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Original article

The predictive value of parameters of clinical presentations for sperm yield in patients with nonobstructive azoospermia receiving microdissection testicular sperm extraction

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ABSTRACT

Objective: We analyzed a cohort of nonobstructive azoospermia (NOA) patients receiving microdissection testicular sperm extraction (mTESE) to examine the relationship of sperm yield and the parameters of clinical presentations. We aim to identify the parameters that might positively predict a positive sperm yield after mTESE.

Materials and methods: A total of 200 patients with NOA who had undergone mTESE were enrolled. Among them, 112 (56%) had received a prior testicular needle biopsy. Clinical data including physical findings, underlying genetic abnormalities, pathologic findings in needle biopsy, and sperm retrieval rate (SRR) during mTESE were reviewed and analyzed.

Results: The pathological findings of prior needle biopsy demonstrate a predictive value of sperm yield during mTESE. Hypospermatogenesis had SRR of 93.3% during mTESE, early maturation arrest had SRR of 13.3%, late maturation arrest (LMA) had SRR of 66.7%, and Sertoli cell-only syndrome had SRR of 18.1%. Regarding parameters of clinical presentation, we found that SRR during mTESE was 85.7% for patients with hypogonadotropic hypogonadism, 60.0% for men with undescended testes (UDT) history, 50.0% for patients who had been exposed to chemotherapeutics due to malignancy of other organs, 100% for prior mumps infection, 50.0% for AZFc deletion, 50.0% for Klinefelter syndrome, and 33.3% for other sex chromosome-related abnormalities. No sperm was found in patients with AZFa or AZFb microdeletion. The consistency of histopathological findings between initial testis biopsy and mTESE was 77.7%. As much as 17.4% of cases had upgraded on spermatogenesis at later mTESE.

Conclusion: Clinical presentations or phenotypes can be used as predictive factors for successful sperm retrieval during mTESE in patients with NOA. Hypogonadotropic hypogonadism and cases with UDT history have a higher chance of sperm retrieval. Initial testicular needle biopsy, if available, can provide valuable information about chances of sperm retrieval. Hypospermatogenesis predicts high sperm yield rate, and LMA can have best upgrade results of sperm yield after mTESE.

1. Introduction

Azoospermia may result from reproductive tract obstruction (obstructive azoospermia) or spermatogenic failure [nonobstructive azoospermia (NOA)]. Approximately 10% of men have problems related to infertility, and 1% of the general population have NOA.[1]

Microdissection testicular sperm extraction (mTESE) has been recognized as the best method to retrieve sperm for patients with NOA, which allows surgeons to identify the most promising large or more opaque seminiferous tubules in the testis under an operative microscope using magnifications up to 15–24×. The sperm retrieval rates (SRRs) for patients with NOA had been reported to vary between 43% and 60% with mTESE, whereas using

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conventional testicular sperm extraction the rates vary between 20% and 45%.[2]

To evaluate the nature of infertility, comprehensive information about reproductive history, symptoms, physical examinations, basic laboratory hormone profiles, and genetic testing is essential. Based on the findings collected from noninvasive assessment, patients with NOA can be categorized into different diagnosis groups or clinical presentation types, including genetic disorders, hormone abnormalities, varicoceles, undescended testis (UDT), postchemotherapy, postmumps infection, and other unclassified or idiopathic group. In the related literature, the SRRs with mTESE for patients with NOA vary based on the diagnosis categories [e.g., 68% in Klinefelter syndrome (KS), 0% in AZFa or AZFb deletions, 70% in AZFc deletions, 37% in Sertoli cell-only syndrome (SCOS), 53% in postchemotherapy, and 74% in patients with UDT].[3,4]

In this study, we aim to evaluate the predictive value of individual clinical presentation for SRR during mTESE in patients with NOA in Taiwan. We also aim to analyze the consistency of the histological findings between the initial testicular needle biopsy and the final mTESE in these patients.

2. Methods

We retrospectively reviewed the case log of patients with NOA at our department from October 2009 to December 2014. A total of 200 patients who had received mTESE were enrolled. Data on reproductive history, physical examination, semen analysis, hormone profile, and genetic testing (including karyotyping, Y-chromosome microdeletion testing, and AZFc partial microdeletion testing) were analyzed. If varicocele(s) was present, the grading of each varicocele site was determined by the same doctor (W.J.H.). We categorized our patients according to different clinical presentations groups, which included genetic disorders (autosome or sex chromosome abnormalities), hypogonadotropic hypogonadism, history of UDT, varicoceles, post chemotherapy, post mumps infection, and idiopathic (or unclassified) group.

Among the 200 patients, 121 had an initial testicular needle biopsy. Patients who did not have testicular needle biopsy either had very small testes, UDT, or wished to have direct mTESE with intracytoplasmic sperm injection treatment. All histopathologic findings of testicular needle biopsy were reviewed and compared with the results of mTESE, respectively. The SRR at mTESE of each histopathologic finding in the initial testicular biopsy was also investigated. The consistency of histopathologic findings between the initial testicular biopsy and the mTESE was also reviewed.

Positive sperm retrieval was defined as presence of spermatozoa within the extracted seminiferous tubules. The motility, viability, or quantity of the extracted sperm is not discussed in this study. The steps for mTESE are similar to other related studies.[2,5] In brief, the tunica albuginea was opened, and the testicular parenchyma was exposed. Optical magnification was used to optimize preservation of the blood vessels under the surface of tunica albuginea. Direct examination of the seminiferous tubules within every part of the testis was performed at 20–25× magnification under the operating microscope. Seminiferous tubules that were larger (diameter > 300 μm) or obviously more opaque were sampled. Touch print smear test on a sterilized slide was also performed for each specimen before it was transferred to the medium. The smear slides were stained and examined under a light microscope by experienced surgeons or specialists to confirm the presence of developing germ cells or spermatozoa. If adequate sperm were identified and retrieved, the procedure was terminated. Mean values of SRR in each group of patients were recorded.

All statistical analysis was performed using SAS 9.2 (SAS Institute, North Carolina University, NC, USA). Fisher exact test and odds ratio analysis were performed for comparing SRR among different groups. All p values <0.05 were determined as statistically significant.

3. Results

A total of 200 patients with NOA (age, 35.1 ± 4.5 years; range, 24–52 years) were enrolled in this study. Among the 200 patients, 121 (61%) had received an initial testicular needle biopsy prior to final mTESE.

The SRR during mTESE was 85.7% for patients with hypogonadotropic hypogonadism ($p = 0.003$) and 60.0% for those with histories of UDT ($p = 0.002$; Table 1). Promising SRRs of 50.0% were also seen in patients with KS, although this was not statistically significant. In our study, patients with varicocele, which was defined as ≥ Grade 2 varicocele in either hemiscrotum, had relatively poorer results. The SRR during mTESE was 16.7% for these patients, and this was significantly lower than that of the other groups.

The SRRs during mTESE were recorded according to the histopathologic diagnosis of the initial testis biopsy results (Table 2). Patients with hypospermatogenesis had SRR of 93.3% ($p < 0.001$), and those with SCOS had SRR of 18.1% ($p = 0.001$).

We also investigated the consistency of histopathologic findings between the initial testicular needle biopsy and the final mTESE. The results are presented in Table 3. Overall, the consistency was 77.7%. The discrepancy in consistency is due to the change in diagnosis after mTESE. We use “upgrade” to represent any diagnosis at mTESE that harbors more advanced stage of spermatogenesis than that detected at the initial testicular biopsy. By contrast, “downgrade” refers to any diagnosis at mTESE that indicates regressed stage of spermatogenesis (Table 3). The most likely upgrading category is late maturation arrest (LMA), with 66% chance.

4. Discussion

mTESE is currently the mainstay of sperm retrieval for patients with NOA. The sperms retrieved are used in further assisted reproductive technology practice, especially for intracytoplasmic sperm injection. Therefore, the female partners need ovarian stimulation and oocyte retrieval. However, in 40–50% of the cases, no sperm can be found after mTESE; thus, such couples have to take significant physical, psychological, and financial risks, including ovulation induction, eggs retrieval, and costs for procedures. It has

Table 1
Sperm retrieval rate during mTESE according to patients' clinical presentations.

Parameter of clinical presentations	No. (%)	SR (+)	SRR (%)	Odds ratio	p
Genetic disorders					
AZFa or AZFb	3 (1.5)	0	0	0.01–10.32	0.557
AZFc deletion	4 (2.0)	2	50.0	0.33–17.64	0.583
Partial AZFc microdeletion	27 (13.5)	7	25.9	0.34–2.11	0.821
Klinefelter syndrome	24 (12.0)	12	50.0	0.98–5.39	0.064
Sex chromosome related	9 (4.5)	3	33.3	0.32–5.26	0.725
Autosomal chromosome abnormality	2 (1.0)	0	0	0.01–19.57	>0.99
Hypogonadotropic hypogonadism	7 (3.5)	6	85.7	1.66–77.98	0.003
UDT	15 (7.5)	9	60.0	1.73–16.04	0.002
Varicoceles	42 (21.5)	7	16.7	0.17–0.98	0.038
Post chemotherapy	4 (2.0)	2	50.0	0.33–7.64	0.582
Post mumps infection	3 (1.5)	3	100.0	0.57–542.98	0.025
Idiopathic	60 (29.5)	13	21.7	0.30–1.21	0.174
Total	200 (100)	64	32.0		

mTESE = microdissection testicular sperm extraction; SR = sperm retrieval; SRR = sperm retrieval rate; UDT = undescended testes.

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