The role of microsurgery in the treatment of male infertility in Romania

Abstract

When facing an infertile male there are two main treatment options: either etiologic treatment or in vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI). Although FIV/ICSI is a remarkable procedure, we must resist the temptation of recommending it out of reflex to infertile couples due to male infertility, without a systematic urologic evaluation. Half of the males with infertility can be cured by a proper etiologic treatment. Microsurgical reconstruction in obstructive azoospermia and microsurgical subinguinal varicocelectomy are procedures with a better cost/efficiency ratio than FIV/ICSI and have the advantage of treating the cause of male infertility. In case of non-obstructive azoospermia, where the couple's only chance of reproduction is FIV/ICSI, micro TESE is the most efficient method of retrieving sperm. Infertility specialists should offer their patients the chance to receive the best possible existing treatment, rather than the best possible treatment they can provide.

Keywords: *male infertility, microsurgery, non-obstructive azoospermia, obstructive azoospermia, varicocele*

Mihai C. Harza[1], Sebastian N. Voinea[1], Radu Vladareanu[2]

1. Centre of Uronephrology and Renal Transplantation, Fundeni Clinical Institute, Bucharest (Romania)
2. "Carol Davila" University of Medicine and Pharmacy, Elias Emergency University Hospital, Bucharest (Romania)

Correspondence:
Dr. Sebastian N. Voinea
e-mail: voiniseb@yahoo.com

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Introduction

In 1667 Antoni van Leeuwenhoek pioneered the area of male reproduction by describing the 'animalculus' - the living spermatozoon. In 1902, E. Martin made a second breakthrough by describing the macroscopic termino-lateral vasoepididymostomy (VES) as a treatment for azoospermia secondary to epididymal obstruction. The results obtained after the 'macro' reconstruction of the spermatic tract were poor, due to the lack of accuracy. Beginning with 1978, when Silber reported the first microsurgical VES (the anastomosis between a single seminiferous tubule and the vas deferent) microsurgery became the most efficient method of treatment for infertile males. Later on, it was proven that the use of a surgical microscope leads to the best results not only in the treatment of spermatic tract obstruction, but also in the cure of varicocele and for sperm retrieval in non-obstructive azoospermia[(1)]. Another important innovation in the field of human reproduction was made by a group lead by van Steirtegheim - the first pregnancy obtained through *in vitro* fertilization (IVF) with intracytoplasmic sperm injection (ICSI). This method involves the injection of a single spermatozoon in an ovule and the development of an embryo which is then transferred in the uterus. The role of microsurgery will be discussed for each of the following entities: obstructive azoospermia, non-obstructive azoospermia and varicocele[(2)].

Vas deferens and epididymal obstruction

Total or partial obstruction of the male genital tract represents 5-10% of the cases of male infertility. In 80% of these cases surgical reconstruction is possible. Vasectomy is a contraceptive method seldom used in Romania. However, it is expected that the incidence of primary obstructive azoospermia within the Romanian population is high, due to the high incidence of sexually transmitted infections - the main cause of primary obstructive azoospermia in Romania. A report published under the auspices of USAID revealed that the prevalence of syphilis and gonorrhea in males between 15 and 49 years old is 10 to 15 times higher than the prediction made by the World Health Organization for our region. Despite this reality, it is a less known fact, even in the medical world, that these patients have similar clinical manifestations with males with obstructive azoospermia secondary to vasectomy: normal hormonal values (FSH, LH, Testosterone, Prolactin, Inhibin B), normal testicular volumes, normal genetic configurations (the absence of Y chromosome microdeletions / normal caryotype). The most common site for primitive testicular obstruction is the epididymal tail. Microsurgical reconstruction is the first line treatment for azoospermia secondary to vasectomy, with a patency and a natural pregnancy rate of 60-95%, respectively 27-49%. Although, the results of reconstruction are essentially the same for patients with primary epididymal obstruction (Table 1), many physicians working in infertility are not aware of this data[(3)].

Our results are similar with the ones published by the cited authors. We performed microsurgical VES according to Berger in 22 patients with azoospermia secondary to primitive epididymal obstruction, with a patency rate of 81% and a pregnancy rate of 22.7%. Goldstein at al. brought two modifications to the original Berger technique: the longitudinal incision of the seminiferous tubule (in opposition to a transverse incision) and the use of double arm fishhook needle, 10, 2.5 cm long suture material - much shorter than the

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ones previously in use. Although we have yet to reach an adequate number of cases, these changes lead to better 3 month patency rates in comparison with the Berger technique, 81% vs. 54% (unpublished data).

Micro TESE

Infertility secondary to non-obstructive azoospermia is most severe and difficult to treat. Until recently, the only options were IVF with a sperm donor or adoption, but recent research has lead to a radical change in this field. Men suffering from non-obstructive azoospermia have a severely altered spermatogenesis, but non-uniform. The testicular histology of men suffering from non-obstructive azoospermia is always modified, showing a combination of Sertoly-cell-only, maturation arrest, associated with microscopic areas of hypospermatogenesis. Testicular biopsy/ aspiration randomly harvests <5% of the seminiferous tubules, with a very small chance of finding the usually inframillimetric areas where the spermatogenesis is present. Micro TESE involves a wide equatorial testicular incision (at least 270°) and the microscopic assisted dissection (X15 – X20) of the testicular tissue, in order to identify dilated, whitish and opaque tubules which often contain viable spermatozoa, suitable for IVF. The dissection is performed under microscopic magnification, along the testicular vessels, decreasing the risk of damaging the testicular blood supply. Small bleedings are promptly controlled using a bipolar coagulation allowing minimum damage of the neighboring seminiferous tubules. The dissection is performed first superficially and, if sperm is not found, deep into the testicular parenchyma. In this way the microdissection allows an inspection of all the testicular tissue and maximizes the chance of finding sperm[4].

Should we perform microTESE for every male with non-obstructive azoospermia? The males with complete deletions of the AZFa and AZFb regions of the Y chromosome (but not in AZFc regions) have a very low likelihood of finding sperm by microTESE. Excepting these genetic anomalies, microTESE is indicated in all males with non-obstructive azoospermia, no matter the etiology (like post chemotherapy or non-mosaic Klinefelter's syndrome). The level of FSH or the volumes of the testis are not predictors of success for retrieving sperm by microTESE. Even in males with very high FSH level (over 90 IU/L) sperm can be retrieved by microTESE[5,6] (Table 1).

MicroTESE allows retrieving sperm in half of the patients with previous failed biopsy or TESE (one or two attempts per testis). The testicular blood supply goes immediately under the albuginea, so serial biopsies/TESE will lead to the formation of more scar tissue in the testicular parenchyma and less chance of finding sperm for subsequent microTESE. In males with non-obstructive azoospermia with more than three biopsies per testis the retrieving rate with microTESE decreases at 22%[7].

Overall, the majority of studies have shown that micro TESE has three advantages: it increases the chance of retrieving spermatozoa (50-70%), it removes a small quantity of testicular tissue (avoiding testicular insufficiency) and it lowers the risk of damaging the testicular vessels, with a subsequent testicular atrophy. However, in Romania microTESE is a very rare procedure. Usually for these patients a small biopsy is performed and if it fails to retrieve sperm, donor sperm fertilization is used depriving many males of the opportunity to have biological children.

Microsurgical subinguinal varicocelectomy with testicle delivery

Varicocele represents the most common cause of male infertility. The surgical cure of varicocele can be performed in a classic manner - open surgery (retroperitoneal, inguinal, subinguinal), or through a minimally invasive approach, such as laparoscopy or embolization. However, conception and complication rates are significantly different. An ideal varicocelectomy should respect the following criteria: spare all arteries (especially the internal spermatic artery - the main blood supply of the testicle), spare lymphatic vessels, as well as the deferent vas with its vessels, ligation of all gubernacular, internal and external spermatic veins, use a mini incision without splitting the fasciae or muscle and no X-ray exposure.

High ligation and laparoscopy represented the standard of treatment for palpable varicocele for many years. With these techniques the internal spermatic artery is not spared in the majority of cases. The internal spermatic artery is the main arterial supply for testis and is very improbable that after its ligation the testicle will have a better function. Moreover, these techniques will miss all the external spermatic and gubernacular veins explaining the higher postoperative recurrence rate. In addition, the retroperitoneal and inguinal approach is associated with a

Table 1 The results of microsurgical reconstruction in the treatment of primitive azoospermia secondary to epydidimal obstruction

Patients number	Potency rate (%)	Natural pregnancy rate (%)	Mean follow-up	Author, year
43	81%	37%	42 ± 17	Lipshultz[2], 1998
61	68.9%	21.3%	24	Paick[3], 2000
29	48%	_	3.2	Kumar[4], 2006

Table 2 The main advantage/disadvantage of treatment options for palpable varicocele

Technique	Internal spermatic veins	External spermatic veins	Morbidity	Recurrence	Restore sperm quality
High ligation	yes	no	+++	+++	++
Inguinal (macro)	yes	yes	++	++	+
Laparoscopy	yes	no	++	++	+
Embolization	yes	yes	+	++	+
Subinguinal (micro)	yes	yes	+	+	+++

Legend: +++ high, ++ medium, + low

longer recovery time due to opening the external oblique fascia. Percutaneous embolization is a minimally invasive technique with a reported success of vein occlusion of 90%. The high complications rate and exposure of the testis to X-ray (with negative effect on spermatogenesis) are the main disadvantages.

Microscopic subinguinal varicocelectomy with testicular delivery meets all the criteria of an ideal surgical cure for varicocele. The spermatic cord was approached through a 2-3 cm transverse incision centered over the external inguinal ring. The delivery of the testicle allows a good exposure of all the veins responsible for varicocele (gubernacular, internal and external spermatic veins). The use of the surgical microscope facilitates not only the preservation of the vas deferens with its vessels, but also that of any other testicular artery and lymphatic. As we passed the learning curve, the results with this technique for our recent series show a natural conception rate of 31% in the first year, 52% after the second year, with a very low complication rate (bleeding 0%, clinical hydrocele 0%, testicular atrophy 0%, recurrence 2.3%).

A comparative evaluation of treatment options for infertile males with palpable varicocele[8-12] is depicted in Table 2.

The current standard of care is to perform open surgical microscopic varicocelectomy with delivery of the testis in order to obtain the best results and minimize possible complications.

Conclusion remarks

Very few assisted reproduction clinics from Romania have an urologist on staff, who can treat the cause of male infertility, or who can collaborate with other infertility specialists when taking a decision regarding the proper treatment. Roughly half of the males with infertility can be cured by a proper etiologic treatment. Although FIV/ICSI is a remarkable procedure, we must resist the temptation of recommending it out of reflex to infertile couples due to male infertility, without a systematic urologic evaluation. This reflex is not in the man's best interest because it denies him the opportunity to benefit from a procedure that can treat the cause of his infertility and can become harmful by overlooking other conditions responsible for male infertility (from the most common - cryptorchidism, hypospadias to the most severe - testicular tumors). Microscopic reconstruction in obstructive azoospermia and microscopic subinguinal varicocelectomy are procedures with a better cost/efficiency ratio than FIV/ICSI and they also have the advantage of treating the cause of male infertility. In case of non-obstructive azoospermia, where the couple's only chance of reproduction is FIV/ICSI, micro TESE is the most efficient method of harvesting spermatozoa, even when other techniques have failed. In the end we consider that infertility specialists should offer their patients the chance to receive the best possible existing treatment, rather than the best possible treatment they can provide. ■

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