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Factors Affecting TESE Success in Infertility Treatment: Preliminary Results of Single-Center Experience

İnfertilite Tedavisinde TESE Başarısını Etkileyen Faktörler: Tek Merkez Deneyimi Ön Sonuçları

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Abstract

Objective: Today, infertility is a health problem with increasing treatment seeking. Testicular sperm extraction (TESE) is the only possible procedure to offer genetic parenting to men with nonobstructive azoospermia (NOA). Our aim in this study is to present our clinical experiences that affect the success of sperm retrieval in men with NOA in the light of the literature.
Materials and Methods: In our study, patients who underwent TESE with a diagnosis of NOA between 2017-2020 were retrospectively analyzed. According to the TESE procedure; the patients were divided into two groups as conventional TESE and TESE performed under microscopic magnification (micro-TESE). Medical histories, hormone values, and physical examination findings of all patients were recorded.
Results: Our micro-TESE success rate was found to be 100%. A positive correlation (rho 0.714, p = 0.009) was found between the factors affecting sperm retrieval , and the application of micro-TESE, and a negative correlation was detected with FSH levels (rho -0.759, p = 0.004).
Conclusion: The success of sperm retrieval increases with the micro-TESE procedure. As FSH levels increase, sperm retrieval success rates decrease.

Keywords: infertility, nonobstructive azoospermia, testicular sperm extraction, TESE

Öz

Amaç: İnfertilite günümüzde tedavi arayışları artan bir sağlık sorunudur. Testiküler sperm ekstraksiyonu (TESE), nonobstrüktif azospermi (NOA) olan erkeklere genetik ebeveynlik sunmak için mümkün olan tek prosedürdür. Bizim bu çalışmamızdaki amacımız NOA'si olan erkeklerde sperm bulma başarısına etki eden klinik deneyimlerimizi literatür eşliğinde sunmaktır.
Gereç ve Yöntemler: Çalışmamızda 2017-2020 yılları arasında NOA tanısı ile TESE uygulanmış hastalar retrospektif olarak incelendi. TESE işlemine göre; geleneksel TESE ve mikroskop altında yapılan TESE (mikro-TESE) olarak iki gruba ayrıldı. Tüm hastaların tıbbi hikayeleri, hormon değerleri, fizik muayeneleri kayıt altına alındı.
Bulgular: Mikro-TESE başarımız %100 olarak saptandı. Sperm elde edilmesine etki eden faktörler olarak; mikro-TESE uygulanması ile pozitif yönde (rho 0,714, p=0,009), FSH seviyeleri ile de negatif yönde (rho -0,759, p=0,004) bir ilişki saptandı.
Sonuç: Sperm elde edilme başarısı Mikro-TESE işlemi ile arttırmaktadır. FSH seviyeleri yükseldikçe sperm elde etme başarı oranları ise azalmaktadır.

Anahtar kelimeler: infertilite; nonobstrüktif azospermi; testiküler sperm ekstraksiyonu, TESE

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Introduction

The World Health Organization (WHO) defines infertility as the inability of a sexually active couple to have spontaneous pregnancy despite unprotected sexual intercourse in the last 1 year [1]. Infertility affects approximately 15% of all couples. In previous studies on the male and female factors, mostly the female factor was prioritized. Although it is stated that 50% of infertility is caused by the female factor and 50% by the male factor, in fact many couples have male and female infertility factors in combination. In the evaluation of male infertility semen analysis plays an important role. Azoospermia, defined as the absence of sperm cells in semen analysis, is responsible for approximately 10-15% of cases with male infertility. Approximately 60% of azoospermic patients have non-obstructive azoospermia (NOA). A disorder in the stages of spermatogenesis of these patients is thought to constitute the underlying pathology [2].

Testicular sperm extraction (TESE) is the possible procedure to offer genetic parenting to men with nonobstructive azoospermia (NOA) [3]. Spermatozoa can be taken directly from the testis in TESE and used for intracytoplasmic sperm injection (ICSI). The first successful fertilization and pregnancy by obtaining spermatozoa from the testis were reported in 1993 [4]. Looking at the current literature, TESE achieves success rates of 100% for men with obstructive azoospermia (OA) and 56% for men with NOA [5–9]. Many predictive factors have been identified that affect the success rates of TESE, such as levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), testicular volume, and the application of microscopic TESE (micro-TESE) [10].

Our aim in this study is to present our clinical experiences that affect the success rates of sperm retrieval in men with NOA in the light of the literature.

Materials and Methods

In our study, patients who underwent TESE with a diagnosis of NOA between 2017-2020 were retrospectively analyzed. The procedures applied in this study are in line with the ethical standards of the institutional research committee. Local ethics committee approval was obtained for the study (Approval Number: 2020/255). Informed consent forms were obtained from all patients before the procedure.

The diagnosis of NOA was confirmed by 2 consecutive semen analysis, medical history, physical examination, follicle stimulating hormone (FSH), luteinizing hormone (LH), and total testosterone levels. Medical history, physical examination, FSH, LH, total testosterone, prolactin values and pathology results of the patients who had TESE were taken from the hospital information management system retrospectively. Testicular volumes of the patients were measured using a Prader orchidometer (ASSI, Westbury, NY, USA). A decrease in testicular volume greater than 2 standard deviations between the evaluated testis and the normal age-matched population was considered as atrophic testis.

Table 1. Comparison of TESE in patients with and without sperm yield

		Group 1 (sperm +) n=7	Group 2 (sperm -) n=5	p
Age (years) (mean ± SD)		34 (27 – 38)	35 (32 – 39)	0.623
Infertility period (months) (median, min.-max.)		48 (36 – 120)	36 (18 – 180)	0.159
FSH IU/L (median, min.-max.)		5.62 (1.75 – 13.17)	19.62 (8.16 – 45.97)	**0.012**
LH IU/L (median, min.- max.)		6.43 (2.64 – 8.59)	6.38 (4.17 – 11.31)	0.465
Total Testosterone ng/dL (median, min.-max.)		3.15 (2.07 – 5.79)	4.89 (2.92 – 5.72)	0.223
Prolactin (median, min.-max.)		9.74 (6.31 – 22.66)	7.60 (5.89 – 10.89)	0.223
Smoking	Yes n (%)	2 (28.6)	0 (0)	0.470
	No n (%)	5 (71.4)	5 (100)	
Physical Examination Findings of the Testes	Normal n (%)	4 (51.7)	1 (20)	0.293
	Atrophic testis n (%)	3 (42.9)	4 (80)	
Previously Applied Assisted Reproductive Treatment Methods	Yes n (%)	3 (42.9)	2 (40)	1.000
	No n (%)	4 (51.7)	3 (60)	
TESE Methods	Conventional TESE n (%)	2 (28.6)	5 (100)	**0.028**
	Micro-TESE n (%)	5 (71.4)	0 (0)	

FSH: follicle stimulating hormone; LH: luteinizing hormone; TESE: testicular sperm extraction; Micro-TESE: microsurgical testicular sperm extraction

Table 2. Correlation analysis between factors affecting sperm detection rates and positivity of sperm detection

		Age	Infertility period	Smoking	Atrophic testis	Micro-TESE application	FSH	LH	Prolactin	Total Testosterone
Positivity of sperm detection	Rho	-0.148	0.424	0.378	-0.371	0.714**	-0.759**	-0.220	0.367	-0.367
	p	0.646	0.169	0.226	0.235	**0.009**	**0.004**	0.491	0.240	0.240
	n	12	12	12	12	12	12	12	12	12

FSH: follicle stimulating hormone; LH: luteinizing hormone; TESE: testicular sperm extraction; Micro-TESE: microsurgical testicular sperm extraction

Two methods were applied to the patients, namely, conventional (traditional) TESE (testicular sperm extraction performed with open surgical method without using any auxiliary enlargement tools and equipment) and micro-TESE (testicular sperm extraction performed by using OPMI VARIO/ S88 System, Karl Zeiss microscope-assisted 20 x magnification). Whether sperm was obtained or not after the procedure was noted and pathology samples were taken from the testis. Patients with incomplete information, chromosomal disorders such as Klinefelter syndrome and Sertoli cell only syndrome were excluded from the study.

Statistical Analysis

For statistical analyses, IBM SPSS version 22.0 (SPSS Inc, Chicago, IL) for Windows was used. Descriptive data were defined as number, percentage, mean, standard deviation, median, minimum and maximum. The normality of distribution of data was tested with the Kolmogorov-Smirnov test. Mann-Whitney U test was used for the analysis quantitative data that did not show normal distribution. For qualitative data, chi-square test, and when chi-square assumptions were not met, Fisher's exact test was used. Spearman correlation analysis was used to evaluate the factors affecting sperm detection. The results were expressed within 95% confidence interval and $p<0,05$ was considered statistically significant.

Results

A total of 17 patients who underwent TESE were included in our study. The mean age of the patients was 33.35 ± 3.96 years. The duration of primary infertility was 53.29 ± 41.94 months. Pathology result was reported as Sertoli –cell only syndrome in 5 patients and they were excluded from the study. A total of 12 patients with sperm maturation disorders were included in the study. No postoperative complications were observed in any patient.

The patients were divided into two groups according to sperm retrieval in TESE procedure; Group 1 was Sperm (+) and Group 2 was Sperm (-). Clinical and laboratory findings of both groups were compared and the results are given in **Table 1**; A statistical difference was found between the groups in terms of FSH levels and TESE methods used. While the median FSH value in Group 1 (minimum - maximum) was 5.62 (1.75 - 13.17), this value was found to be statistically significantly higher in Group 2 (9.62 (8.16 - 45.97) ($p = 0.012$). Micro-TESE application was effective in achieving successful results in Group 1 ($p = 0.028$). Sperm was found in all 5 patients who underwent micro-TESE and its success rate was 100%.

When the correlation analysis of the factors affecting sperm retrieval is examined; a positive relationship with micro-TESE application (rho 0.714, $p = 0.009$) and a negative relationship with FSH levels (rho -0.759, $p = 0.004$) were detected. A statistically significant relationship was not found with other parameters (**Table 2**).

Discussion

Today, diagnosis and treatment rates of infertility are increasing. This case raises a successful assisted reproductive technology centers and foreground. It is stated that female and male factors are responsible at similar rates in infertility. Azoospermia, defined as the absence of sperm cells as a male factor, is responsible for approximately 10-15% of the cases with male infertility. Approximately 60% of azoospermic patients have non-obstructive azoospermia (NOA). Testicular sperm extraction (TESE) is the only possible procedure to offer genetic parenting to men with nonobstructive azoospermia (NOA) [3]. Patients with NOA have a higher sperm retrieval rate in microdissection TESE (micro-TESE) application compared to conventional TESE [3]. Sertkaya et al. [3] reported a 78.3% success rate in 60 patients they applied micro-TESE. Ortaç et al. [10] stated that they obtained sperm with a success rate of 46.7% with micro-TESE in a total of 379 patients. In other studies, the success rates of this procedure ranged between 42.9, and 63% [5–9,11–13]. Patients with Sertoli cell -only syndrome and those with Klinefelter syndrome were included in these studies. In our study, the success rate of micro-TESE was 100%. The low number of patients, exclusion of patients with Sertoli cell -only syndrome and those with genetic anomalies such as Klinefelter syndrome from our study may be the reason for our high success rates. In accordance with the literature, we can say

that micro-TESE application increases the success rates of sperm retrieval compared to conventional TESE procedure.

When other factors affecting success rates are examined; many studies in the literature have indicated that the success rates of micro-TESE increase in direct proportion to testicular volume [10,14,15]. The limit testicular volumes that reduce the chance of sperm retrieval were reported by various authors as < 8 ml (Marconi et al. [16]), < 4ml (Bromage et al. [17]) and < 5.7 ml (Ziaee et al. [18]). Bryson CF et al. [19], on the other hand, stated that spermatozoa will be found in testes with volumes less than 2 ml. In our study, due to the low number of patients, testicular volume measurement was grouped only according to the presence or absence of atrophy, and the effect of atrophic testis on sperm retrieval was not investigated.

FSH is stated to be another ffactor that affects success of TESE. FSH has an important role in the regulation of spermatogenesis due to its effect on germ cells responsible for spermatogenesis. In the literature, the cut-off FSH value for the presence of sperm in the TESE procedure has not been shown [14]. Bernie et al. [8] found higher FSH levels such as 19.7 ± 12.8 IU / L in patients with, and 25.3 ± 15.5 IU / L in patients without testicular sperm. In studies investigating the cut-off value of FSH, Ramasamy et al. [20] , and Souza et al. [15] reported that sperm retrieval rates decreased in patients with FSH levels <15 IU / L, and <17 IU / L, respectively. In our study, we found that the median FSH value (19.62 IU / L) in patients who could not yield sperm was higher than the FSH median value (5.62 IU / L) of the patients in whom sperm retrieval was realized Our findings were consistent with the literature. We showed that FSH levels have a prognostic value in predicting sperm retrieval, and correlation analysis has demonstrated that the success rates of sperm retrieval decrease as the FSH levels increase.

Our study has some limitations. In this study, we examined a relatively small number of patients. We did not include a control group in the study as in similar publications. Not mentioning the amount of sample retrieved by micro-TESE or whether unilateral or bilateral TESE was performed may be the limitation of our study.

Conclusion

It is possible to retrieve sperm with TESE in cases with nonobstructive azoospermia. Micro-TESE procedure increases the success rates of sperm retrieval. As FSH levels increase, success rates of sperm retrieval decrease. The results should be supported by prospective studies performed in large patient groups.

Ethics Committee Approval: The study was approved by Hitit University Faculty of Medicine Clinical Research and Ethics Committee, Corum, Turkey (Decision No: 2020/255).
Informed Consent: An informed consent was obtained from all the patients.
Publication: The results of the study were not published in full or in part in form of abstracts.
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References

[1] Rowe PJ, Comhaire FH, Hargreave TB, Mellows HJ. WHO manual for the standardized investigation and diagnosis of the infertile couple. Cambridge: Cambridge University Press; 2000.

[2] Schlegel PN, Li PS. Microdissection TESE: sperm retrieval in non-obstructive azoospermia. Hum Reprod Update 1998;4:439. https://doi.org/10.1093/humupd/4.4.439.

[3] Sertkaya Z, Tokuç E, Özkaya F, Ertaş K, Kutluhan MA, Çulha MG. Acute effect of microdissection testicular sperm extraction on blood total testosterone and luteinising hormone levels. Andrologia 2020;52:e13655. https://doi.org/10.1111/and.13655.

[4] Craft I, Bennett V, Nicholson N. Fertilising ability of testicular spermatozoa. Lancet 1993;342:864. https://doi.org/10.1016/0140-6736(93)92722-6.

[5] Cissen M, Meijerink AM, D'Hauwers KW, Meissner A, Van Der Weide N, Mochtar MH, et al. Prediction model for obtaining spermatozoa with testicular sperm extraction in men with non-obstructive azoospermia. Hum Reprod 2016;31:1934–41. https://doi.org/10.1093/humrep/dew147.

[6] Corona G, Pizzocaro A, Lanfranco F, Garolla A, Pelliccione F, Vignozzi L, et al. Sperm recovery and ICSI outcomes in Klinefelter syndrome: A systematic review and meta-analysis. Hum Reprod Update 2017;23:265–75. https://doi.org/10.1093/humupd/dmx008.

[7] Bernie AM, Mata DA, Ramasamy R, Schlegel PN. Comparison of microdissection testicular sperm extraction, conventional testicular sperm extraction, and testicular sperm aspiration for nonobstructive azoospermia: A systematic review and meta-analysis. Fertil Steril 2015;104:1099-1103.e3. https://doi.org/10.1016/j.fertnstert.2015.07.1136.

[8] Bernie AM, Ramasamy R, Schlegel PN. Predictive factors of successful microdissection testicular sperm extraction. Basic Clin Androl 2013;23:5. https://doi.org/10.1186/2051-4190-23-5.

[9] Ishikawa T. Surgical recovery of sperm in non-obstructive azoospermia. Asian J Androl 2012;14:109–15. https://doi.org/10.1038/aja.2011.61.

[10] Ortaç M, Çilesiz NC, Kadıoğlu A. Factors affecting the success of microdissection testicular sperm extraction in men with non-obstructive azoospermia. Androl Bul 2020;22:12–5. https://doi.org/10.24898/tandro.2020.72473.

[11] Chan PTK, Schlegel PN. Nonobstructive azoospermia. Curr Opin Urol 2000;10:617–24. https://doi.org/10.1097/00042307-200011000-00015.

[12] Kalsi JS, Shah P, Thum Y, Muneer A, Ralph DJ, Minhas S. Salvage micro-dissection testicular sperm extraction; Outcome in men with non-obstructive azoospermia with previous failed sperm retrievals. BJU Int 2015;116:460–5. https://doi.org/10.1111/bju.12932.

[13] Donoso P, Tournaye H, Devroey P. Which is the best sperm retrieval technique for non-obstructive azoospermia? A systematic review. Hum Reprod Update 2007;13:539–49. https://doi.org/10.1093/humupd/dmm029.

[14] Sofikitis N, Giotitsas N, Tsounapi P, Baltogiannis D, Giannakis D, Pardalidis N. Hormonal regulation of spermatogenesis and spermiogenesis. J Steroid Biochem Mol Biol 2008;109:323–30. https://doi.org/10.1016/j.jsbmb.2008.03.004.

[15] Souza CAB, Filho JSC, Santos D, Gratão A, Freitas FM, Passos EP. Predictive factors for motile sperm recovery using testicular biopsy in nonobstructive azoospermic patients. Int Urol Nephrol 2003;35:53–7. https://doi.org/10.1023/A:1025900112600.

[16] Marconi M, Keudel A, Diemer T, Bergmann M, Steger K, Schuppe HC, et al. Combined trifocal and microsurgical testicular sperm extraction is the best technique for testicular sperm retrieval in "low-chance" nonobstructive azoospermia. Eur Urol 2012;62:713–9. https://doi.org/10.1016/j.eururo.2012.03.004.

[17] Bromage SJ, Falconer DA, Lieberman BA, Sangar V, Payne SR. Sperm Retrieval Rates in Subgroups of Primary Azoospermic Males. Eur Urol 2007;51:534–40. https://doi.org/10.1016/j.eururo.2006.08.032.

[18] Ziaee SA, Ezzatnegad M, Nowroozi M, Jamshidian H, Abdi H, Hosseini Moghaddam SMM. Prediction of successful sperm retrieval in patients with nonobstructive azoospermia. Urol J 2006;3:92–6. https://doi.org/10.22037/uj.v3i2.202.

[19] 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. J Urol 2014;191:175–8. https://doi.org/10.1016/j.juro.2013.07.065.

[20] Ramasamy R, Lin K, Gosden LV, Rosenwaks Z, Palermo GD, Schlegel PN. High serum FSH levels in men with nonobstructive azoospermia does not affect success of microdissection testicular sperm extraction. Fertil Steril 2009;92:590–3. https://doi.org/10.1016/j.fertnstert.2008.07.1703.