Evaluation of diagnostic testis biopsy and the repetition of testicular sperm extraction surgeries in infertility patients

Alayman Hussein, M.B.B.C.H., M.Sc., M.D.

Urology Department, Minia University, El-Minia, Egypt

Objective: To evaluate the use of a diagnostic testis biopsy and a repetition of testicular sperm extraction (TESE) surgeries in azoospermic patients and its impact on the outcome of TESE.
Design: Retrospective, case–control study.
Setting: University IVF center and hospital.
Patient(s): A total of 552 azoospermic patients undergoing TESE for intracytoplasmic injection.
Intervention(s): At the time of the TESE, a piece of testicular tissue was prepared for histopathologic evaluation.
Main Outcome Measure(s): Sperm retrieval rate.
Result(s): Testicular sperm retrieval was successful in 100% of patients with obstructive azoospermia, 95.6% of patients with hypospermatogenesis, 47.9% of patients with maturation arrest, and 28.6% of patients with Sertoli cell–only syndrome in cases with no previous testicular surgery; in 100%, 91.4%, 32%, and 13.3%, respectively, in cases with a history of one testicular surgery; and in 100%, 10%, 0, and 0, respectively, in cases with a history of two testicular surgeries.
Conclusion(s): Testicular sperm retrieval may be successful for some patients in each histopathologic category of azoospermia, with variable degrees of success for different histopathologic categories. The repetition of testicular surgeries decreases the chance of finding sperm in subsequent testicular sperm retrieval procedures. (Fertil Steril® 2013;100:88–93. ©2013 by American Society for Reproductive Medicine.)
Key Words: Testis biopsy, TESE, ICSI

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A diagnostic testis biopsy with a histologic examination of the seminiferous tubules was used classically in azoospermic patients to distinguish obstructive from nonobstructive azoospermia and to assess the type and degree of impairment of spermatogenesis in nonobstructive azoospermia (1). For men with nonobstructive azoospermia, intracytoplasmic sperm injection (ICSI) remains the only treatment option in case of successfully retrieving sperm from the testis.

Finding sperm for ICSI is a challenge in some cases of nonobstructive azoospermia (2). Modifications of conventional testicular sperm extraction (TESE) to increase the chance of sperm retrieval in nonobstructive azoospermia include testicular mapping and microsurgical dissection of the seminiferous tubules (3–5).

The aim of any investigation in medicine is to make a correct therapeutic decision with a high degree of confidence. A trend in the previous years is to avoid invasive diagnostic procedures if it does not help in choosing the optimum line of treatment, even if it helps to determine the exact etiology.

In this study we tried to determine whether knowing the details of the histopathology of the testicular tissue would change the decision for TESE. In addition, we studied the complications of a diagnostic testis biopsy and the effect of repetition of TESE surgeries on the probability of finding sperm in TESE for ICSI.

MATERIALS AND METHODS

This retrospective study was conducted between July 2002 and June 2011 at Minia National Hospital and Minia University Center of Assisted Reproduction, El-Minia, Egypt, with approval of the Institutional Review Board of the

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Reprint requests: Alayman Hussein, M.B.B.C.H., M.Sc., M.D., Minia University Hospital, Urology Department, Kornish El-Nile Street, El-Minia 61111, Egypt (E-mail: alaymanh@hotmail.com).

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Faculty of Medicine, Minia University. A total of 552 azoospermic patients undergoing TESE for ICSI were included in this study. All included patients were evaluated by a routine history, physical examination, and multiple semen analyses. At a minimum, three semen analyses with centrifugation of the specimen and a microscopic examination of the pellet were performed on each patient to confirm azoospermia. In all patients, we measured the morning plasma T and FSH levels and performed a scrotal ultrasound and Doppler ultrasound to measure the size of the testis and to detect a varicocele or any other associated pathology before and 3–6 months after TESE. We excluded patients with a varicocele, patients with a history of testicular malignancy, and those who received radiotherapy or chemotherapy. Additionally, we excluded patients with a history of varicocele ligation and those who were receiving hormonal treatment to stimulate spermatogenesis.

Of the 552 azoospermic patients, 176 patients had a history of conventional TESE and a diagnostic testicular biopsy and histopathologic assessment in other centers. In 72 of them, the conventional TESE was successful, whereas the conventional TESE failed to recover sperm in 104 patients. A microscopic slide revision of a previously performed testicular biopsy for each patient was performed by a single pathologist. The histopathologic diagnosis was based on the predominant histology. All patients were included, regardless their histopathologic pattern.

We performed a microsurgical testicular sperm retrieval on one side of all patients. If we did not find sperm in the fresh examination, we opened the other testis and dissected the seminiferous tubules under an operating microscope, and a piece of fully dilated tubules was taken and examined for sperm. The size and number of pieces of testicular tissue taken in each patient varied according to the presence of sperm in the fresh biopsy and the size of the testis. For patients with no previous histopathologic assessment, a piece of testicular tissue was prepared for histopathologic evaluation by the same pathologist at the time of the micro-TESE.

The micro-TESE was repeated once in 64 patients (24 had a previous conventional TESE and diagnostic testis biopsy) and twice in 36 patients (none had a previous conventional TESE and diagnostic testicular biopsy). In all cases, the micro-TESE was performed at least 6 months after any previously successful TESE.

Three to six months after the micro-TESE, libido was assessed by an open-ended question by the physician, and the patients were examined for any scrotal mass, indurations, or tenderness. Additionally, we measured the morning plasma T and FSH levels and performed a scrotal ultrasound to measure the size of the testis and to detect any postoperative complications.

In addition to measuring the size of the testis, we used a scrotal ultrasound and Doppler ultrasound to detect and evaluate testicular focal lesions, which reflect postoperative chronic testicular changes, including fibrotic and ischemic areas and old hematomas. We did not use the testicular ultrasound findings in the first month because a diffuse heterogeneity of the testis may be due to temporary testicular edema, and hypoechoic areas may indicate an absorbable hematoma.

A statistical analysis was performed to study the correlation between successful sperm retrieval and the size of the testis, FSH level, histopathologic pattern, and the number of previous testicular surgeries. Statistics software (SPSS) was used for the statistical analysis. Continuous variables were expressed as the mean ± SD. When appropriate, we used the Pearson's correlation coefficient test and independent-sample t test for comparison of continuous variables and the χ^2 test and Mann-Whitney U tests to compare categoric variables, and we considered $P<.05$ a significant value.

RESULTS

Our study included 552 azoospermic patients undergoing TESE for ICSI. The mean age of the patients was 31.6 ± 5.5 years. We added the testicular size of the right testis to that of the left testis in each patient and used the sum as one unit that corresponded to the total testicular size. The mean total testicular volume, which was measured by ultrasound, was 24.2 ± 3.3 cm^3. The mean FSH level was 18.4 ± 11.9 IU/L (range 1.8–58.2 IU/L). The mean total T level was 684.2 ± 211.3 ng/dL. We performed unilateral TESE in 116 cases with obstructive azoospermia and in 108 cases with nonobstructive azoospermia, and we performed bilateral TESE in 328 cases of nonobstructive azoospermia.

We studied the effect of the repetition of testicular surgery on the success of the testicular sperm retrieval and found a significant decrease in the testicular sperm retrieval rate with the repetition of testicular surgeries ($P=.001$). The testicular sperm retrieval was successful in 80.3% of patients with no previous testicular surgery, 57.4% of patients with a history of one previous testicular surgery, and 16.6% of patients with a history of two testicular surgeries.

In the 216 patients with a history of one previous testicular surgery, 40 patients had a history of a successful micro-TESE (2 obstructive and 38 nonobstructive azoospermia), 72 patients had a history of a successful conventional TESE (39 obstructive and 33 nonobstructive azoospermia), and 104 patients had a history of a negative conventional TESE (all of them nonobstructive azoospermia). We did not find a significant difference in the sperm retrieval rate in all patients, obstructive and nonobstructive, using the microdissection technique in patients with a history of successful conventional TESE and in patients with a history of successful micro-TESE ($P=.091$). The micro-TESE was successful in 82.5% of patients (33 of 40) with a history of a successful micro-TESE and in 87.5% of patients (63 of 72) with a history of a successful conventional TESE. Sperm retrieval was successful in all patients with obstructive azoospermia. In nonobstructive azoospermic patients, we found that the sperm retrieval rate using the microdissection technique is higher in patients with a history of successful micro-TESE (81.6%, 31 of 38) than in patients with a history of successful conventional TESE (72.7%, 24 of 33), but the difference was not statistically significant ($P=.063$). The application of micro-TESE in patients with a history of a negative conventional TESE (all of them nonobstructive azoospermia) successfully recovered testicular sperm in 26.9% of cases (28 of 104).