for diagnostic or therapeutic purposes. Loupe magnification may be used to avoid injuring small vessels seen through the scrotal skin.

Percutaneous epididymal sperm aspiration: The epididymis is stabilized between the index finger, thumb and forefinger while the testis is held with the palm of the hand. A 13-gauge needle attached to a 1 ml tuberculin syringe is inserted into the epididymis through the scrotal skin (Figure 6A). Negative pressure is created and the tip of the needle is gently moved in and out within the epididymis until fluid enters the syringe. The amount of epididymal fluid obtained during aspiration is often minimal (~0.1 ml), except in cases of CAVD in which 0.3–1.0 ml may be aspirated. The needle is withdrawn from the epididymis and the aspirate is flushed into a 0.5–1.0 ml 37°C sperm medium. The tube containing the epididymal aspirate is transferred to the laboratory for microscopic examination. PESA is repeated at a different site of the same epididymis (from cauda up to the caput) and/or at the contralateral one until adequate number of motile sperm is retrieved. If PESA fails to retrieve motile sperm for ICSI, TESA is performed at the same operative time.

The adoption of strict criteria to diagnose OA is crucial for obtaining high success retrieval rate using percutaneous techniques. Using PESA, our approach is to perform the first aspiration at the corpus epididymis then proceed up to the caput if necessary, since aspirates from the cauda are usually rich in poor quality senescent spermatozoa, debris and macrophages. Most cases of PESA failures are not necessarily technical failures because immotile spermatozoa are found. However, in certain cases of epididymal fibrosis due to multiple PESA attempts or postinfection, PESA may be ineffective to retrieve sperm.

Testicular sperm aspiration: The epididymis is stabilized between the index finger, thumb and forefinger while
the anterior scrotal skin is stretched. A 23-gauge needle attached to a 20 ml syringe is connected to a syringe holder and is inserted through the stretched scrotal skin into the anteromedial or anterolateral portion of the superior testicular pole in an oblique angle towards the medium and lower poles (Figure 6B). Negative pressure is created by pulling the syringe holder while the tip of the needle is moved in and out within the testis in an oblique plane to disrupt the seminiferous tubules and sample different areas. When a small piece of testicular tissue is aspirated, the needle is gently withdrawn from the testis while the negative pressure is maintained. A pair of microsurgery forceps is used to grab the seminiferous tubules that exteriorize from the scrotal skin, thus aiding in the removal of the specimen. The specimen is flushed into a tube containing 0.5–1.0 ml warm sperm medium and is transferred to the laboratory for microscopic examination. TESA or TESE may be performed at the contralateral testis if insufficient or no sperm are obtained.

Microsurgical Sperm Retrieval

The microsurgical approach allows direct visualization of epididymal and seminiferous tubules with high magnification. These techniques have been associated with retrieval of higher sperm numbers and of better quality in OA and higher retrieval success rates in NOA. Microsurgical epididymal sperm aspiration: A transverse 2 cm incision is made through the anesthetized layers, and the testis is exteriorized. The epididymis is examined and its tunica is incised. An enlarged tubule is dissected and opened with sharp microsurgical scissors. Fluid exuding from the tubule is aspirated with a silicone tube or blunted needle attached to a 1 ml tuberculin syringe (Figure 7). The aspirate is flushed into a 0.5–1.0 ml 37°C sperm medium. The tube containing the epididymal aspirate is transferred to the laboratory for microscopic examination. MESA is repeated at a different site of the same epididymis (from cauda up to the caput) and/or at the contralateral one until adequate number of motile sperm is retrieved. If MESA fails to retrieve motile sperm, testicular sperm retrieval may be performed at the same operative time.

Microsurgical testicular sperm extraction: First, the testis is delivered out of the scrotum. Then, a single, large, mid-portion incision is made in an avascular area of the tunica albuginea under 6–8X magnification, and the testicular parenchyma is widely exposed (Figure 7A). Dissection of the testicular parenchyma is carried out at 16–25X magnification searching for enlarged seminiferous tubules. The superficial and deep testicular regions may be examined, if needed, and microsurgical-guided testicular biopsies are performed by removing enlarged tubules which are more likely to harbor active spermatogenesis (Figures 7B to D). If enlarged tubules are not seen, then any tubule different than the remaining ones in size is excised. If all tubules are identical in appearance, random microbiopsies (at least three at each testicular pole) are performed. Testicular tissue specimens

---

Figures 6A and B Percutaneous sperm retrieval techniques. (A) Percutaneous epididymal sperm aspiration (PESA). Epididymis is stabilized between the index finger, thumb and forefinger. A needle attached to a tuberculin syringe is inserted into the epididymis through the scrotal skin, and fluid is aspirated; (B) Testicular sperm aspiration (TESA). A 20 ml needle-syringe connected to a holder is percutaneous inserted into the testis. Negative pressure is created and the tip of the needle is moved within the testis to disrupt the seminiferous tubules and sample different areas.
Figures 7A to D  Microsurgical sperm retrieval techniques. Operating microscope and microsurgical technique are used throughout the procedures. On top: Microsurgical epididymal sperm aspiration (MESA). After exposure of epididymis, a dilated epididymal tubule is dissected and opened. Fluid is aspirated, diluted with sperm medium and sent to the laboratory for examination. On bottom: Microsurgical testicular sperm extraction (micro-TESE). (A) After the testicle is exteriorized, a single and large incision is made in an avascular area of the albuginea to expose the seminiferous tubules. (B) Dilated tubules are identified and removed with microforceps (intraoperative photograph at 40X magnification). (C) Illustration of the histopathology cross-section of a dilated seminiferous tubule with active spermatogenesis. (D) Illustration of the histopathology cross-section of a thin tubule with Sertoli-cell-only syndrome.
are placed at an outer-well dish containing sperm media. Specimens are washed grossly to remove blood clots and are sent to the laboratory for processing and search for sperm. The albuginea and scrotal layers are closed using nonabsorbable and absorbable sutures respectively.

**Conventional Testicular Open-Biopsy Sperm Extraction**

Single or multiple open testicular biopsies may be taken to obtain sperm both in OA and NOA, but mainly in cases of NOA. TESE can be also used as a diagnostic tool to obtain testicular parenchyma for histology analysis and search of sperm previous to the ICSI cycle. A transverse 2 cm incision is made through the anesthetized skin, cremaster and parietal tunica vaginalis. Conventional TESE is carried out without magnification. A small self-retaining eyelid retractor is placed to improve exposure of the tunica albuginea, since the testis is not exteriorized. The tunica albuginea is incised for approximately 0.5–1 cm. Gentle pressure is made onto the testis to extrude testicular parenchyma out of the small incision. A fragment of approximately 5x5x5 mm is excised with sharp scissors and placed promptly in sperm culture media (Figure 8). The specimen is sent to the laboratory for processing and microscopic examination. The albuginea is closed using nonabsorbable sutures. TESE can be repeated in a different testicular pole, if the multiple biopsies approach is selected.

**POSTOPERATIVE CARE AND RESULTS**

Patients are discharged in the same day and can return to normal activities 1 day and 3 days after percutaneous and open techniques respectively. Scrotal ice packing and supporter is recommended to control edema and alleviate pain. Patients should refrain from ejaculation and strenuous physical activity for approximately 7–10 days. Oral analgesics are prescribed, but pain complaint is often minimal.

The best technique for sperm retrieval in men with OA and NOA is yet to be determined. To date, no randomized controlled trial has compared the efficiency of these strategies and thus current recommendations are based on cumulative evidence provided by descriptive, observational and controlled studies. Meta-analysis results demonstrated no significant difference in any outcome measure between the use of epididymal or testicular sperm in men with OA. The etiology of the obstruction and the use of fresh or frozen-thawed epididymal/testicular sperm do not seem to affect ICSI outcomes in terms of fertilization, pregnancy or miscarriage rates. In cases of NOA, the efficiency of TESA for retrieving spermatozoa is lower than TESE except in the favorable cases of men with previous successful TESA or testicular histopathology showing hypospermatogenesis. In these circumstances, sperm retrieval rates (SRR) may be as high as 100%. In a recent systematic review, the mean reported SRR for TESE was 49.5%. TESE with multiple biopsies resulted in higher SRR than fine-needle aspiration, a variation of TESA, especially in cases of SCO syndrome and maturation arrest. In NOA, current evidence suggests that micro-TESE performs better than conventional TESE or TESA in cases of SCO syndrome, where tubules containing active focus of spermatogenesis can be positively identified using microsurgery. Sperm retrieval rates ranging from 35% to 77% have been reported with micro-TESE. To allow for adequate healing and the resumption of spermatogenesis, the minimum recommended interval between sperm retrieval procedures in NOA is 3–6 months.
Postoperative complications of sperm retrieval techniques include persistent pain, swelling, infection, hydrocele and hematoma.\textsuperscript{121-127} The development of intratesticular hematoma has been observed in most patients undergoing TESE with single or multiple biopsies based on ultrasounds results performed after surgery, but they often resolve spontaneously without compromising testicular function.\textsuperscript{126} In the larger-volume standard testicular biopsy, the risk of transient or even permanent testicular damage (such as complete devascularization) can result in decreased serum testosterone levels.\textsuperscript{123,125} Less invasive techniques, such as TESA and micro-TESE, aim to reduce the incidence of complications and long-term consequences of these surgical approaches. Several studies have documented a lower incidence of complications following micro-TESE compared with the conventional technique.\textsuperscript{122,123,125,127} Using micro-TESE, proper identification of testicular vessels under the tunica albuginea is made prior to the placement of an incision into the testis. The use of optical magnification and microsurgery technique allows the preservation of intratesticular blood supply, as well as the identification of tubules more likely to harbor sperm production.\textsuperscript{124} Therefore, efficacy of sperm retrieval is improved while the risks of large tissue removal are minimized. The small amount of tissue extracted also facilitates sperm processing.\textsuperscript{124} In certain groups of patients, however, such as those with Klinefelter’s disease who already have diminished androgen production, a significant decrease on serum testosterone has been documented following micro-TESE.\textsuperscript{124} However, testosterone levels return to the presurgical values in most Klinefelter men in a 12-month follow-up period. It is recommended that sperm retrieval should be performed by surgeons who have training in the procedures, because of the potential serious postoperative complications.\textsuperscript{125}

The clinical outcomes of ICSI using testicular sperm extracted by TESA or micro-TESE in NOA are significantly lower than those obtained with either ejaculated or epididymal/testicular sperm from men with OA.\textsuperscript{118,128,129} Testicular spermatozoa of men with severely impaired spermatogenesis have decreased fertility potential and may have a higher tendency to carry deficiencies, such as the ones related to the centrioles and genetic material, which ultimately affect the capability of the male gamete to activate the egg and trigger the formation and development of a normal zygote and a viable embryo.\textsuperscript{130} From the limited data available, it is suggested that the sperm retrieval technique itself has no impact on ICSI success rates.\textsuperscript{122} However, frozen-thawed surgically-retrieved sperm from NOA men have significantly impaired reproductive potential than fresh ones.\textsuperscript{118,131} Meta-analysis results showed that fertilization rates by ICSI remained similar, but implantation was significantly higher (by 73\%) with the use of fresh testicular sperm compared to frozen-thawed testicular sperm.\textsuperscript{118}

The question of whether or not ICSI using sperm retrieved from men with either OA or NOA might be associated with increased risk for birth defects is still unresolved. IVF, in general, is associated with multiple gestation and an increased risk of congenital abnormalities (including hypospadias).\textsuperscript{132} ICSI in particular, carries an increased risk of endocrine abnormalities, as well as epigenetic imprinting effects.\textsuperscript{132} Although the absolute risk of any of these conditions remains low,\textsuperscript{132,133} current data is limited and study populations are heterogenic. It is, therefore, recommended that well-defined groups of ICSI with ejaculated sperm, ICSI with epididymal sperm and ICSI with testicular sperm, and a control group of naturally conceived children are closely followed up.

\section*{REFERENCES}

Chapter 6  Surgical Management of Male Infertility


Section 2 Male Factor Infertility


Section 2  Male Factor Infertility


