Infertility: Surgical Management

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Key Points

- Varicocele repair can be offered for the palpable symptomatic varicocele.
- Epididymal or testicular sperm have similar efficacy in assisted reproductive techniques (ART) in men with obstructive azoospermia.
- No apparent differences exist in either fertilization or pregnancy rates between fresh vs. cryopreserved/thawed sperm in both obstructive and non-obstructive azoospermia.
- Microscopic assisted testicular sperm extraction is associated with higher rates of successful sperm retrieval compared to conventional sperm extraction.

1. Introduction

Conditions leading to impaired male fertility potential can often be successfully treated with surgical intervention. Significant advances in operative techniques and assisted reproductive technology have resulted in important opportunities for urologists to advance the reproductive health of infertile couples.

The surgical management of male infertility can be organized into (i) **diagnostic procedures**, (ii) **procedures that optimize spermatogenesis**, (iii) **procedures that improve sperm delivery**, and (iv) **sperm retrieval procedures.**[1]

1.1 Key Words

azoospermia, epididymis, epididymovasostomy, MESA, micro-TESE, PESA, sperm, TESA, TESE, testicle, varicocele, varicocelectomy, vasovasostomy

2. Diagnostic Surgical Procedures

Per the **AUA/ASRM Guidelines on Treatment of Infertility in Men**, **a testicular biopsy should not routinely be performed to establish the cause of azoospermia** for patients who have clinical findings (abnormally high FSH, testicular atrophy) that suggest a diagnosis of non-obstructive azoospermia. [2] However, for **azoospermic** patients who have **normal testicular volume, at least one palpable vas deferens, a nondilated epididymis, and a normal serum FSH level, diagnostic**

testicular biopsy may be helpful.[3] It should be noted that failure to find sperm on a diagnostic biopsy can indicate non-obstructive azoospermia. However, failure to find sperm does not predict an unsuccessful retrieval procedure such as TESE or micro-TESE. Therefore, it is not necessary to perform a diagnostic biopsy before proceeding to a sperm retrieval procedure.[4]

2.1 Testicular Aspiration (Diagnostic)

Indications: In the rare cases where a diagnostic biopsy is indicated, it is important to remember that all testicular sperm retrieval procedures can serve therapeutic (i.e. obtain sperm for use with in vitro fertility (IVF)/intracytoplasmic sperm injection (ICSI) and diagnostic purposes. Testicular aspiration can help establish the diagnosis of obstructive versus nonobstructive azoospermia.

Procedure: With smaller gauge needles (such as, 22 or 23G), the procedure is generally referred to as an aspiration. When larger caliber needles are used, (16 or 18G), the procedure is sometimes referred to as a needle aspiration biopsy or cutting needle biopsy. Large gauge needles can often facilitate preservation of the testicular architecture. Some clinicians prefer use of a tissue-cutting biopsy needle (such as a prostate spring-loaded biopsy gun). In this case, a small skin incision is usually made to aid the needle passage. Several passes may be necessary to ensure aspiration of adequate sperm numbers.

Operative Considerations: Under local anesthesia, with or without conscious sedation, a needle is passed percutaneously into the testis. Suction is then applied, sometimes with the aid of a Cameco syringe pistol, and seminiferous tubule tissue is collected. More than one pass can be performed to increase sperm yield.

Outcomes: Generally, thousands to millions of sperm can be obtained in cases of obstructive azoospermia. Yields in cases of nonobstructive azoospermia range from zero to thousands of sperm.

Complications: While minimally invasive, the blind nature of needle passage can lead to hematocele or intratesticular hematoma formation as well as delayed development of hydroceles or spermatoceles.

2.2. Open Testicular Biopsy (Diagnostic)

Indications: To establish the diagnosis of obstructive versus nonobstructive azoospermia or to obtain sperm for use with assisted reproductive techniques (ART).

Operative Considerations: Under local anesthesia with or without sedation, while firmly grasping and fixing the testis, a 1-2 cm anterior scrotal incision is made. This incision is extended down through the Dartos and tunica vaginalis layers until the anterior aspect of the tunica albuginea of the testis is exposed. An eyelid retractor can aid in exposure. A stay suture can be placed in the tunica albuginea to fix exposure. A tunica albuginea incision is made using an 11 blade. Seminiferous tubules are extruded with application of gentle posterior testicular pressure. Fine forceps and microscissors may also be used to aid in testicular parenchyma extrusion and excision. Bipolar electrocautery is used to achieve hemostasis, and the incision is closed in layers using 4-0 or 5-0 absorbable suture.

Outcomes: The procedure can be done entirely as a diagnostic procedure with the specimen sent in preservative (e.g. Bouin's solution) to pathology. Alternatively, the sperm may be retrieved the day of or the day before the partner's egg retrieval for use in an ART cycle. In addition, testicular tissue may be cryopreserved for use in future ART cycles. The literature and AUA/ASRM Infertile Male Guidelines report similar ART outcomes for use of fresh and frozen testicular sperm and supports the use of either.[2]

Complications: As the procedure is performed under direct vision, bleeding complications and testicular injury are low (<1%).

3. Procedures That Optimize Sperm Production

At this time, surgical procedures that optimize sperm production are limited to those involving varicocele correction. **The AUA/ASRM Infertile Male Guideline has three separate guidelines on the management of varicoceles.**[2]

3.1 Varicoceles

3.1.1. Definition

Varicoceles are a common condition that result from an **abnormal dilation of the pampiniform plexus of veins** located within the spermatic cord.[5]

3.1.2. Risk Factors and Pathophysiology

Although the pathophysiology of varicoceles is well described, risk factors are less clear. **Congenital absence of valves in the spermatic veins** are thought to contribute to the development of varicoceles, but the exact role that this condition plays in varicocele formation is unclear. Additionally, the **acquired incompetence of venous valves via external venous compression** is another possible cause of varicoceles. Venous compression can result in increased intravascular pressure and dilation of the pampiniform plexus. **Pathological retroperitoneal processes**, such as large tumors, can thus be the root cause of an acquired varicocele. **Varicoceles are 3-8 times more likely among first degree relatives of men with a varicocele**, but the current data do not support additional screening of siblings and offspring.[6] In contrast, increasing body mass index (BMI) portends a decreased likelihood of varicoceles.[7] The reason for this is unknown at this time, but could be due to the difficulty of detecting clinical varicoceles in obese men due to their body habitus.

Incompetent venous valves in the spermatic veins are **more common on the left side due to the right-angled insertion of the left spermatic vein into the left renal vein**. This results in turbulent backflow and increased intravascular back-pressure. The **nutcracker phenomenon**, which is characterized by compression of the left renal vein between the superior mesenteric artery and the aorta, can also cause left sided varicoceles.[8] **While varicoceles are known to detrimentally affect spermatogenesis, the exact pathophysiology remains unclear**. Possible mechanisms include increased intratesticular temperature due to impairment of the scrotal countercurrent cooling mechanism, increased oxidative stress, and reflux of gonadotoxic renal and adrenal metabolites.[9]

3.1.3. Epidemiology

Varicoceles occur in 15-25% of males overall and up to 35-60% of men seen in an infertility clinic. The majority (**75-90%**) of varicoceles are left sided, and **33%** are bilateral. While varicoceles are extremely common, **they do not cause infertility in most affected men**.

3.1.4. Diagnosis and Evaluation

The diagnosis of a varicocele is made on physical exam with the patient in the standing and supine positions.[9] The **Valsalva maneuver** can facilitate diagnosis by causing a palpable impulse and venous distension. Classically, varicoceles are described as a scrotum having a **"bag of worms"** feeling and appearance. While recent studies have explored a possible benefit to repair of subclinical varicoceles, [10] the abundance of existing data only establishes a benefit of repair for clinical (i.e. palpable varicoceles). **Only palpable varicoceles have been shown to be associated with male factor infertility**, so imaging is not recommended to detect subclinical varicoceles when no palpable abnormality is present. Similarly, the AUA/ASRM guidelines do not recommend repair of subclinical varicoceles.[2]

Varicoceles are graded using a scale ranging from I-III[1] (**Table 1**). **Grade I** varicoceles are small, not grossly visible, and are palpable **only during Valsalva maneuver**. **Grade II** varicoceles are of medium size, are not grossly visible, but are palpable with the patient standing without the Valsalva maneuver. **Grade III** varicoceles are large and are grossly visible with the patient standing. Although the optimal criteria for further evaluation of varicoceles have not been defined, varicoceles occurring **prior to puberty**, those that are **rapid in onset**, or those that **fail to decompress in the supine position** warrant additional investigation to rule out retroperitoneal pathology (tumor). Right-sided varicoceles are not necessarily associated with a higher risk of pathologic findings and current AUA/ASRM guidelines do not recommend routine imaging to evaluation isolated right sided varicoceles.[2] Although most varicoceles are asymptomatic, **men can present with pain**. A dull ache that increases after standing for long periods of time or with activity and improves in the recumbent position is characteristic.

The routine evaluation of an infertile male with a varicocele consists of a medical and reproductive history, a physical examination, and a minimum of two semen analyses. In men with abnormalities on the semen analysis, sexual dysfunction, or other findings of endocrinopathy, an endocrine panel consisting of at least a testosterone and FSH level is warranted, as an elevated FSH (>4.5 IU/mL) may indicate a detrimental effect of the varicocele on spermatogenesis. [11,12] As noted above, abdominal/retroperitoneal imaging may be obtained in select cases, and scrotal ultrasonography is appropriate if the testicles are unable to be assessed (e.g. hydrocele, tight scrotum) or in cases of indeterminate findings. However, it is important to note that the diagnosis of a varicocele is not made or confirmed by scrotal ultrasonography, and varicoceles found on ultrasound that are not confirmed by examination may not be clinically relevant. Similarly, correction of varicoceles identified only on ultrasonography (sub-clinical) does not result in clinically relevant increases in semen parameters or pregnancy rates.[13]

Table 1. Varicocele Grading System	
Varicocele Grade	**Physical Examination Findings**
Subclinical	Nonpalpable varicocele, only identified on imagining
I (Small)	Varicocele is palpable *only* with Valsalva maneuver
II (Medium)	Variococele is palpable *without* Valsalva maneuver
III (Large)	Varicocele is visible (“bag of worms” appearance)

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3.1.5. Indications for Varicocele Treatment

(see **Table 2**)[11]

Decision making in the male with a varicocele can be aided by considering three separate scenarios: (i) **the male partner in a couple attempting to conceive** (ii) **the adult male not currently attempting to conceive** (iii) **adolescent male.** **Table 2** delineates the criteria required for proceeding with varicocele ligation surgery in these cases.

Young males with a varicocele and normal semen analyses should undergo **semen analysis testing every one to two years**. Adolescents with a varicocele and normal ipsilateral testicular size should be offered annual follow-up including objective measures of testicular size and/or semen analyses. Varicocele correction is often considered in the context of other therapeutic options, such as assisted reproductive techniques (ART), including intrauterine insemination (IUI) and in vitro fertilization (IVF). Very limited data suggest that **an uncorrected varicocele <u>may</u> cause a progressive decline in semen parameters <u>or fertility</u> over time**, particularly in subfertile males, thus further decreasing a male's overall reproductive potential.[14,15,16,17]

Table 2. Indications for Varicocele Treatment in Selected Populations

Patient Population	Criteria for varicocelectomy (when ALL of the following are met)
Male partner in couple trying to conceive	1. a varicocele is palpable; 2. the couple has documented infertility; 3. the female has normal fertility, subfertility or potentially correctable infertility; *and* 4. the male partner has one or more abnormal semen parameters or sperm function test results, including DNA fragmentation index
Male partner in couple undergoing IVF/ICSI	1. a varicocele is palpable; *and* 2. the male partner has either oligo or azoospermia; *or* 3. testicular pain is present consistent with a varicocele
Adult male not currently attempting to conceive	1. a varicocele is palpable; *and* 2. the male partner has one or more abnormal semen parameters; *or* 3. testicular pain is present consistent with a varicocele
Adolescent Male	1. a varicocele is palpable; *and* 2. the ipsilateral testicle is smaller than the contralateral; *or* 3. abnormal semen parameters are present

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3.1.6. Surgical Repair

There are two major approaches to varicocele correction, **percutaneous embolization** and **surgical repair**. Surgical options include both **open** and **laparoscopic** approaches. Open techniques consist of **subinguinal**, **inguinal**, and **retroperitoneal approaches**. Although definitive data are lacking, currently available meta-analyses comparing techniques suggest that microscopic inguinal or subinguinal approaches may have superior outcomes and lower complication rates compared to other approaches.[18,19,20,21] Most adult urologists currently perform an inguinal or subinguinal approach with the assistance of an operative microscope, while the majority of pediatric urologists employ laparoscopic approaches.

Indications: as described above in *section 3.1.5*

Operative Considerations: Most experts use the inguinal or subinguinal approach for surgical correction. Intraoperative magnification (loupes, operating microscope) is commonly used to facilitate preservation of the testicular artery and lymphatics and isolation of the internal spermatic veins. Keys of this procedure are:

- Proper identification of the cord in its entirety in order not to leave any dilated veins posteriorly.
- 50% of the time, the testicular artery is adherent to the posterior surface of one of the veins.
- Use of a Doppler to avoid accidental ligation of the testicular artery. A forceps or partially tied silk ligatures can be used to temporarily occlude the vessel while the Doppler probe remains on the testicular artery. This will allow the surgeon to test whether the testicular artery is the packet to be ligated.
- Once all veins have been ligated, the surgeon should perform complete inspection of the field to ensure patency of the testicular artery and ligation of all venous structures.

The use of optical magnification has been shown to decrease varicocele persistence and recurrence.[22]

Outcomes: Surgical treatment of varicoceles results in successful correction in greater than 90% of men with low rates of recurrence and complications.[11,18,19] Although debatable, available meta-analyses suggest that microscopic inguinal and subinguinal approaches may be preferred over other approaches.[19,20,21] Current meta-analyses also suggest that varicocelectomy in men with clinically-palpable varicoceles and subfertility results in improved semen parameters and pregnancy rates. [23,24,25] It is notable that an older Cochrane review failed to demonstrate statistically significant improvements in pregnancy rates following varicocelectomy. However, the study was limited by inclusion of men with normal semen parameters and subclinical varicoceles.[26] Other populations have also exhibited benefits with varicocelectomy. Among men with oligo- or azoospermia and clinical varicoceles undergoing IVF/ICSI, varicocelectomy may improve live birth rates, pregnancy rates, and sperm retrieval rates. [27] However, limited data in this regard leads to lack of consensus. The current AUA/ASRM guidelines recommend that when the man has nonobstructive azoospermia and a palpable varicocele, couples should be informed of the absence of definitive evidence supporting varicocele repair prior to ART.[2] Varicocele management in children and adolescents has also demonstrated significant improvements in testicular volume and sperm concentration.[28] The extent of improvements expected may correlate linearly with the severity of the varicocele, and outcomes appear to be durable to at least 12 months.[29,30] In contrast to the above data, surgical management of subclinical varicoceles does not result in a clinically-relevant increase in semen parameters or pregnancy rates.[13]

Complications: The most common complications of varicocelectomy are hydrocele formation and varicocele recurrence.[31] Hydrocele formation can be mitigated with use of optical magnification. Microsurgical varicocelectomy is associated with very low **hydrocele formation rates** compared to **conventional inguinal** and **laparoscopic** techniques. Lower varicocele recurrence rates are also noted with microscopic visualization, as **microsurgical** inguinal varicocelectomy has a very low recurrence rate **(1-2%)** compared to the **non-magnified inguinal (9-16%),** high **retroperitoneal (11-15%)**, and **radiographic balloon occlusion (4-11%)** approaches.[32,31,33] When varicocele persistence or recurrence is noted, either surgical ligation or percutaneous embolization are therapeutic options. Another very rare, but significant, complication of varicocelectomy is testicular atrophy or loss due to inadvertent injury of the testicular artery. Oftentimes, the presence of alternate blood supplies to the testis (vasal artery, cremasteric artery), as well as additional testicular arteries present in the spermatic cord, are sufficient enough to prevent testicular atrophy or loss. **Wound infections in contemporary series occur in <1%, while hematoma rates are not clearly defined.**[34]

3.1.7 Percutaneous Embolization

The refluxing internal spermatic veins are accessed and embolized using a combination of fluid and/or coils. This technique involves local anesthesia and then femoral vein access and catheter insertion. Once the catheter is inserted, the venographic placement of a balloon or coil in the internal spermatic vein is performed. This technique may offer the advantage of less postoperative pain, but intravascular coil migration, extension coil placement with chronic pain, and inadequate management of distal accessory veins are key risks and limitations. Expertise in interventional radiology is needed, and technical difficulties, in particular those relating to challenging anatomy, can prevent successful access to the internal spermatic veins in some patients. **Unfortunately, late recurrence (2-5 years) after percutaneous embolization is common and occurs more frequently with embolization compared to other approaches.**[35] **Furthermore, most men will need to follow up with a urologist, not an interventional radiologist, after their procedure.**

4. Procedures That Improve Sperm Delivery

Transurethral resection of the ejaculatory ducts (TURED) procedures, vasovasostomy, and epididymovasostomy procedures enable the urologist to correct underlying obstruction in the male excurrent ductal system and **can potentially restore fertility to a previously azoospermic male**. Because many of these men present with azoospermia, the AUA/ASRM Infertile Male Guideline is an excellent comprehensive resource that details the requisite preoperative evaluation of these patients and men with other forms of azoospermia. A companion to this manuscript, **“The Management of Obstructive Azoospermia: AUA Best Practice Statement”**, provides guidance for the treatment of azoospermic men, including surgical procedures that aim to overcome obstructive processes that hinder the delivery of sperm in the ejaculate (**Table 3**). The AUA guidelines note that patients with obstructive azoospermia can be managed with surgical correction or sperm extraction / IVF.

Table 3: Obstructive Azoospermia Sperm Retrieval Techniques (From AUA best practice statement on obstructive azoospermia). Microsurgical Epididymal Sperm Aspiration (MESA); Percutaneous Epididymal Sperm Aspiration (PESA); Testicular Sperm Aspiration (TESA); Testicular Sperm Extraction (TESE)

Sperm Retrieval Techniques	Advantages	Disadvantages
Microsurgical epididymal sperm aspiration (MESA)	• Large quantity of sperm obtained suitable for several IVF/ICSI cycles in one procedure	• Requires microsurgical skills • Incision with post-op discomfort • Higher cost compared to percutaneous procedures
Percutaneous epididymal sperm aspiration (PESA)	• No microsurgical skills required • Rapid • Minimum post-op discomfort	• Fewer sperm retrieved • Higher risk of epididymal damage
Testicular sperm extraction (TESE) and microTESE	• Large quantity of sperm obtained (when sufficient sperm present) suitable for several IVF/ICSI cycles in one procedure • No microsurgical skills required except when microTESE performed	• Risk of testicular damage with multiple biopsies • Incision with post-op discomfort • Higher cost compared to percutaneous procedures

Percutaneous testicular sperm aspiration (TESA)	• No microsurgical skills required • Rapid • Minimum post-op discomfort • Minimally invasive	• Fewer sperm retrieved
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4.1 Ejaculatory Duct Obstruction

4.1.1. Definition

Ejaculatory duct obstruction (EDO) results from a partial or complete blockage of the ejaculatory ducts. This blockage impairs the secretion of vasal fluid (including sperm) and seminal vesicle fluid into the prostatic urethra during seminal emission. [3]

4.1.2. Risk Factors and Pathophysiology

Mechanical obstruction of the ejaculatory duct may be due to congenital or acquired causes. Understanding the embryologic origins of the ejaculatory duct can elucidate its obstruction. In the male, the **mesonephric (Wolffian) duct** forms the epididymis, vas deferens, seminal vesicle, and ejaculatory duct. The **paramesonephric (Mullerian) duct** generally involutes to form the prostatic utricle and appendix testis. The ejaculatory ducts are continuous with the seminal vesicles and are joined by the ampulla of the vas deferens. The ejaculatory ducts are typically 1-2 cm in length and vary in caliber from 1.7 mm at the origin to 0.3 mm distally. [36] Congenital EDO causes can occur due to **utricular, mesonephric,** or **paramesonephric cysts**. Moreover, congenital ejaculatory duct atresia or stenosis has also been described. Acquired causes can arise due to a number of conditions, including **infections** (sexually transmitted diseases, prostatitis), **calculi, tumors, urethral instrumentation** or **prior transurethral surgery**.

4.1.3. Epidemiology

It is estimated that **1-5% of infertile men have ejaculatory duct obstruction** whether it be partial or complete.[37] The incidence of partial obstruction may be higher as prostate screening studies have suggested that up to 5% of the male population have prostatic cysts, although most of them do not cause clinical infertility. [38]

4.1.4. Diagnosis and Evaluation

The evaluation for EDO must begin with a detailed history and physical examination.

The most common complaint of men with EDO is infertility, as most affected men are otherwise asymptomatic. Patients may also report **perineal pain, ejaculatory pain, hematospermia, scrotal pain, decreased ejaculate volume, and lower urinary tract symptoms**. In order to establish the diagnosis, one has to demonstrate **normal spermatogenesis and patency of the proximal genital tract including the epididymis and vas deferens**.

A **semen analysis** can also help determine the diagnosis. **As most of the ejaculate volume consists of seminal vesicle fluid, a semen analysis in the setting of EDO commonly reveals low volume (< 1mL). In addition, without seminal vesicle secretions, the ejaculate is often acidic (pH<7) and lacks fructose**. Azoospermia is the classic finding of complete obstruction, but partial obstruction may present with oligospermia, asthenospermia, or necrospermia. [12]

Imaging studies can also assist in making the diagnosis. Transrectal ultrasound (**TRUS**) can identify the presence of cysts, calculi, or other prostate/ejaculatory duct abnormalities; however, it is unable to definitely diagnose EDO. The presence of larger (>0.1 ml) midline prostatic cysts or proximal genital tract dilation suggests the presence of ejaculatory duct obstruction.[39] Similarly, **dilated seminal vesicles (>15 mm) or dilated ejaculatory ducts (>2.3 mm) have historically been used to suggest EDO**. However, despite these associated findings, TRUS has relatively low specificity and low positive predictive value.[40] This poor specificity has led some to suggest a need for adjunctive procedures at the time of TRUS, including seminal vesicle aspiration (presence of >3 sperm / HPF suggests EDO), seminal vesicle chromotubation (to visually test patency of system), ejaculatory duct manometry, or possible use of MRI. [41,42,43,,44,45] Despite the lack of an optimal method of diagnosing EDO, **the most commonly performed preliminary assessment includes TRUS with or without confirmatory procedures**.

4.1.5. Operative Management

Indication: Ejaculatory duct obstruction

Operative Considerations: Transurethral resection of the ejaculatory ducts (TURED) was first described in 1973.[46] Since its original description, refinements to the technique have been made to improve efficacy and decrease complications. With the patient under general or spinal anesthesia in the dorsal lithotomy position, **the seminal vesicles and ejaculatory duct are ideally opacified with indigo carmine and/or contrast dye injected into the seminal vesicles under TRUS guidance to improve intraoperative identification of the relevant anatomy**. Resection is performed with a standard resectoscope. With cutting current, the proximal verumontanum is resected to allow drainage of the ejaculatory ducts. Intraoperative TRUS and digital rectal compression of the prostate and seminal vesicles via a sterile rectal drape can help guide resection. If the obstruction is due to a prostatic cyst, cyst unroofing alone is generally sufficient. In the case of stenosis or calculi, resection along the ejaculatory duct may be required. Confirmation of patency may be confirmed by efflux of dye from the ejaculatory ducts or retrograde seminovesiculography under fluoroscopic imaging. A urethral catheter is generally left in overnight and semen analyses are evaluated starting at 3-12 weeks post resection. While ejaculatory duct dilation using **percutaneous transluminal angioplasty** balloons (3-4 mm in diameter) or **9F endoscopes** has also been described, TURED remains the most widely utilized procedure to correct EDO.[47,48] Patients with EDO may also be managed with surgical sperm extraction.[2]

Outcomes: After TURED, approximately **50-92% of men will have return of sperm** to their ejaculate, and pregnancy rates are approximately 13-42%.[49,50] (**Table 4**).

Complications: The complication rate from TURED procedures is up to **33%.**[51,52] With the ejaculatory duct anti-reflux mechanism disrupted, urine can pool in the duct. This commonly causes decreased sperm motility and even sperm death as the urine admixes with the sperm during seminal emission. Over time, urine can reflux via the ejaculatory duct and vas deferens to the epididymis, where it can cause chronic epididymo-orchitis (2-9%). In addition, watery ejaculate (10-13%), post-void urinary leakage, worsening of semen parameters or iatrogenic azoospermia can result after TURED. In some cases, delayed stenosis of the resected ducts can cause recurrent obstruction (up to 43%), necessitating a repeat procedure. Given the high complication rate of TURED, performing this procedure should be done with caution.

Table 4. Summary of studies describing outcomes of transurethral resection of ejaculatory duct (TURED) for ejaculatory duct obstruction (EDO).

Study	Number of Patients (n)	Patients with Improved Semen Parameters (%)	Pregnancy Rate after TURED Procedure (%)
El-Assmy et al, 2012	23	61	13
Tu et al, 2011	60	85	27
Yurdakul et al, 2008[49]	12	92	25
Turek et al, 1994	46	65	20
Meacham et al, 1993	24	50	29
Pryor et al, 1991	12	83	42

View Image.

4.2 Vasal and Epididymal Obstruction

4.2.1. Definition

Vasovasostomy (VV) and Epididymovasostomy (EV) are most commonly performed in order to **re-establish excurrent ductal patency after a prior vasectomy**, although additional indications include numerous other forms of congenital and acquired excurrent ductal obstruction. Both procedures are highly effective at relieving obstruction if performed correctly, as will be detailed below.

4.2.2. Risk factors and Pathophysiology

Although most men present for a VV and/or EV after a prior vasectomy, up to **7% of men with primary infertility will have excurrent ductal obstruction**, either from congenital or acquired causes. Many patients will be candidates for reconstructive surgery to re-establish patency. Examples of congenital excurrent ductal obstruction include **congenital epididymal tubule point blockage** or **epididymal atresia**, which can be seen in some men with CFTR mutations. Examples of acquired excurrent ductal obstruction include epididymal tubule obstruction arising from a prior episode of **epididymitis** and **iatrogenic vasal obstruction** occurring after inguinal hernia repair.

4.2.3. Epidemiology

There are **3.6 million vasectomized men aged 15-45 years in the United States**, which represents an overall **vasectomy prevalence of 6-8%** based on several large national cohorts.[53,54,55] Overall, **2% of men with a history of vasectomy also report having a subsequent VV and/or EV.**[53] VV and/or EV are more cost-effective treatment options than IVF for men with a history obstructive azoospermia, and successful re-establishment of continuity of the excurrent ductal system can facilitate conception attempts via natural means. [50,56] However, the published literature is not uniform in the cost effectiveness findings, due in part to the absence of randomized controlled trials and the use of different clinical parameters in each analysis. While cost is an important consideration when deciding between vasectomy reversal and sperm retrieval with IVF/ICSI, additional factors such as female partner age, ovarian reserve, and preferred form of future contraception are among other important factors influencing decision making. [57]

4.2.4. Surgical Reconstruction

Indications: Typically, men will present for VV and/or EV after having had a vasectomy. Men requesting a vasectomy reversal do not require further workup, although some authors have reported that a preoperative serum FSH level can help identify patients with a higher likelihood of ultimately requiring post-reversal use of assisted reproductive techniques. [58] Fortunately, most men who present for VV/EV have the best proof of optimal fertility possible, prior paternity. Among men with suspected obstructive azoospermia, optimal surgical candidates include those with **a low FSH (<7.6 mIU/ml) and a normal longitudinal testicular axis (>4.5 cm), as these criteria are associated with a 96% chance of having obstructive azoospermia** .[59] Physical exam in azoospermic men can help to identify the presence or absence of a vasal defect or granuloma and the distance from the vasal defect to the testis in centimeters.[60,61] The **female partners of men considering VV and/or EV should also undergo evaluation** to determine if female infertility factors are present, as female factors might affect the decision to pursue microsurgical reconstruction vs sperm extraction with IVF/ICSI.[50]

Operative Considerations: VV and/or EV are typically performed with an operating microscope, and this approach is historically associated with very favorable patency and pregnancy rates.[62] Most surgeons use either a median raphe incision, transverse scrotal, or bilateral linear incisions over the defect. Once the incision is made, dissection is carried down to the level of the vas deferens, which is mobilized both proximal and distal to the defect. Once the vasal defect is isolated, the operating microscope is typically brought into the field. The vas deferens is meticulously mobilized to provide adequate length, taking care to preserve the blood supply by leaving the vasal sheath intact. If length is an issue, the external ring can be opened to increase the available abdominal vasal length and permit a tension free anastomosis. Alternatively, the convoluted vas can be dissected from the epididymal tunic. **Combined, these techniques can provide up to 5 cm of additional length**. The two ends of the vas should be transected both proximal and distal to the defect. **Microscopic examination of the vasal fluid (from testicular end)** is then performed by placing a drop of fluid mixed with saline on a slide.

The optimal intra-operative decision tree for proceeding with a VV or EV has not been conclusively defined. Historically, a combination of gross and microscopic vasal fluid was utilized, with the presence of whole sperm or clear fluid leading to VV, while thick or pasty fluid with or without sperm parts led to EV.[63,64] More recently, data have demonstrated patency rates >90% among men with sperm or sperm parts, independent of vasal fluid, leading some to utilize this approach in selecting the intra-operative procedure.[65,66] The appropriate management for no fluid seen remains debatable and unknown, with some suggesting that an EV should be performed while others proceed with VV.

Following transection of the abdominal vas, some microsurgeons choose to perform vasal injection with **saline by placing a 24-30G angiocatheter** and injecting saline into the abdominal vasal end to ensure patency. The vasal ends are then re-approximated with either a suture (typically 4-0 or 5-0) or an approximator clamp to remove tension. The microscopic anastomosis is then performed. Multiple techniques for re-anastomosis have been described, including multilayer or modified single layer techniques. A meta-analysis evaluating outcomes demonstrated equivalent patency rates with either procedure, although data are very limited and other studies have indicated that results may vary between techniques depending on time interval since vasectomy.[67,68] Suture choice is also variable, with most microsurgeons electing to use a combination of 10-0 and 8-0 or 9-0 sutures to achieve the anastomosis. To assist with suture placement into the abdominal vas, the mucosal lumen can be gently dilated with a microvessel dilator. The completed anastomosis should be leak proof and tension free. To facilitate a tension free anastomosis, additional sutures may be placed in the vasa proximal to the anastomosis bilaterally (ReVas technique), with one study suggesting improved outcomes over more traditional approaches.[69] Once one side is completed, an identical process is undertaken on the contralateral side.

Should an EV be necessary, most microsurgeons will perform an end-to-side anastomosis (vasal end to side of epididymis).[38] The set-up for an EV is more complex and requires a high degree of microsurgical skill. The epididymal tunic is inspected to determine an optimal site for EV, proximal to the obstruction **as evidenced by the abrupt change in diameter of the epididymal tubules** (dilated behind the obstruction and flat beyond site of obstruction). The vas deferens is then anchored to the peri-epididymal tissue to facilitate a tension free anastomosis. Once the desired target is chosen, the epididymal tubules are exposed by opening the epididymal tunic with microscissors. For an intussuscepted EV, two double armed 10-0 sutures are placed into and out of a single tubule in a parallel fashion and also placed into and out of the vas.[70] An ophthalmic blade is then used to incise the intervening epididymal tubule, and the sutures are tied down. An outer layer of closure is then placed from the epididymal tunic to the seromuscular layer of the vas deferens with 9-0 suture. A VV or EV is then repeated on the contralateral side. Once the anastomosis is completed, the wound is closed in layers and a scrotal support is placed on the patient.

Outcomes: **Microsurgical VV** for vasectomy reversal results in return of sperm to the ejaculate in **70-95%** of patients, and **pregnancies** are achieved without use of assisted reproductive techniques in **30-75%** of couples.[50] When **EV** must be performed, patency rates range from **50-85%** and **pregnancy** rates range from **20-40%** with intercourse.[47] Other factors which have been associated with improved outcomes include the length of the vas segment from the epididymis to the vasectomy site (longer is better), use of surgical clips at time of vasectomy, duration since vasectomy, presence of granuloma, increased alpha-glucosidase, placement of additional vasal support sutures (ReVas technique), and use of angled cutting of the vas.[5071,72,73,74] When pregnancy is used as the definition for success, additional favorable factors include younger female partner age and prior pregnancy together.[75] Although the length of time since the vasectomy (longer interval portends worse outcome) has historically been associated with worse outcomes, this has been called into question and may be less significant or variably associated depending on surgical technique.[76,77] A successful pregnancy outcome may also be predicted based on post-operative semen parameters. However, in contrast to the WHO 2010 criteria, semen results post reversal likely require a lower threshold. Majzoub and colleagues noted that men with counts >5 million/ml had similar pregnancy rates compared to higher numbers while those <5 million/ml were significantly less likely to achieve a spontaneous pregnancy.[78]

Complications: Potential self-limiting complications include wound infection, hematoma, scrotal edema, orchalgia and primary or delayed anastomotic failure. Although the true rate of complications is likely underreported, one analysis of 2500 cases reported hematomas in 0.3%, granulomas in 5%, and delayed failure in 5%.[34]

5. Procedures for Sperm Retrieval

Azoospermia can be either “obstructive” or “non-obstructive” in nature. Sperm retrieval for use in assisted reproductive techniques can be a primary treatment for both obstructive and non-obstructive azoospermia (NOA). Since the advent of intracytoplasmic sperm injection (ICSI) in 1992, surgical sperm retrieval evolved from a purely diagnostic procedure to a therapeutic one.[79] While sperm from men with obstructive azoospermia was first used successfully, subsequent studies demonstrated that sperm from men with spermatogenic failure (NOA) could also be used with ICSI.[80] It is important to note that all surgically retrieved sperm obligates the couple to use IVF/ICSI given the poor overall results when used with intrauterine insemination or conventional IVF. Sperm from the vas deferens, epididymis, or testis can be used to successfully fertilize an oocyte and facilitate a healthy pregnancy.

Although surgical sperm retrieval had historically been reserved for cases where viable sperm fails to reach the ejaculate, it is increasingly used in cases where sperm are of suboptimal quality (e.g. high DNA fragmentation). Specific instances include (i) **Obstructive azoospermia** (vasectomy, congenital bilateral absence of the vas deferens, ejaculatory duct obstruction) where surgical reconstruction is not desired or possible (ii) **Non-obstructive azoospermia** (i.e. spermatogenic failure) (iii) **Inability to ejaculate** (spinal cord injury, retroperitoneal surgery, religious beliefs) where assisted ejaculation (penile vibratory stimulation, electroejaculation) fails or is not desired (iv) **Complete necrospermia**. (v) **Ejaculated sperm with elevated DNA fragmentation index**.

The overall aim of sperm retrieval is to obtain the best quality sperm in sufficient numbers for immediate use and/or cryopreservation, while minimizing risk of injury to the reproductive structures. Several different sperm retrieval procedures are available, and the selection of a specific method depends on the experience and preference of the physician performing the procedure and the embryologist who will be working with the specimen in the laboratory.[50]

The literature supports the following (i) **No apparent differences exist in either fertilization or pregnancy rates between fresh vs. cryopreserved/thawed sperm in both obstructive and non-obstructive azoospermia**. Thus, the timing of sperm retrieval in regard to oocyte retrieval should be determined by the expertise and preference of the physician and embryologist (ii) In obstructive azoospermia, the choices of either percutaneous vs. open surgery and testis vs. epididymis extraction site should be determined based on local preference and expertise, as **neither site nor method of sperm retrieval affects outcome in IVF/ICSI. (iii) Open surgical testicular sperm retrieval with or without microsurgical magnification is recommended for patients with non-obstructive azoospermia.** [2,50]

5.1 Epididymal Sperm Retrieval

5.1.1 Percutaneous Epididymal Sperm Aspiration (PESA)

Indications: Obstructive azoospermia. The procedure can be more difficult in men without dilated epididymides or with epididymal atresia.

Operative Considerations: Under local anesthesia, a small gauge needle (23-26G) is passed percutaneously into the epididymis. Epididymal fluid is then aspirated and examined by light microscopy for the presence of sperm. Gentle pressure on the epididymis and several passes of the needle may be required to improve yields.

Outcomes: Generally, thousands to millions of sperm can be obtained for IVF/ICSI or sperm cryopreservation. However, retrieval rates can be variable with 25-40% of attempts having rare motile sperm or no sperm.[81,82]

Complications: The procedure is minimally invasive, repeatable, and surgical reconstruction afterwards has been described. However, as the needle passage is blind, sperm yields can be variable and bleeding can occur (<1%).

5.1.2 Microsurgical Epididymal Sperm Aspiration (MESA)

Indications: Obstruction azoospermia.

Operative Considerations: An incision in made in the scrotum and carried down through the tunica vaginalis. The testis is then delivered. Under 15-25x magnification, the epididymal tunic is opened and individual tubules are isolated. Beginning at the epididymal tail, tubules are opened and the fluid is aspirated. Dissection proceeds toward the caput until an adequate number of sperm are obtained. In many cases, the entire epididymis may need to be inspected to maximize yields. Bipolar electrocautery is then used for hemostasis. Modifications to the MESA technique allow for preservation of the epididymis and smaller incisions.

Outcomes: The procedure generally provides millions of sperm for IVF/ICSI or sperm cryopreservation with retrieval rates of 95-100%.[83] The cost of the procedure is higher in cases where general anesthesia is utilized.[84]

Complications: Bleeding, fibrosis, and postoperative pain are the most commonly described complications (<1%).

5.2 Testis

5.2.1 Testicular Sperm Aspiration (TESA)

Indications: All testicular sperm retrieval procedures can serve therapeutic and diagnostic purposes. Testicular sperm aspiration can aid the diagnosis of azoospermia and can provide sperm to be used with assisted reproductive techniques.

Operative Considerations: Under local anesthesia a needle is passed percutaneously through the scrotal layers and penetrates the tunica albuginea. Suction is the applied, usually via a 10-20cc syringe, and seminiferous tubules are aspirated. One or more passes can be performed to increase sperm yield. With smaller gauge needles (22-23G), the procedure is generally referred to as an **aspiration**. When larger caliber needles are used, (16-18G), the procedure is sometimes referred to as a **needle aspiration biopsy** or **cutting needle biopsy**. Large gauge needles are often better able to cut testicular parenchyma and preserve architecture. Some prefer use of the **tissue-cutting biopsy needle**, which uses a spring-loaded biopsy gun. A small skin incision is often made to aid passage of the needle. Several passes may be necessary for adequate sperm numbers.

Outcomes: Can provide adequate sperm (thousands to millions) in up to 100% of men with obstructive azoospermia.[85]

Complications: The blind nature of needle passage can lead to hematocele or intratesticular hematoma formation (<1%).

5.2.2 Testicular Sperm Extraction (TESE)

Indications: To obtain sperm for use with ART.

Operative Considerations: Under local and/or general anesthesia a scrotal incision is made. This is extended down through the Dartos and tunica vaginalis until the tunica albuginea of the testis is exposed. An eyelid retractor can aid in exposure. A tunical holding stitch is placed to mark the apex of the tunica albuginea incision, which is made using an 11 blade. Seminiferous tubes are extruded with gentle testicular pressure. Fine forceps and microscissors may also be used to aid in testicular parenchyma removal. Cautery is used for hemostasis and the incision is closed.

In cases of cryptozoospermia or non-obstructive azoospermia, the use of an operating microscope (microTESE) has been described to aid in the identification of rare pockets of spermatogenesis. Under general anesthesia or IV sedation, a scrotal incision in made and the larger testis is delivered from the scrotum. A transverse tunica albuginea incision in made to expose the seminiferous tubules. Incisions along the equatorial plane or lateral longitudinal plane have been described. The operating microscope allows improved seminiferous tubule assessment. Intact spermatogenesis is often found in larger and more opaque tubules. In addition, more targeted tubule sampling can limit testicular tissue removal thus improving recovery and allowing repeat procedures if necessary.

Outcomes: **If the patient is azoospermic due to an obstructive process, retrieval rates of up to 100% can be expected.**

In cases of NOA or severe cryptozoospermia, retrieval rates are lower. Although early studies suggested that microTESE had a significantly higher successful retrieval rate compared to TESE alone, its true role has been under increasing scrutiny in recent years. Meta-analyses indicate that successful sperm retrieval was 43-63%, which was 1.5x more likely than if TESE (17-45%) were used.[86,87] In addition, complication rates are also low. Given the data, the AUA guidelines state that for men with NOA undergoing sperm retrieval, microdissection testicular sperm extraction (TESE) should be performed. Although the optimal algorithm for the evaluation and management of men with azoospermia is debatable, a potential algorithm is provided in **Figure 1**.

Complications:

<u>Conventional TESE</u>

As the procedure is performed under direct vision, bleeding complications are low, with few studies reporting complications from TESE or microTESE. Longer-term impacts on testosterone, testicular size, and other similar complications likely depend on the extent of dissection and tissue removal performed. Although very limited comparative data exist, one study which randomly assigned men to TESE, microTESE, TESA, and fine-needle TESA demonstrated lower post-operative testosterone levels in the TESE and microTESE groups compared to TESA and fine-needle TESA.[88]

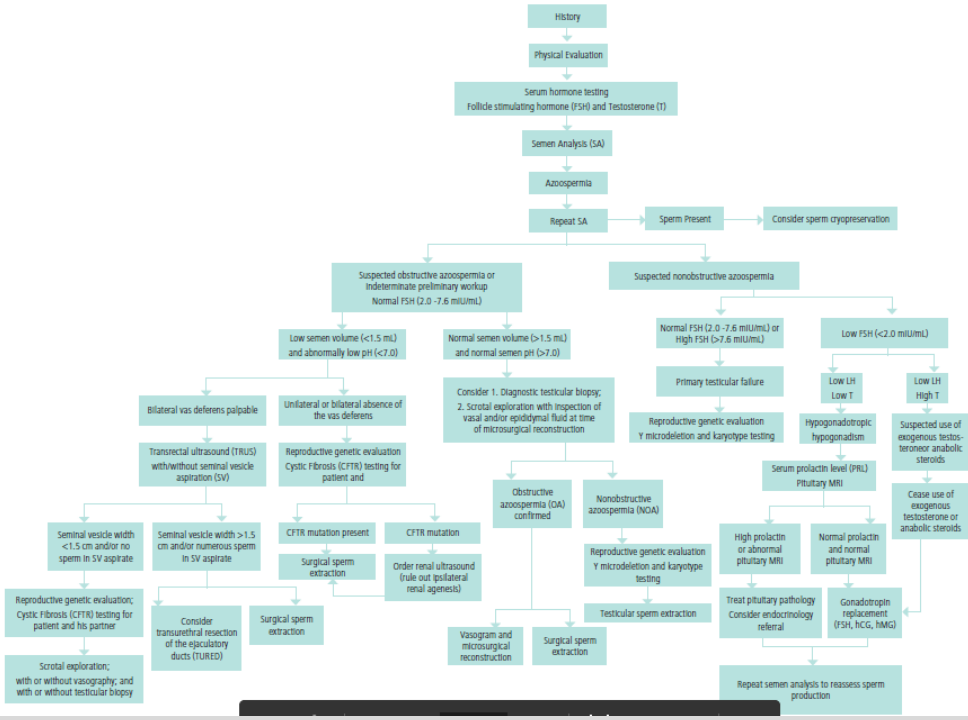

Figure 1

6. Summary

The surgical management of male infertility can be organized into (i) **diagnostic procedures**, (ii) **procedures that optimize spermatogenesis**, (iii) **procedures that improve sperm delivery**, and (iv) **sperm retrieval procedures**.[1] In order to deliver effective diagnostic and therapeutic care, clinicians must be knowledgeable about the causes and treatments for male infertility. ***More specifically, a fundamental understanding of the proper evaluation and treatment of the azoospermic male is essential in order to deliver effective surgical care. Figure 1 provides one proposed algorithm for the evaluation and surgical treatment of azoospermia.***

7. Abbreviations

Surgical Management of Male Infertility

- **ART –** Assisted reproductive techniques
- **AUA –** American Urological Association
- **BMI –** Body mass index
- **CFTR –** Cystic fibrosis transmembrane conductance regulator
- **EDO –** Ejaculatory duct obstruction
- **EV -** Epididymovasostomy
- **FSH –** Follicle stimulating hormone
- **G -** Gauge
- **HPF –** High power field
- **ICSI –** Intracytoplasmic sperm injection

- **IUI –** Intrauterine insemination
- **IVF –** In vitro fertilization
- **MESA –** Microsurgical epididymal sperm aspiration
- **mL –** milliliter
- **mm –** millimeter
- **mTESE –** Microdissection testicular sperm extraction
- **mIU –** microInternational Units
- **MRI –** Magnetic resonance imaging
- **PESA –** Percutaneous epididymal sperm aspiration
- **TESA –** Testicular sperm aspiration
- **TESE –** Testicular sperm extraction
- **TURED –** Transurethral resection of ejaculatory ducts
- **TRUS –** Transrectal ultrasonography
- **VV -** Vasovasostomy

8. Additional Reading

Diagnosis and Treatment of Infertility in Men: **AUA/ASRM Guideline (2020)**

9. Patient Resource Materials

- *"Sperm retrieval"* **https://urologyhealth.org/urologic-conditions/sperm-retrieval**
- *"Varicoceles"* **https://urologyhealth.org/urologic-conditions/varicoceles**
- *"Vasectomy Reversal"* **https://urologyhealth.org/urologic-conditions/vasectomy-reversal**

Videos

Varicocelectomy: Microscopic subinguinal (Marmar) technique

Vasovasostomy Larry I. Lipshultz MD Baylor College Of Medicine

Epididymovasostomy - A two suture technique

Presentations

SURGICAL MANAGEMENT Presentation 1

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