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Surgical Treatment of Male Infertility

Erkek İnfertilitesinin Cerrahi Tedavisi

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ABSTRACT

Male infertility may occur due to obstructive and non-obstructive reasons, and some pathologies may be corrected with surgical and medical treatment. Such treatment may increase the possibility of spontaneous pregnancy, the success of assisted reproductive technology, and also testicular sperm retrieval rate. This review will focus on surgical treatment alternatives in infertile males. Although treatment options for varicocele in infertile men include open surgical, radiologic, and laparoscopic approaches; microsurgical varicocele repair has the highest improvement in postoperative sperm parameters with lower complication rates. Recent advances in microsurgical anastomosis techniques have increased the patency rate for proximal epididymal obstruction. Although treatment options for distal ejaculatory duct obstruction include endoscopic resection, balloon dilatation, and laser incision/excision, transurethral resection of the ejaculatory duct (TURED), is still the primary gold standard treatment of distal ejaculatory duct obstruction. The testicular sperm retrieval rate has increased with the management of correctable pathologies in men with non-obstructive azoospermia. In case of treatment failure of correctable or uncorrectable pathologies of male factor infertility, surgical sperm obtained from the urogenital tract may necessary for assisted reproductive technology. Surgical success rates for male infertility and the success of surgical sperm obtained procedures have increased dramatically over the last decades attributable to the development of microsurgical techniques and endoscopic equipment, instrumentation, and techniques.
Keywords: Male infertility; varicocele; obstructive azoospermia; surgical treatment.

ÖZ

Erkek infertilitesi obstrüktif ve obstrüktif olmayan sebeplerle oluşabilir ve bunların bazıları cerrahi ve medikal tedavi ile düzeltilebilir. Bu tedavi yöntemleri çiftlerde spontan gebelik şansını artırabildiği gibi bu tedaviler ile üremeye yardımcı tedavi yöntemleri başarısı ve testiküler sperm bulma şansı artabilir. Bu derlemede infertil erkeklerde cerrahi tedavi yöntemleri irdelenecektir. Varikoselli infertil erkeklerde tedavi opsiyonları açık ve laparoskopik cerrahi ve radyolojik tedavi olmakla birlikte, mikrocerrahi varikoselektomi postoperatif sperm parametrelerinde en yüksek artış oranı ve en düşük komplikasyon oranlarına sahiptir. Proksimal epididimal obstrüksiyonların cerrahi tedavisinde mikrocerrahi anastomoz yöntemlerindeki ilerlemeler kanalın açılma başarısını artırmaktadır. Distal ejakülatör kanal tıkanıklığının cerrahi tedavisinde endoskopik rezeksiyon, balon dilatasyon, lazerle insizyon/eksizyon yöntemleri bulunmakla beraber, transüretral ejakülatör kanal rezeksiyonu (transurethral resection of the ejaculatory duct, TURED) hala altın standart tedavi yöntemidir. Nonobstrüktif azospermide düzeltilebilir patolojilerin giderilmesiyle testiküler sperm elde etme oranlarında artış gösterilmiştir. Düzeltilebilir veya düzeltilemez patolojilere bağlı erkek infertilitesinde tedavi başarısızlığı durumunda yardımcı üreme teknolojisi için ürogenital sistemden cerrahi olarak sperm elde etmek gerekli olabilir. Erkek infertilitesi cerrahi tedavilerinin başarı oranları ve cerrahi olarak sperm elde etme başarı oranları, mikro cerrahi tekniklerinin, endoskopik ekipman, enstrümantasyon ve tekniklerin gelişmesine bağlı olarak son dekatlarda çarpıcı bir şekilde artmıştır.
Anahtar kelimeler: Erkek infertilitesi; varikosel; obstrüktif azospermi; cerrahi tedavi.

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INTRODUCTION

Male infertility may occur due to obstructive (ejaculatory duct, vas deferens, and epididymal obstruction) and non-obstructive (varicocele, secondary hypogonadism, gonadotoxins exposure) reasons as correctable pathologies, and may also occur due to genetic disorders and testicular atrophy after mumps orchitis and undescended testis as uncorrectable pathologies (1-11). The aim of the evaluation of men for infertility is to point out to diagnose correctable pathologies, to detect genetic diseases, and also to diagnose life-threatening diseases (2,3,12-14). In addition, to increase the probability of spontaneous pregnancy, medical and surgical treatment may increase assisted reproductive technology (ART) success, and also testicular sperm retrieval rate (15-20). This review will focus on surgical treatment alternatives in infertile males.

Surgical Treatment of Varicocele

Varicocele is an excessive dilation of the pampiniform plexus. It is also the most commonly seen and correctable cause of male factor infertility (1,21). Varicocele is among the cost-effective treatments for infertility. The pampiniform plexus consists of the internal spermatic veins, external spermatic vein, deferential vein, and gubernacular vein. The left internal spermatic vein drains into the left renal vein at a straight angle, whereas the right internal spermatic vein drains directly into the inferior vena cava at an oblique angle. Therefore, left-sided varicocele is more common than right-sided. However, there are some variations, such as the number of gonadal veins, localization of drainage, and termination angle in some cases that could explain a higher incidence of bilateral varicoceles and also causes varicocele recurrences after the surgery or intervention (22). These variations were found more frequently on the left side (30%), as compared to the right side (10%). In some cases (10%), the variations were present bilaterally. Venous reflux is likely to be induced via collateral pathways, whereas in adolescents congenital venous abnormalities (renospermatic bypass, Nutcracker phenomenon, and valve abnormalities) are predominantly present (23). In addition, obesity is another risk factor for varicocele recurrence. Increased body mass index in men with varicocele is associated with larger spermatic vein diameters when supine (24).

Physical examination is the reference standard to diagnose varicoceles in subfertile men. Additional radiologic imaging is not necessary to diagnose subclinical varicocele, because only a varicocele detected by physical examination should be considered potentially significant (6).

When clinical palpable varicocele coexists with impaired semen quality, surgical repair may potentially restore spermatogenesis and fertility. Recent meta-analyses suggested that varicocele repair has a beneficial effect on fertility status in infertile men with palpable varicocele. Ficarra et al. (25) reviewed randomized clinical trials for varicocele repair and found a significant increase in pregnancy rate in patients who underwent varicocele treatment (36.4%) compared with patients having no treatment (20%). Marmar et al. (26) reported a 33% pregnancy rate in patients who underwent surgical varicocelectomy and a 15.5% pregnancy in the controls receiving no varicocelectomy.

Indications for the treatment of varicocele are the presence of clinical palpable varicocele with infertility history and abnormal semen parameters, and pain, if medical conservative treatment such as analgesics/anti-inflammatory drugs fails (25).

The aim of the treatment of infertile men with varicocele is to improve semen parameters and also to achieve pregnancy with or without the use of ART (2,4,20,27,28). Treatment options for varicocele in infertile men include open surgical, radiologic, and laparoscopic approaches (29,30). However, anatomic variations of testicular veins affect outcomes of surgical and radiologic treatment of varicocele. In a venographic study, the most anatomic reason for surgical failure was gonadal vein duplication (66% of the cases) (31). In this series, most cases had laparoscopic or open surgery at the suprainguinal level. Therefore, other veins at the lower level could not be identified.

The best treatment modality for varicocele in infertile men should include higher seminal improvement and spontaneous pregnancy rates with lower complication rates such as recurrence or persistence, hydrocele formation, and testicular atrophy. Even if we do our best to treat varicocele, only 35-50% of the patients will have a positive response to varicocele treatment, and 50% will not respond to varicocele treatment due to recurrence, genetic abnormality, or technical failure. Therefore, the best method should have the lowest complication rates, and the ideal technique should aim for ligation of all internal and external spermatic veins with preservation of spermatic arteries and lymphatics (19,29,30).

Radiologic treatment of varicocele seems to have some advantages including a shorter recovery period, no anesthesia, and lower cost, however, has some disadvantages such as operation failure, higher recurrence rate, thrombosis, and contrast agent allergy. Patients with bilateral grade 3 varicocele should not be considered for embolization because of significantly higher technical failure rates for right-sided varicocele. Patients who present for treatment of varicocele due to infertility should be recommended for surgery rather than embolization, due to evidence-based data that suggests pregnancy rates are improved following surgery but not with embolization (32).

Laparoscopic varicocelectomy can be performed either transperitoneally or extraperitoneally and seems to have a postoperative recovery period. However, it is not possible to ligate external spermatic veins and other veins at the lower level which might cause recurrence.

High ligation has a less arterial injury at the proximal level, however, it is unable to ligate external spermatic, gubernacular veins, and other internal spermatic vein branches originating from the duplicated gonadal vein at the lower level.

Microsurgical varicocele repair can be performed via an inguinal or subinguinal approach. Although the subinguinal approach to microsurgical varicocelectomy obviates the need to open the aponeurosis of the external oblique, it is associated with a greater number of internal spermatic veins and arteries compared with the inguinal

approach. Subinguinal microscopic varicocelectomy has disadvantages, needing more skills because of the higher number of internal spermatic vein channels, and a higher risk for arterial injury due to smaller artery in diameter at the level of the external inguinal ring (33). In a study, conducted with 102 consecutive men who underwent subinguinal microsurgical varicocelectomy, a mean number of 12.9 internal spermatic veins, 0.9 external spermatic veins, 1.8 internal spermatic arteries, and 2.9 lymphatics were identified per cord. In addition, 88.2% of the internal spermatic arteries were surrounded by a dense complex of adherent veins, and the incidence of dilated external spermatic veins was 49.4% (34).

Open microsurgical inguinal or subinguinal varicocelectomy techniques have been shown to result in higher spontaneous pregnancy rates and fewer recurrences and postoperative complications than conventional varicocelectomy techniques in infertile men. The use of higher magnification allows surgeons to preserve the internal spermatic artery and lymphatics and also to visualize and ligate all spermatic veins (33).

We published a review/meta-analysis to compare all techniques (29). Overall spontaneous pregnancy rates were 37.69% in the Palomo technique series, 41.97% in the microsurgical varicocelectomy techniques, 30.07% in the laparoscopic varicocelectomy techniques, 33.2% in the radiologic embolization, and 36% in the macroscopic inguinal (Ivanissevich) varicocelectomy series, revealing significant difference among the techniques. Overall recurrence rates were 14.97% in the Palomo technique series, 1.05% in the microsurgical varicocelectomy techniques, 4.3% in the laparoscopic varicocelectomy techniques, 12.7% in the radiologic embolization, and 2.63% in the macroscopic inguinal (Ivanissevich) or subinguinal varicocelectomy series, revealing significant difference among the techniques. Overall hydrocele formation rates were 8.24% in the Palomo technique series, 0.44% in the microsurgical varicocelectomy techniques, 2.84% in the laparoscopic varicocelectomy, and 7.3% in the macroscopic inguinal (Ivanissevich) or subinguinal varicocelectomy series revealing significant difference among the techniques. We conclude that the microsurgical varicocelectomy technique has higher spontaneous pregnancy rates and lower postoperative recurrence and hydrocele formation than conventional varicocelectomy techniques in infertile men.

Postoperative pregnancies occur with a mean duration of 7 months (3-11 months) after surgery (2). The current treatment modality is microsurgical inguinal or subinguinal varicocelectomy with high improvement in postoperative semen parameters (50% at least 50% increase in total motile sperm count) and pregnancy rates (36-43%) and highly low complication and recurrence rates (0-1%) (29,30).

Microsurgical varicocele repair has a significant potential not only to obviate the need for ART but also to downstage the level of ART needed to bypass male factor infertility (2). After varicocelectomy, intrauterine insemination (IUI) may be tried again for men who had not achieved pregnancy by natural intercourse. Following varicocelectomy, the results with IUI seem to improve or 11-21% pregnancy rates per cycle (34). The initial sperm concentration is predictive of unassisted pregnancy outcome in this population (13,35). Varicocelectomy may also enhance spermatogenesis within the testis, potentially increasing the chance of successful testicular sperm extraction surgery in patients with previously failed in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) (2). Varicocele repair may also increase IVF success in men who have had a varicocele. Agarwal and Esteves (36) reviewed 4 retrospective randomized studies, including 870 cycles with regard to varicocele presence and ICSI. They concluded that performing varicocelectomy in patients with clinical varicocele prior to ICSI is associated with improved pregnancy outcomes.

Surgical Treatment of Ejaculatory Duct Obstruction

Ejaculatory duct obstruction is detected in 1-5% of azoospermic men (1). Ejaculatory duct obstruction, although rare, is a surgically correctable cause of male infertility (6,9,18). The etiology is congenital (ejaculatory duct atresia, stenosis, and cyst) and acquired (trauma, infection, inflammatory, stone, dysfunction of seminal vesicle, and prostate cancer) (9,18,19). Calculus formation secondary to infection may also cause obstruction (15). Cyst formation from prior instrumentation or infection may also occur (15). In many cases, patients with ejaculatory duct obstruction have no significant antecedent history.

It is diagnosed with low ejaculate volume and seminal fructose level, acidic pH, and dilated seminal vesicle on transrectal ultrasound.

Although treatment options for distal ejaculatory duct obstruction include endoscopic resection, balloon dilatation, and laser incision/excision, transurethral resection of the ejaculatory duct (TURED), first described by Farley and Barnes in 1973, is the primary gold standard treatment of distal ejaculatory duct obstruction (15). A 24 French resectoscope is placed into the urethra, and resection is carried out at the level of the verumontanum. Overall results from surgical correction of ejaculatory duct obstruction show a 60-70% improvement in semen parameters and a 20-30% pregnancy rate (37). In cases who did not achieve spontaneous pregnancy, TURED may increase the chance for ART and also downstage the level of ART from ICSI to IUI (9).

A common complication of TURED is the reflux of urine into the ejaculatory ducts and subsequently into the seminal vesicles, vas deferens, or even the epididymis. This reflux into the epididymis can lead to acute or chronic epididymitis. Other complications include retrograde ejaculation secondary to a bladder neck injury, incontinence secondary to external sphincter injury, and, although rare, rectourethral fistula secondary to rectal injury (6,9,13,15). Postoperative bleeding, bladder neck contractures, and erectile dysfunction are also known complications. Large defects within the prostate can allow the mixing of semen and urine, which can further impair sperm quality.

Surgical Treatment of Obstructive Azoospermia

Treatment includes vasovasostomy (VV) or vasoepididymostomy (VE) in proximal obstruction and TURED in distal obstruction. Sperm for ART may be achieved from vas deferens, epididymis, testis, and seminal vesicle in cases who failed treatment or unpossible treatment due to localization of obstruction. Vasectomy

reversal can be done with VV and VE, using microsurgery. After a vasectomy reversal, spontaneous pregnancy is possible. Patency and pregnancy rates are 70-90% and 50-70%, respectively although the success rate varies with the duration of vasectomy, pathology of obstruction, and experience of the surgeon (38). In cases who failed surgery, IVF/ICSI can be done with epididymal sperm.

Surgical Treatment of Proximal Obstructions

Epididymal obstruction can be secondary to vasectomy, congenital, inflammatory, or idiopathic (39). In an azoospermic man with normal semen volume, normal testicular size, bilateral palpable vas deferens and a normal testicular biopsy demonstrating sufficient spermatogenesis, the most likely site of obstruction is the epididymis. Prior to performing VE, vasography should be performed to document vasal patency. Vasography should only be performed at the time of a planned surgical reconstructive procedure. If vasography is performed as a separate procedure, then an additional site of obstruction can be created. Vasography can be performed with either an open or a puncture technique. The puncture technique eliminates the need for closure of the vas deferens. Radiographic contrast can be injected distally toward the abdomen, and a plain x-ray is taken to define the anatomy of the vas deferens. The patency of the vas deferens can also be verified by simply injecting saline distally. If it flows easily, then the vas deferens is assumed to be patent. Injection should not be performed toward the epididymis, because this could cause injury.

Recent modifications address one of the main technical difficulties encountered in VE, that is, suture placement in an open collapsed epididymal tubule. These newer intussusception techniques involve the placement of sutures in a distended epididymal tubule before it is opened. The technique reported by Berger uses three 10-0 sutures and that by Marmar uses 2. The main theoretical advantage of these newer intussusception techniques is that the resultant invagination of the epididymis may reduce leakage from the anastomosis. Whether these modifications will translate into improved pregnancy rates is not known (40,41).

Vasal obstruction can occur secondary to vasectomy and other scrotal surgery besides vasectomy, or lower abdominal or inguinal surgery, such as renal transplantation or herniorrhaphy. Reconstruction after renal transplantation is usually not feasible, as the abdominal end of the vas deferens retracts proximally in the retroperitoneum. Obstruction caused by hernia repair may be correctable, though these repairs are technically challenging. Crossover transseptal procedures (VV or VE) is possible when a normal testis with unreconstructable obstruction is present on one side and an atrophic testis and patent ductal system are present on the contralateral side (42).

Vasal obstruction secondary vasectomy can be corrected with microsurgical VV. When a secondary epididymal obstruction occurs after vasectomy, VE is required. Patency and pregnancy rates for VV range from 75% to 93% and from 46% to 82%, respectively (42). VE is more technically demanding and less successful than VV. Patency rates range from 67% to 85%, and pregnancy rates range from 27% to 49%. Patency can take as long as 6 months for VV and as long as 1 year following VE. The average time to achieve pregnancy was 1 year for VV.

Several investigators have attempted to use fewer sutures, augmented by fibrin glue or laser soldering for both VV and VE procedures, allowing for a shorter operative time. In addition, robotics have been used for both VVs and VEs, with the hope that it may help with microsurgical technical issues, including eliminating tremor and improving dexterity with microsurgical instruments (43). While these techniques are not the current clinical standard, they appear to yield similar patency rates and may represent alternatives for the surgeon who performs only an occasional vasectomy reversal.

Surgical Sperm Retrieval Methods

In cases surgical treatment options fail or are not possible due to localization of obstruction or the presence of older female age, sperm for the use of ART can be obtained from the urogenital tract including vas deferens, epididymis, testis, and seminal vesicles. Sperm can be obtained by microsurgical testicular sperm extraction (micro-TESE) from the testis with a success rate of 36 to 78% in non-obstructive cases, and by microsurgical epididymal sperm aspiration (MESA) from the epididymis with a success rate of 60 to 98% in the obstructive cases (44).

Men with non-obstructive azoospermia (NOA) can now be treated by using intra-oocyte round spermatid injection (ROSI) or elongated spermatid injection (ELSI) in cases for which no mature sperm are available, sperm precursors, obtained from either the ejaculate or the testis. But the rates of fertilization and pregnancy with spermatids have been disappointing (45).

CONCLUSION

Varicocele is the most commonly seen and surgically correctable cause of male factor infertility. The other reasons of male factor infertility that are surgically correctable are congenital or acquired obstructive pathologies. Treatment strategies and surgical success rates for male infertility have increased dramatically over the three decades attributable to the development of microsurgical techniques and endoscopic equipment, instrumentation, and techniques. In case of treatment failure of correctable or uncorrectable pathologies of male factor infertility, surgical sperm obtained from the urogenital tract may necessary for ART. The success of surgical sperm obtained procedures has increased dramatically over the last decades attribute to technological progress similar to surgical techniques.

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