

Testicular Sperm Extraction in Non-Obstructive Azoospermic Patients with Sertoli Cell-Only Syndrome Testicular Histology

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Abstract

Aim: Sertoli cell-only syndrome (SCOS) is a prevalent cause of non-obstructive azoospermia (NOA) in males, where seminiferous tubules exclusively contain Sertoli cells, leading to minimal or absent spermatogenesis. Success rates for sperm retrieval in these cases vary significantly. We aimed to investigate the sperm retrieval rate with microdissection TESE (mTESE) in NOA patients with SCOS testicular histology and the factors that may affect it.

Methods: Patients who underwent mTESE due to NOA were retrospectively evaluated. Only patients with a histopathological diagnosis of SCOS were included in the study. Those with other histopathological diagnoses, those who underwent conventional TESE (cTESE) were excluded from the study. The sperm retrieval rate after mTESE was calculated for patients with a pathology result of SCOS. The age, testicular volume, and Follicle-Stimulating Hormone (FSH) level of the groups with and without sperm were compared.


Results: In our study, 186 patients with testicular histopathology diagnosed as SCOS were included. The rate of sperm retrieval after TESE in these patients was 28%. In patients with retrieved sperm, the mean age was 33.8 ± 5.4 years, the mean testicular volume was 11.1 ± 6.3 ml, and the mean FSH level was 22.5 ± 12.7 mIU/ml. In patients without retrieved sperm, the mean age was 33.8 ± 6.1 years, the mean testicular volume was 10.3 ± 6.1 ml, and the mean FSH level was 21.0 ± 9.8 mIU/ml. There was no significant difference observed in mean age, testicular volume, and FSH level between the group with retrieved sperm and the group without retrieved sperm ($p=0.97$, $p=0.24$, $p=0.38$, respectively).

Conclusions: The findings of our study can be used for counseling men with NOA. Obtaining intratesticular sperm is possible in the presence of NOA and a diagnosis of SCOS histology. Therefore, patients undergoing testicular biopsy with TESE for histological examination can simultaneously prepare for intracytoplasmic sperm injection if sperm is found.

Keywords: Sertoli cell-only syndrome, non-obstructive azoospermia, infertility, testicular sperm extraction

1. Introduction

Non-obstructive azoospermia (NOA) means the absence of spermatozoa in semen analysis.¹ Testicular failure is observed as a result of NOA in approximately 1% of all men and 10% of infertile men.² The primary treatment for NOA is testicular sperm extraction (TESE) followed by intracytoplasmic sperm injection (ICSI).¹ The testicular histopathology of NOA patients may include hypospermatogenesis, complete or incomplete maturation arrest, and Sertoli cell-only syndrome (SCOS). SCOS is a significant clinical condition where azoospermia and germ cells are not observed, and the success rate of TESE is low.³

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In studies, SCOS has been reported in 10.8-44% of infertile men with NOA.³

We aimed to investigate the sperm retrieval rate (SRR) in patients with SCOS testicular histology undergoing microdissection TESE (mTESE) and identify potential influencing factors.

2. Materials and methods

This study has been approved by the Başkent University Medical and Health Sciences Research Council (Project No: KA24/70) and conducted in accordance with the principles of the Helsinki Declaration. In our clinic, patients who underwent mTESE due to NOA were retrospectively evaluated. Only patients with a histopathological diagnosis of SCOS were included in the study. Individuals with other histopathological diagnoses, those who underwent conventional TESE (cTESE), and those with incomplete

data were excluded from the study. SRR after mTESE was calculated for patients with a pathology result of SCOS. The age, testicular volume, and Follicle-Stimulating Hormone (FSH) level of the groups with and without sperm were compared.

2.1. Surgical Technique

With sedoanalgesia and/or local anesthesia combination, mTESE procedures were performed by applying approximately 2 cm vertical incision to the scrotum. The tunica albuginea of the unilateral testis was opened with a vertical incision. Subtunical vessels were identified and avoided under the surgical microscope. Direct examination of the testicular parenchyma was performed at magnifications of x20 to x40 using an operating microscope. Small samples were taken from large, opaque seminiferous tubules. The procedure was terminated when a sufficient volume of sperm was obtained for ICSI. In the instance no sperm was found in one testis, the same procedure was repeated on the contralateral testis. A small tissue sample obtained surgically during the same session was placed in Bouin's solution and sent to the histopathology laboratory.

2.2. Statistical Analysis

Statistical analysis was performed using the SPSS V 22.0 statistical package. Normality of each continuous variable was checked using Kolmogorov-Smirnov and Shapiro-Wilk tests, along with histograms. Between-group comparisons were conducted using the Mann-Whitney U test for non-normally distributed data. P-values less than 0.05 were considered statistically significant.

3. Results

In our study, 186 patients with testicular histopathology diagnosed as SCOS were included. SRR after mTESE in these patients was 28%. In patients with retrieved sperm, the mean age was 33.8 ± 5.4 years, the mean testicular volume was 11.1 ± 6.3 ml, and the mean FSH level was 22.5 ± 12.7 mIU/ml. In patients without retrieved sperm, the mean age was 33.8 ± 6.1 years, the mean testicular volume was 10.3 ± 6.1 ml, and the mean FSH level was 21.0 ± 9.8 mIU/ml. There was no significant difference observed in mean age, testicular volume, and FSH level between the group with retrieved sperm and the group without retrieved sperm ($p=0.97$, $p=0.24$, $p=0.38$, respectively). The parameters evaluated in the study are shown in Table 1.

Table 1
Comparison of clinical and laboratory data of patients in groups

Parameters	Group I*	Group II**	p
Age (year)	33.8 ± 5.4	33.8 ± 6.1	0.97
Testicular Volume (ml)	11.1 ± 6.3	10.3 ± 6.1	0.24
FSH (mIU/ml)	22.5 ± 12.7	21.0 ± 9.8	0.38

FSH: Follicle-Stimulating Hormone *group with retrieved sperm **group without retrieved sperm

4. Discussion

The most common histological diagnosis in patients with NOA is SCOS¹. It is expected that in patients diagnosed with SCOS, there would be a lower SRR compared to other histological diagnoses¹. However, due to the heterogeneity of testicular histology, it has been reported that spermatozoa can still be found in these patients as well⁴. In two different studies examining the success rate of sperm retrieval in patients with testicular histopathology diagnosed

as SCOS, the success rate was found to be 27.6% and 23.6%, respectively^{4,5}. In our study, this rate was 28%, which is consistent with these studies. However, in another study, an SRR of 14.8% was found⁶. The reason for this discrepancy may be attributed to the multicenter nature of the study, resulting in heterogeneous patients and TESE being performed by different surgeons.

Due to the emergence of accompanying diseases that negatively affect testicular perfusion and germ cell loss with age, theoretically, lower success rates in terms of SRR are expected in elderly patients⁷. It is known that age is one of the important factors affecting the SRR after TESE⁸. In a study involving a limited number of patients ($n=64$), the patient age was found to be similar between the groups with no sperm retrieved during TESE (36.4 years) and the groups with sperm retrieved (37.2 years), with slightly higher age observed in the TESE-positive group⁷. Similarly, Guneri et al.⁹ also identified age as an important factor in their study (38 years versus 42 years). Okada et al.¹⁰ also demonstrated that patient age is a factor influencing TESE outcomes, determining that the median age was significantly different between the unsuccessful and successful TESE groups (38 (28-43) and 31 (25-40) years, respectively). However, studies evaluating only SCOS patients have reported that age does not have an effect on the SRR^{4,5}. In our study, it was also determined that age did not have an effect on the SRR, and we believe this is due to the selection of patients being homogeneous in terms of age.

It is known clinically that testicular volume correlates with spermatogenesis. Turunc et al.¹¹ found a positive correlation between testicular volume and SRR in patients with NOA, and determined that SRR was significantly lower in patients with testicular volume below 5 mL. However, in this study, distinction based on testicular histopathology was not made. In our study, it was found that testicular volume was not a determining factor for the presence or absence of sperm in the groups. This result differs from studies that only examined SCOS patients and reported lower SRR in men with smaller testicular volumes who underwent cTESE^{12,13}. However, recent mTESE studies with large series of NOA patients have shown that testicular volume does not have any effect on SRR^{6,14,15}. This suggests that performing mTESE or cTESE in SCOS patients may lead to different outcomes in terms of testicular volume.

There are studies suggesting that serum FSH levels can predict the presence of sperm retrievable by cTESE¹⁶. Conversely, it has also been reported that FSH has poor predictive value for sperm retrieval via TESE^{13,17}. In addition to studies indicating that FSH levels are determinant for patients with testicular histopathology diagnosed as SCOS, there are also studies showing that it has no effect⁴⁻⁶. The discrepancy in the relationship between FSH levels and SRR success may stem from differing demographic characteristics across studies. A study by Silber et al.¹⁸ demonstrated that FSH concentration is inversely proportional to the number of germ cells in the testis, yet it lacks correlation with more advanced stages of spermatogenesis. Additionally, it has been noted that FSH can only reflect the global function of spermatogenesis and cannot evaluate the function of an isolated region within the testis¹⁸. By allowing for more detailed examination of each part of the testis, the mTESE method increases the chance of finding spermatogenic areas¹⁹. Therefore, mTESE can increase the SRR rate even when the overall spermatogenesis function of the testis is very low¹⁹. This may explain why FSH cannot accurately predict the SRR of mTESE.

4.1. Limitation

Our study has two main limitations. The first of these is that it is a retrospective study. The other is that parameters related to ICSI and its outcomes, such as fertilization rate, implantation rate, clinical pregnancy rate, and live birth rate, were not evaluated. The high

number of patients in this special group is one of the strengths of our study.

5. Conclusion

The results of our study provide valuable insights for counseling men with NOA. Testicular sperm retrieval is feasible in cases of NOA with a SCOS histology. Consequently, patients undergoing testicular biopsy with TESE for histological assessment can concurrently consider preparation for ICSI if sperm is obtained.

Statement of ethics

This study has been approved by the Başkent University Medical and Health Sciences Research Council (Project No: KA24/70) and conducted in accordance with the principles of the Helsinki Declaration.

Conflict of interest statement

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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Author Contributions

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Originality Assertion

The authors have not submitted this article to another journal previously.

References

- 1.Chiba K, Enatsu N, Fujisawa M. Management of non-obstructive azoospermia. *Reproductive medicine and biology*. 2016;15:165-73. <https://doi.org/10.1007/s12522-016-0234-z>
- 2.Kumar R. Medical management of non-obstructive azoospermia. *Clinics*. 2013;68:75-9. [https://doi.org/10.6061/clinics/2013\(Sup01\)08](https://doi.org/10.6061/clinics/2013(Sup01)08)
- 3.Sasagawa I, Yazawa H, Suzuki Y, et al. Reevaluation of testicular biopsies of males with nonobstructive azoospermia in assisted reproductive technology. *Archives of andrology*. 2001;46(1):79-83. <https://doi.org/10.1080/01485010150211191>
- 4.Gul U, Turunc T, Haydardedeoglu B, Yaycioglu O, Kuzgunbay B, Ozkardes H. Sperm retrieval and live birth rates in presumed Sertoli-cell-only syndrome in testis biopsy: a single centre experience. *Andrology*. 2013;1(1):47-51. <https://doi.org/10.1111/j.2047-2927.2012.00003.x>
- 5.Modarresi T, Hosseini H, Hampa AD, et al. Predictive factors of successful microdissection testicular sperm extraction in patients with presumed sertoli cell-only syndrome. *International journal of fertility & sterility*. 2015;9(1):107.
6. Taitson PF, Mourthé Filho A, Radaelli MRM. Testicular sperm extraction in men with sertoli cell-only testicular histology-1680 cases. *JBRA Assisted Reproduction*. 2019;23(3):246. <https://doi.org/10.5935/1518-0557.20190023>
- 7.Pavan-Jukic D, Stubljarić D, Jukic T, Starc A. Predictive factors for sperm retrieval from males with azoospermia who are eligible for testicular sperm extraction (TESE). *Systems biology in reproductive medicine*. 2020;66(1):70-5. <https://doi.org/10.1080/19396368.2019.1680764>
- 8.Tsujimura A. Microdissection testicular sperm extraction: prediction, outcome, and complications. *International journal of urology*. 2007;14(10):883-9. <https://doi.org/10.1111/j.1442-2042.2007.01828.x>
- 9.Güneri Ç, Alkibay T, Tunç L. Effects of clinical, laboratory and pathological features on successful sperm retrieval in non-obstructive azoospermia. *Turkish Journal of Urology*. 2016;42(3):168. <https://doi.org/10.5152/tud.2016.45403>
- 10.Okada H, Goda K, Yamamoto Y, et al. Age as a limiting factor for successful sperm retrieval in patients with nonmosaic Klinefelter's syndrome. *Fertility and sterility*. 2005;84(6):1662-4. <https://doi.org/10.1016/j.fertnstert.2005.05.053>
- 11.Turunc T, Gul U, Haydardedeoglu B, et al. Conventional testicular sperm extraction combined with the microdissection technique in nonobstructive azoospermic patients: a prospective comparative study. *Fertility and sterility*. 2010;94(6):2157-2160. <https://doi.org/10.1016/j.fertnstert.2010.01.008>
- 12.Tournaye H, Verheyen G, Nagy P, et al. Are there any predictive factors for successful testicular sperm recovery in azoospermic patients? *Human reproduction (Oxford, England)*. 1997;12(1):80-6. <https://doi.org/10.1093/humrep/12.1.80>
- 13.Ezeh U, Taub N, Moore H, Cooke I. Establishment of predictive variables associated with testicular sperm retrieval in men with non-obstructive azoospermia. *Human reproduction*. 1999;14(4):1005-12. <https://doi.org/10.1093/humrep/14.4.1005>
- 14.Berookhim BM, Palermo GD, Zaninovic N, Rosenwaks Z, Schlegel PN. Microdissection testicular sperm extraction in men with Sertoli cell-only testicular histology. *Fertility and sterility*. 2014;102(5):1282-6. <https://doi.org/10.1016/j.fertnstert.2014.08.007>
- 15.Bryson CF, Ramasamy R, Sheehan M, Palermo GD, Rosenwaks Z, Schlegel PN. Severe testicular atrophy does not affect the success of microdissection testicular sperm extraction. *The Journal of urology*. 2014;191(1):175-8. <https://doi.org/10.1016/j.juro.2013.07.065>
- 16.Ishikawa T. Surgical recovery of sperm in non-obstructive azoospermia. *Asian journal of andrology*. 2012;14(1):109. <https://doi.org/10.1038/aja.2011.61>
- 17.Jezek D, Knuth U, Schulze W. Successful testicular sperm extraction (TESE) in spite of high serum follicle stimulating hormone and azoospermia: correlation between testicular morphology, TESE results, semen analysis and serum hormone values in 103 infertile men. *Human reproduction (Oxford, England)*. 1998;13(5):1230-4. <https://doi.org/10.1093/humrep/13.5.1230>
- 18.Silber SJ, Van Steirteghem A, Nagy Z, Liu J, Tournaye H, Devroey P. Normal pregnancies resulting from testicular sperm extraction and intracytoplasmic sperm injection for azoospermia due to maturation arrest. *Fertility and Sterility*. 1996;66(1):110-7. [https://doi.org/10.1016/S0015-0282\(16\)58396-4](https://doi.org/10.1016/S0015-0282(16)58396-4)
- 19.Li H, Chen L-P, Yang J, et al. Predictive value of FSH, testicular volume, and histopathological findings for the sperm retrieval rate of microdissection TESE in nonobstructive azoospermia: a meta-analysis. *Asian journal of andrology*. 2018;20(1):30. https://doi.org/10.4103/aja.aja_5_17