Severe Testicular Atrophy does not Affect the Success of Microdissection Testicular Sperm Extraction

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Purpose: Men with azoospermia and severe testicular atrophy may be counseled to avoid sperm retrieval due to perceived limited success. We evaluated the outcomes of microdissection testicular sperm extraction in men with severe testicular atrophy (volume 2 ml or less).

Materials and Methods: We reviewed the records of 1,127 men with nonobstructive azoospermia who underwent microdissection testicular sperm extraction followed by intracytoplasmic sperm injection. They were classified into 3 groups based on average testicular volume, including 2 ml or less, greater than 2 to less than 10 and 10 or greater. Sperm retrieval, clinical pregnancy and live birth rates were calculated. Clinical features evaluated included age, follicle-stimulating hormone level, cryptorchidism history, Klinefelter syndrome, varicocele and testicular histology on diagnostic biopsy.

Results: Testicular sperm were successfully retrieved in 56% of the men. The sperm retrieval rate in those with a testicular volume of 2 ml or less, greater than 2 to less than 10 and 10 or greater was 55%, 56% and 55%, respectively. Clinical pregnancy and live birth rates were similar in men in the 3 groups who underwent sperm retrieval (55.2%, 50.0% and 47.0%, and 47.2%, 43.0% and 42.2%, respectively). Of the 106 men with an average testis volume of 2 ml or less those from whom sperm were retrieved were younger (31.1 vs 35.2 years) and more likely to have a history of Klinefelter syndrome (82.2% vs 55.6%) than men in whom sperm were not found ($p < 0.05$). Men in this group had a higher prevalence of Klinefelter syndrome than men with a testis volume of greater than 2 ml (72.6% vs 5.3%, $p < 0.0001$). Men younger than 30 years with Klinefelter syndrome had a higher sperm retrieval rate than men older than 30 years without Klinefelter syndrome (81.8% vs 33%, $p < 0.01$). There was no cutoff point for age beyond which sperm could not be retrieved in men with small testes. On multivariable analysis younger age was the only preoperative factor associated with successful sperm retrieval in men with small testes (2 ml or less).

Conclusions: Testicular volume does not affect the sperm retrieval rate at our center for microdissection testicular sperm extraction. Of men with the smallest volume testes those who were younger with Klinefelter syndrome had the highest sperm retrieval rate. Severe testicular atrophy should not be a contraindication to microdissection testicular sperm extraction.

Key Words: testis; organ size; azoospermia; sperm injections, intracytoplasmic; spermatozoa

Abbreviations and Acronyms

FSH = follicle-stimulating hormone

KS = Klinefelter syndrome

micro-TESE = microdissection TESE

NOA = nonobstructive azoospermia

SR = sperm retrieval

TESE = testicular sperm extraction

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In patients with NOA micro-TESE has become a recognized and effective procedure to isolate sperm for intracytoplasmic sperm injection. We previously reported a 50% to 60% SR rate using micro-TESE.[1] Several factors have been evaluated and reported for predicting SR rates, including but not limited to FSH.[2–4] However, no single factor correlates with success. Men with NOA usually have smaller testicles than men with obstructive azoospermia[5] except those with an early or late maturation arrest histology.[6] Studies to date have only shown poor correlations between testicular size and SR rates,[7,8] although to our knowledge no study has specifically evaluated the effectiveness of micro-TESE in men with severe testicular atrophy.

The primary aim of our study was to evaluate the outcomes of micro-TESE, including SR, pregnancy and live birth rates, in patients with severe testicular atrophy, defined as an average testicular volume of 2 ml or less. We also identified identify preoperative clinical parameters that could help predict successful SR in men with small testes.

PATIENTS AND METHODS

We retrospectively collected data from the records of 1,127 men with NOA who underwent micro-TESE, as performed by a single urologist in the 12-year period between 1999 and 2011. Azoospermia was confirmed by analyzing 2 specimens according to WHO guidelines. An additional centrifuged semen sample was confirmed to be azoospermic on the day of planned TESE. Testicular volume was measured at physical examination by a single surgeon using a standardized orchidometer.[9] The average volume of the 2 testes was used for analysis. If only 1 testis was present, it was used in the calculation. Men were classified into 3 groups based on an average testicular volume of 2 or less, greater than 2 to less than 10 and 10 ml or greater. Clinical pregnancy in female partners was defined by identification of a gestational sac in which a fetal heartbeat could be seen on transvaginal ultrasound 6 weeks after embryo transfer. Confirmation of live birth was obtained by telephone interviews of couples identified with clinical pregnancy.

Micro-Testicular Sperm Extraction

The procedure was described previously.[10] Briefly, a midline incision was made in the scrotum and the scrotal content was pushed out preferentially from the side with the larger testis. The tunica vaginalis was opened, the testis was uncovered and the tunica albuginea was visualized. The remainder of the procedure was performed under an operative microscope. After the tunica albuginea was opened the testicular parenchyma was directly examined at 12× to 18× magnification. Examination included as much of the testicular parenchyma as possible. In some cases it was necessary to use a right angle clamp to open the tunica albuginea to adequately expose the testicular parenchyma for dissection.

Small samples (1 to 3 mg) of the larger, more opaque[11] tubules were dissected. Each sample was dropped in a suspension, passed through a 24 gauge angiocatheter and examined immediately by a skilled embryologist for the presence of the testicular spermatozoa.

A droplet of dispersed tissue suspension was placed on a glass slide under a phase contrast microscope at 200× magnification. If no spermatozoa were identified in the initial sample, subsequent samples were taken from the same testis and from the contralateral testis, as needed. Dissection was performed through all regions of testicular tissue, preserving the testicular blood supply. After TESE the best testicular samples were pooled in 5 ml tubal fluid medium. The suspension was centrifuged at 1,800 × gravity and examined carefully for even a single spermatozoon. The procedure was terminated when spermatozoa were retrieved or further dissection was thought likely to jeopardize the testicular blood supply. If no spermatozoa were seen, the sedimented testicular tissue was digested[10] and analyzed.

Statistical Analysis

Data were analyzed with Stata®, version 9. The 2-tailed Fisher exact test was used to compare testicular volume for the outcome of SR, pregnancy, live birth and other categorical outcomes, such as cryptorchidism. The unpaired Student t-test was used to compare continuous data, such as FSH level, and male and female age. The Fisher exact test, chi-square analysis and Student t-test was used to calculate p values between the 2 ml or less and greater than 10 ml groups for all dichotomous and continuous variables, respectively, with $p < 0.05$ considered statistically significant.

RESULTS

Testis volume was 2 ml or less in 106 men (9.4%), greater than 2 to less than 10 ml in 573 (50.8%) and 10 ml or greater in 448 (39.8%). SR was successful in 631 (56%) men. Average ± SD testicular volume in men in whom sperm were not retrieved was similar to that in men with successful SR (9.1 ± 4.85 and 9.1 ± 5.6 ml, respectively, $p = 0.9$). The SR rate was similar among men with different testicular sizes, including 54.7%, 56.2% and 55.1% for 2 or less, greater than 2 to less than 10 and 10 ml or greater, respectively ($p = 0.53$). Similarly, no significant difference was seen in the pregnancy rate of female partners of men from whom sperm were retrieved (55.2%, 50.0% and 47.0%, respectively, $p = 0.39$). In women who achieved clinical pregnancy there was no difference in the live birth rate (87.5%, 83.2% and 82.8%, respectively, $p = 0.30$).

Men with a testicular volume of 2 ml or less had higher mean FSH than men with testes 10 ml or greater (39.9 ± 17.6 vs 18.3 ± 12.3 IU/ml, $p < 0.001$). They also showed a higher rate of KS than men with testes greater than 2 ml (72.6% vs 5.3%, $p < 0.0001$, table 1). In the 33 men without KS who had a testicular volume of 2 ml or less the SR rate was 34.4%.