available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Sperm Cells for Artificial Reproduction and Germ Cell Transplantation

Wolfgang H.G. Weidner *, *Hans-Christian Schuppe*, *Adrian Pilatz*, *Bora Altinkilic*, *Thorsten Diemer*

Department of Urology, Pediatric Urology and Andrology, Justus Liebig-University, Giessen, Germany

Article info

Keywords:
Sperm retrieval
Azoospermia
TESE
IVF/ICSI
Germ cell transplantation

Abstract

Sperm retrieval for in vitro fertilization/intracytoplasmic sperm injection is the only medical procedure that enables a man with testicular azoospermia to father a child. In obstructive azoospermia after failed refertilization, microsurgical epididymal sperm aspiration is the gold standard, with retrieval rates up to 100%. In nonobstructive azoospermia (NOA), testicular spermatozoa (spermatids) can be recovered by testicular sperm extraction (TESE) in approximately half of the men. No parameters are available to definitively predict a successful recovery individually, but genetic factors, reduced testicular volume, and high serum follicle-stimulating hormone levels are associated with an unfavorable outcome. Retrieval surgery is well standardized, chiefly performed with microsurgical assistance and without severe local complications. Microsurgically assisted TESE (M-TESE) and TESE that is not microscopically supported in low-chance NOA patients may result in hypogonadism in the long term. In patients with Klinefelter syndrome, the outcome is worse with increasing age. For children before chemotherapy, M-TESE for stem cell preservation must be performed with minimal damage to the testicles.

* Corresponding author. Department of Urology, Pediatric Urology and Andrology, Justus Liebig-University Giessen, Rudolf-Buchheim-Strasse 7, D-35392 Giessen, Germany. Tel. +49 0641 985 44501; Fax: +49 0641 985 44509.
E-mail address: Wolfgang.Weidner@chiru.med.uni-giessen.de (Wolfgang H.G. Weidner).

1. Introduction

For years, males without spermatozoa in their ejaculate were regarded as irreversibly infertile. With the introduction of intracytoplasmic sperm injection (ICSI) in 1992 [1], azoospermic patients could be offered infertility treatment by surgical sperm retrieval from their reproductive tract. Standardized technologies were established worldwide, and viable pregnancies were reported from ICSI using sperm from testicular or epididymal origin [2,3]. Child birth rates were shown to be similar for sperm that had been prepared mechanically or enzymatically or that were cryopreserved [4].

There is worldwide consensus on the indications for sperm retrieval (Table 1). Generally, two different clinical scenarios must be distinguished. First, in men with obstructive azoospermia (OA), epididymal sperm aspiration and conventional, not microscopically supported testicular sperm extraction (TESE) or testicular fine-needle sperm aspiration have been used successfully to retrieve elongated spermatids with a success rate of up to 100% [5]. Second, in patients with nonobstructive azoospermia (NOA), the

http://dx.doi.org/10.1016/j.eursup.2014.07.001

Table 1 – Indications for sperm retrieval

Surgery of the seminal duct
• Not feasible (congenital bilateral absence of the vas deferens)
• Not indicated (eg, female age, female pathologies)
• Not desired by the couple
• Surgical failure
Ejaculatory disorders
Nonobstructive azoospermia

probability of finding elongated spermatids in the testes is significantly lower, with retrieval rates of up to 66% depending on the patient population, a multifocal approach, and the use of microsurgically assisted TESE (M-TESE) during the procedure [6–11].

2. Sperm retrieval in obstructive azoospermia

2.1. *Sperm retrieval during or after failed refertilization (vasovasostomy and tubulovasostomy)*

In the age of modern artificial reproduction techniques, the usefulness of "redo" procedures for refertilization is questioned by many gynecologists, although there has been consensus for years that sperm retrieval and ICSI should be used only when reconstructive microsurgery has definitely failed [12,13]. Even in cases of repeat bilateral vasovasostomy, patency rates are reported in up to 85.9% of patients [14,15] and for tubulovasostomy, in approximately 41–69% of patients [16]. The mean pregnancy rates achieved are approximately 74%, whereas the mean pregnancy rates for ICSI/sperm retrieval are only approximately 25–39% [12]. Thus, we and others are counseling couples after failed refertilization procedures that sperm retrieval for in vitro fertilization (IVF)/ICSI should be used only when repeat reconstructive microsurgery has definitely failed.

In some cases, couples ask for sperm retrieval during refertilization procedures. During vasovasostomy, direct duct aspiration may be helpful, although older data demonstrated no spermatozoa in duct aspirates in up to 27% of patients [17]. For tubulovasostomy procedures, we suggest adding a trifocal TESE if the couple requires this additional procedure as a backup.

2.2. *Epididymal sperm retrieval*

Microsurgical epididymal sperm aspiration (MESA) for the retrieval of sperm for IVF/ICSI is the standard procedure for men with OA who have had a failed microsurgical reversal or who have an underlying morbidity hindering reconstruction [18]. The operation provides a sperm retrieval rate of as high as 95%, and these sperm can be used for multiple IVF/ICSI cycles [3,18]. A special indication for all types of epididymal sperm retrieval is OA patients with a low-volume ejaculate, acidic pH, absence or low concentrations of seminal plasma fructose, lack of seminal α-glucosidase, and agenesis of the vasa deferentia [19]. In these cases, palpation is decisive for the identification of the vasa. Genetic examination of the couples for abnormalities of the cystic fibrosis transmembrane conductance regulator (ATP-binding cassette sub-family C, member 7) gene (*CFTR*) is mandatory to counsel the couple about the risks of having offspring with cystic fibrosis and/or infertility.

MESA is the treatment of choice [19], with the possibility of retrieving a high number of motile sperm with minimal blood contamination [3,18,19]. Usually MESA is performed under general anesthesia. Percutaneous epididymal sperm aspiration seems to be equally effective and can be performed under local anesthesia. For both techniques, complications are negligible [18].

2.3. *Testicular sperm retrieval in obstructive azoospermia*

Theoretically, in OA, epididymal and testicular sperm retrieval seem to be equally effective in outcome, with delivery rates of approximately 100% [5]. The retrieval location, either epididymal or testicular, does not matter for fertilization, clinical pregnancy rates, or live births [3]. Percutaneous sperm aspiration may also be successful [5]. A decreased rate of pregnancies using testicular sperm in these cases demonstrates a questionable advantage for epididymal retrieval in the obstructive situation [20,21]. Pragmatically, we advise such couples to retrieve sperm from the epididymal head first, especially in cases of congenital bilateral absence of the vas deferens [19], and to switch to testicular retrieval if the MESA procedure fails.

3. Testicular sperm extraction in nonobstructive azoospermia

Since the first successful ICSI procedure using sperm retrieved from the testis approximately 20 yr ago [22,23], numerous studies have addressed the best surgical technique for testicular sperm retrieval in NOA patients [5,20,24,25]. Two surgical innovations have been proposed to improve surgical sperm recovery rates. First, based on the heterogeneity of spermatogenesis with a random distribution of focal intact areas in patients with NOA [6,26], trifocal TESE [5,8,11,27] using the upper, middle, and lower pole of the testis has frequently been used to increase retrieval rates. Second, with the introduction of M-TESE [28], a technique that identifies the dilated tubules with foci of intact spermatogenesis more reliably, a further option of retrieving elongated spermatids (testicular sperm) has become available. The results are generally excellent, with retrieval rates of up to 60%, even in patients with a poor prognosis [27,9,29,10].

In spite of these surgical improvements, a Cochrane database review in 2008 came to the conclusion that there is insufficient evidence to recommend any sperm retrieval technique for azoospermic men, leaving this important field of surgical andrology still open to debate [30]. Nevertheless, there seems to be a rationale to suggest a multifocal approach in NOA patients and to consider M-TESE as an additional option for better results in different forms of mixed pathology with heterogeneous tubular size [5]. Especially in a subgroup of NOA men with small testes and/or high follicle-stimulating hormone (FSH) levels