Effect of surgical repair of varicocele in non-obstructive azoospermic patients with varicocele on the outcome of TESE

Thesis

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Presented by

Amr Sarwat Al -Ahwani

M.B.B.Ch, MSc

Supervised by

Dr. Ahmad Ateyah Awwad

Professor of Andrology and STDs,
Faculty of Medicine, Cairo University

Dr. Ibrahim Fahmy

Professor of Andrology and STDs ,
Faculty of Medicine, Cairo University

Dr. Osama Kamal Zaki

Assisstant professor of Andrology and STDs,
Faculty of Medicine, Cairo University

Faculty of Medicine

Cairo University

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Abstract

We evaluated the impact of varicocelectomy on the sperm retrieval success rate using microsurgical testicular sperm extraction in men with clinical varicocele and nonobstructive azoospermia.

The study included 100 men with complete nonobstructive azoospermia with a clinical unilateral or bilateral varicocele grades II and III. Of the patients 50 underwent successful varicocelectomy and the other 50 patients underwent directly MicroTESE without varicocelectomy.

Key words:

Effect of surgical repair of varicocele in non- obstructive azoospermic patients with varicocele on the outcome of TESE

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LIST OF ABBREVIATIONS

ASRM	American Society of Reproductive Medicine
AZF	Azoospermia factor
C1 arrest	Primary spermatocyte arrest
CDUS	Colour Doppler UltraSound
E2	estradiol
ER	Estrogen receptor
FSH	Follicle-stimulating hormone
ICSI	Intracytoplasmic Sperm Injection
LH	Lutinizing Hormone
MDA	malodialdehyde
MMP	Mitochondrial Membrane Potential
NOA	Non-Obstructive Azoospermia
OAT	Oligoasthenoteratozoospermia
RI	Resistive Index
ROS	Reactive Oxygen Species
SCO	Sertoli Cell Only
SRR	Sperm retrieval rate
TAC	Total Antioxidant Capacity
TEM	Transmission electron microscope
TESE	Testicular Sperm Extraction

Introduction

Varicocele is observed in 10-20% of the general male population, in 35-40% of men with primary infertility, and in up to 80% of men with secondary infertility ***(Witt and Lipschultz, 1993; Schlesinger et al., 1994; Kamal et al., 2001).*** Although pathogenesis of varicocele remains enigmatic, gross testicular alterations associated with varicocele are documented ***(Pasqualotto et al., 2003).*** The effect of varicocele is diverse but often can result in generalized impairment of sperm production characterized by abnormal semen quality, ranging from oligozoospermia to azoospermia ***(Gorelick and Goldstein, 1993)***.

Observation of azoospermia or severe oligozoospermia with varicocele is reported to range from 4.3% to 13.3%. It is suggestde that spermatogenesis in damaged testes may vary within a single testis, resulting in focal or ''patches'' of sperm production ***(Turek et al., 1997)***.

A primary benefit of varicocele repair in azoospermic men with spermatogenic failure is the possibility of producing motile sperm in the ejaculate **(*Palermo et al., 1992)***. Although these men had no sperm in their ejaculate, it was discovered on testicular biopsy that they often had isolated pockets of sperm production in their testes from which sperm could be retrieved ***(Jow et al., 1993)*** The success rate of varicocele repair in nonobstructive azoospermia (NOA) is still controversial.

A history of prior varicocele repair does not seem to affect the chance of sperm retrieval by TESE for men with clinical varicoceles and NOA (***Schlegel et al., 2004).*** However, after varicocele repair, one study found a return of sperm to the ejaculate in 12 of 28 (43%) men with NOA at an average follow-up of 24 months ***(Kim et al., 1999).*** Furthermore, motile sperm in the ejaculate of azoospermic patients yields superior ICSI success rates compared with sperm obtained by TESE ***(Aboulghar et al., 1997).***

Thereby, varicocele repair in completely azoospermic men has also prompted investigators to determine the effect of this procedure on spermatogenesis in NOA.

Few reports have independently found that microsurgical technique of varicocele repair in men with azoospermia resulted in induction or enhancement of spermatogenesis in some of patients ***(Esteves and Glina, 1999; Kim et al., 1999; Kadioglu et al., 2001)***.

Aim of the Work:

To evaluate the tceffe of varicocelectomy in Non-Obstructive Azoospermia (NOA) cases on the outcome of TESE.

Anatomy of the Testis

The testicular tissue is serrounded by a tough white fibrous capsule, the tunica albuginea, and invaginated anteriorly into a double serous covering, the tunica vaginalis. Posterolaterally to the testis ,lies the epididymis, which is divided into an expanded head, a body and a pointed tail inferiorly. Medially, there is a distinct groove, the sinusepididymis, between it and the testis. The epididymis is covered by the tunica vaginalis except at its posterior margin which is 'extra-peritoneal'. The testis and epididymis each bear at their upper extremities a small stalked body, termed respectively the appendix testis and appendix epididymis (hydatid of Morgagni). The appendix testis is a remnant of the upper end of the paramesonephric (Müllerian) duct; the appendix epididymis is a remnant of the mesonephros. These structures, being stalked, are liable to undergo torsion ***(Harold et al., 2006)***.

Arterial Blood Supply:

The internal spermatic artery is the main arterial supply of the testis. It arises from the aorta at or immediately below the level of the renal vessels (at the level of the second lumbar vertebra) and runs its course with the spermatic cord through the inguinal canal giving a branch to the epididymis. At the back of the testis it divides into medial and lateral branches which do not penetrate the mediastinum testis but sweep around horizontally within the tunica albuginea where their branches penetrate the testicular parenchyma (***Sinnatamby et al., 1999)***.

The testicular artery has different types of terminations; it can end up by dividing into upper polar or segmental and lower polar or segmental branches, or by giving upper polar, middle segmental and lastly it continues to the lower end of the testis. *Another type* by dividing into upper, middle and lower segmental branches. *Sometimes* it gives upper polar only and continues by itself along the mediastinum towards the lower end of the testis then it is directed to supply the antero-lateral aspect of the testis. *Lastly* it can descends without extra-testicular branches along the mediastinum testis ***(Taymour et al., 2002)***.

The testis is also supplied by the vasal artery and the cremastric artery. The artery of the vas (differential artery) arises from the inferior vesical artery and lies in contact with the vas until it reaches the epididymal head where it branches into capillary network supplying the tail and body of the epididymis. The cremastric (external spermatic artery) arises from the inferior epigastric artery and runs its course towards the internal inguinal ring where it enters the coverings of the spermatic cord and continues to anastmose with the capillary network of the differential and internal spermatic arteries ***(Sinnatamby et al., 1999)***.

The testicular artery anastomoses with the artery to the vas, supplying the vas deferens and epididymis, which arises from the inferior vesical branch of the internal iliac artery. This cross-connection means that ligation of the testicular artery is not necessarily followed by testicular atrophy ***(Beck et al., 1992; Yamamoto et al., 1995)***.

Contrary to classical anatomical descriptions, Jarow and his team observed that often more than 1 branch of the internal spermatic artery is present at the level of the proximal inguinal canal. Many surgeons who perform varicocelectomy assume that only 1 artery is present at this level and ligate all other vascular structures once an artery has been identified. they determined the frequency and number of internal spermatic arteries present within the spermatic cord in the proximal inguinal canal. The number of internal spermatic arteries present at this level was studied in 15 spermatic cords of 12 patients undergoing varicocelectomy using loupe magnification and intraoperative Doppler ultrasound. The number of arteries ranged from 1 to 3, with a mean of 2 arteries. Histological studies of the same area of 17 spermatic cords obtained from cadavers revealed a mean of 2.4 arteries (range 1 to 3). Knowledge of the frequent early branching of the internal spermatic artery will prevent inadvertent interruption of testicular arterial blood flow during operations performed upon the spermatic cord within the inguinal canal.***(Jarow, Ogle et al. 1992***)

Reporting on the intraoperative anatomy of 83 infertile men who underwent microsurgical varicocel-ectomy at the inguinal level, 1 artery was identified in 69% of dissections, 2 arteries in 27% of dissections, and 3 or more arteries in 4% of spermatic cords ***(Beck et al, 1992).*** In a follow-up report, the same group identified 2 arteries in 42% of all dissections and 3 arteries in 33% of the spermatic cords during microsurgical varicocelectomy at the subinguinal level ***(Hopps et al, 2003)***.

Venous Drainage:

Classically the venous drainage system of the scrotal contents includes the testicular (internal spermatic) vein, which, drains into the renal vein on the left side or the inferior vena cava, on the right side. The vasal (differential) vein, which, drains into the vesicular veins. The cremastric (external spermatic) vein, which, drains into the inferior epigastric vein. These vessels are highly anastmotic and form the pampiniform plexus ***(Fretz & Sandlow, 2002)***.

The venous drainage system is divided into the superficial system via the scrotal veins and the deep system that drains the pampiniform plexus. The superficial system consists of the external spermatic, cremastric, ductus deferens, and scrotal, gubernacular, superficial epigastric, and external pudendal, superficial circumflex iliac, saphenous and femoral veins. The deep system includes the penile, crural, ureteric, obturator, renal capsular, colonic and lumbar veins ***(Coolaset et al., 1980; Wishahi et al., 1991 a; Beck et al., 1992)***.

At the fourth lumbar vertebra ,the internal spermatic vein divides into medial and lateral divisions. The lateral division terminates at the inferior vena cava or the renal vein, whereas the medial branch anastomoses with the urethral veins and may cross-communicate with the contra-lateral vein ***(Wishahi et al., 1991 b)***.

Left to right venous communication is also present at various levels, at the ureteric, spermatic, scrotal, retro-pubic and sacral veins. Also, at the saphenous system and deep pampiniform plexi. The complex anatomic nature of the venous drainage of the scrotal contents may explain the failure of surgery in treating varicocele, in particular procedures performed above the level of the fourth lumbar vertebra ***(Wishahi et al., 1991 a; Turek & Lipshultz, 1995)***.

The testicular vein presents numeric variations and also variations in its local of termination. In approximately 30% of the cases, there are collaterals that communicate the testicular vein with retroperitoneal veins. These anatomic findings can help understanding the origin of varicocele and its recurrence after surgical interventions. At the right side , One testicular vein occurred in 85% and 2 veins in 5% of the cases. There were communicating veins with the colon in 21% of the cases. While at the left side , One testicular vein occurred in 82%, two veins in 15%, three veins in 2% and four veins in 1% of the cases. There were communicating veins with the colon in 31% of the cases **(Luciano et al.,2007).**

Variations of gonadal veins were more frequent on the left side, as observed by **Asala et al (2001)**, who found only 2 cases of right gonadal vein draining into right renal vein out of 150 cadavers dissected. The testes are important organs whose veins and arteries play major role in their thermo-regulation that is essential for efficient functioning of the organs. Thus variations of testicular venous drainage are very significant while performing surgery or radiology. During endo-urological procedures, anatomical variations of renal and gonadal veins have got immense significance as lesions in them may cause severe back bleeding during and after surgery. These variations may remain clinically silent and usually unnoticed until discovered during operation or autopsy **(Hoeltlet al., 1990).**

In a recent study done by Biswas and his colleges, they report the presence of an additional renal vein on the right side draining directly into IVC. This variation was observed during a routine dissection in a middle-aged male cadaver. On further dissection it was seen that this additional vein received the right testicular vein. Both the renal veins of the right side had a normal course, lying anterior to the renal artery and ureter. On the left side, two veins were coming out from the upper and lower ends of the hilum and they joined to form a single left renal vein, which passed in front of the aorta. The lower tributary of the left renal vein rather than the left renal vein received the testicular vein of the left side **(Biswas et al.,2006)**.

Regarding the total number of valves, except for those of the pampiniform plexuses, the left side was found contain a greater number of valves. As regards valve types, there is a predominance of double semilunar one on both sides rather than single semilunar valves

(Chopard et al., 1992).

Kuypers and his group studied thirty-one in male dissecting room cadavers and fifteen male autopsy subjects. On the left side, valves were absent throughout the course of the main testicular vein in 20 subjects, and on the right they were absent in eight. However, on the left side six subjects also had an accessory testicular vein; in five of these, valves were absent. On the right, two subjects had an accessory vein, but both had valves present. Thus a valveless venous pathway of drainage was present in 25 of the subjects on the left and eight on the right. This difference was statistically significant to $P < 0.001$ **(Kuypers et al.,2005).**

Lymph Drainage:

The lymphatic system drains to the para-aortic lymph nodes at the level of the renal vessels. Free communication occurs between the lymphatics on either side. ***(Sinnatamby et al., 1999)***.

Nerve Supply:

Sympathetic fibers emerge from the tenth thoracic vertebra via the renal and aortic plexus. These convey afferent (pain) fibers, hence, refer pain from the testis to the loin ***(Harold et al., 2006)***.

Impact of Varicocele on Fertility:

I. Pathogenesis of Varicocele:

The incidence of varicocele is approximately 15% of the general population, 35% of men with primary infertility and in 75-81% of men with secondary infertility ***(Gorelick et al., 1993)***. The term `varicocele', refers to an abnormal dilatation, elongation and tortuosity of the testicular veins within the pampiniform plexus ***(Benoff & Gilbert, 2001)***.

Varicocele is classically divided into primary and secondary types. Secondary varicocele occurs when the renal or internal spermatic vein is compressed by a mass or neoplasm, whether renal or retroperitoneal. Secondary varicocele characteristically does not disappear when the patient attains the supine position ***(Bowse, 1991)***. ***)***. Pathologically, a varicocele is the result of the retrograde reflux of blood down the internal spermatic vein causing dilatation of the pampiniform plexus ***(Jequire et al., 2000)***.

Varicocele occurs more frequently on the left side, most probably due to asymmetry of the internal spermatic veins resulting in alterations in biochemical properties ***(Lund et al., 1998).***The length of the left internal spermatic vein has been determined to be 8-10 cm longer than the right spermatic vein. Additionally, the left internal spermatic vein enters the left renal vein perpendicularly; while on the right, the internal spermatic vein drains obliquely into the inferior vena cava. These combined anatomic realities may result in increased hydrostatic pressures transmitted to the left pampiniform plexus, perhaps resulting in varicocele formation ***(Colpi et al., 2006 a).***On the other hand it was mentioned that valves may be absent in the internal spermatic vein in men without varicocele ***(Wishahi, 1991 b)***.