



## **Prognostic Factors for Successful Microdissection Testicular Sperm Extraction (Micro-TESE)**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** There are some men suffer from infertility, non-obstructive azoospermia is one of the causes of infertility, these men need sperm retrieval from testes like microdissection testicular sperm extraction (Micro-TESE). This work aims to assess the different preoperative and intraoperative factors that predict successful sperm retrieval with Microdissection Testicular Sperm Extraction (Micro-TESE) in men with non-obstructive azoospermia.

**Methods:** Our study is a cohort prospective one, conducted on 52 male patients with non-obstructive azoospermia who attended to the outpatient andrology and infertility clinic of Urology Department, Tanta University Hospitals during the period between December 2018 to November 2019. All patients were subjected to detailed medical history, physical examination, two semen analysis on two different laboratories. Microdissection Testicular Sperm Extraction is performed to all patients after Estimation of serum FSH, LH, testosterone, prolactin, estradiol and scrotal Doppler ultrasonography

**Results:** From 52 patients who have done, Patients were divided in to 2 groups according to the result of Micro-TESE procedure: negative SSR group (28 patients) and positive SSR group (24 patients). In comparison between the two groups according to preoperative factors as age, FSH,

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LH, estradiol, testosterone, prolactin and testicular volume, there was no significant difference between these groups. On comparison of intraoperative size of seminiferous tubules in relation to results of Micro-TESE, we found that presence of large convoluted seminiferous tubules was statistically significant in prediction of successful sperm retrieval with Micro-TESE

**Conclusions:** The chances of sperm retrieval in men with NOA by Micro-TESE are not related to preoperatively age, FSH, LH, testosterone, estradiol, prolactin and testicular volume. The detection of large seminiferous tubules intraoperatively is a good predictor for successful sperm retrieval with Micro-TESE as it was statistically significant.

*Keywords: Infertility; non-obstructive azoospermia; Microdissection testicular sperm extraction; Micro-TESE; surgical sperm retrieval.*

## 1. INTRODUCTION

Infertility is defined as the inability of a couple to conceive after 1 year of unprotected intercourse [1]. Worldwide, about 10 – 20% of couples at the reproductive age were affected by infertility [2]. Male factor of infertility contributes about 50% of cases, and this proportion is increasing rapidly [3]. Men undergoing evaluation for infertility are found to have azoospermia, or lack of sperm in the ejaculate, up to 10% of this case. About 60% of these cases are due to non-obstructive azoospermia (NOA) a condition in which men have impaired production of sperm [4].

Men with NOA are usual in need for some form of sperm retrieval procedure in conjunction with intra-cytoplasmic sperm injection (ICSI) to father their own children [5]. Microdissection testicular sperm extraction (Micro-TESE) is currently one of the most popular sperm retrieval procedures for men with NOA [6].

From several previous studies, there is a debate between different authors as regarding to preoperative and intraoperative factors that predict the result of Micro-TESE as age, FSH, LH, testosterone, estradiol, prolactin, testicular volume and tubular diameter and opacity.

In our study we have the different preoperative and intraoperative factors that predict successful sperm retrieval with Microdissection Testicular Sperm Extraction in men with non-obstructive azoospermia.

## 2. METHODS

The study is a cohort prospective one, conducted on 52 male patients with NOA who attended to the outpatient andrology and infertility clinic of Urology Department, Tanta University Hospitals during the period between December-2018 to November-2019.

Inclusion criteria were: (males with non-obstructive azoospermia- males with small sized testes (testis longitudinal axis (TLA)<4.5 cm)- males with high/normal FSH- Males did not undergo a previous testicular biopsy- males who are complaining of male infertility > one year- males have normal female partner).

The exclusion criteria were history of previous testicular biopsy, patient who unfit for surgery (e.g., heart, liver, renal failure or bleeding problems) and suspected or diagnosed female factor infertility.

All patients were evaluated as regards to: Full medical history, Physical Examination to detect Signs of feminization, testicular size and consistency, Presence of varicocele and vas deferens.

**Patients were investigated preoperatively regarding:** 1- CBC, blood sugar tests, liver and renal function tests, bleeding profile and urine analysis. 2-Semen analysis (twice on two different occasions). 3- Serum levels of testosterone, FSH, LH, prolactin and estradiol. 3- Color flow scrotal Doppler ultrasound examination.

**Micro-TESE was done to all patients with aid of LEICA M530 surgical microscope:** On a supine position and after sterilization of scrotum, A midline incision is made in the scrotum and the scrotal content is pushed out from the side of the larger testis and the tunica vaginalis is opened then the tunica albuginea is bivalved. Direct examination of the testicular parenchyma is performed with aid of the operative microscope. The examination is to detect the shape, size and opacity of seminiferous tubules. Small samples are excised from the larger, more convoluted opaque tubules. Each sample is examined for the presence of the testicular spermatozoa under a phase-contrast microscope at x200

magnification. If no spermatozoa were identified in the initial sample, subsequent samples were taken from the same testis and if needed, from the contralateral testis. Tunica albuginea and other layers are closed anatomically with synthetic braided suture (polyglactin (Vicryl) 4/0). Closure of skin with simple sutures with synthetic braided suture polyglactin (Vicryl) 3/0.

### 2.1 Statistical Analysis

The collected data were organized, tabulated and statistically analyzed using SPSS version 19 (Statistical Package for Social Studies) created by IBM, Illinois, Chicago, USA. For numerical values the range mean ( $\pm$ median) and standard deviations were calculated. The differences between two mean values were used using Mann-Whitney test as the variables were not found to follow the normal distribution. Chi-square test of significance was used in order to compare proportions between qualitative parameters. For comparison between more than

two groups, Kruskal-Wallis test was used and pairwise analysis was performed if the test was positive by using Mann-Whitney test. The level of significant was adopted at  $p < 0.05$ .

### 3. RESULTS

The success rate of surgical sperm retrieval (SSR) by Micro-TESE procedure in our study was 46.15%. As there were 24 patients with positive SRR out of 52 patients. (Fig. 1)

Patients were divided in to 2 groups according to the result of Micro-TESE procedure: negative SSR group (28 patients) and positive SSR group (24 patients).

Regarding Age distribution, the age of our patients was ranged from 23-52 years old and it was found non-significant as the mean age of the negative SSR group was (31.79 $\pm$ 5.83) years and positive group with (32.54 $\pm$ 7.31) years. Table (1)

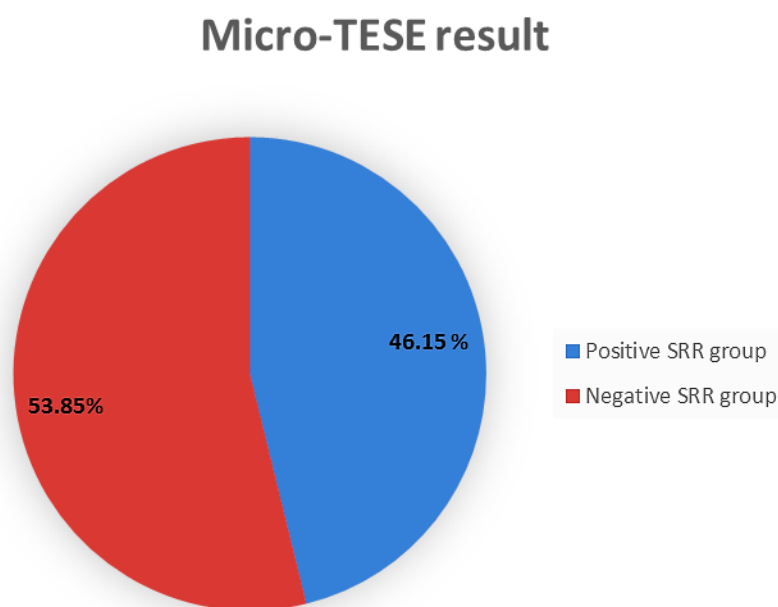


Fig. 1. Micro-TESE result in percentage.

Table 1. Comparison between groups according to Age distribution

Age in years	Micro-TESE results	
	Negative	Positive
Range	23-48	24-52
Median	31.5	31.5
Mean $\pm$ SD	31.79 $\pm$ 5.83	32.54 $\pm$ 7.31
Z	0.092	
p	0.972	

Regarding hormonal profile of patients in relation to results of Micro-TESE, there were no significant difference between the negative SSR group and positive SSR group according to FSH, LH, testosterone, prolactin, and estradiol as p. value was (0.660), (0.802), (0.485), (0.378), and (0.485) respectively. Table (2).

Regarding Testicular volume in relation to results of Micro-TESE, the difference was insignificant (P value=0.083). Although, the mean +SD of positive SSR group higher than that of negative one. Table (3).

Regarding Intraoperative size of seminiferous tubules in relation to results of Micro-TESE, Statistically, Presence of large seminiferous tubules was significant in prediction of successful

sperm retrieval with Micro-TESE (P value < 0.001).

Regarding pregnancy rate, the number of patients with positive SSR was 24 cases. Twenty-two cases had successful ICSI (91.7%). While the number of patients' wives who got pregnant was 13 wives (54.2%) of positive SSR cases. Fig. (2).

#### 4. DISCUSSION

Our data showed no statistically significant difference as regarding Age, testicular volume and hormonal profile including FSH, LH , estradiol , testosterone and prolactin, while high statistically significant difference between groups according to intraoperative diameter of Seminiferous tubules.

**Table 2. Comparison of hormonal profile of patients in relation to results of Micro-TESE**

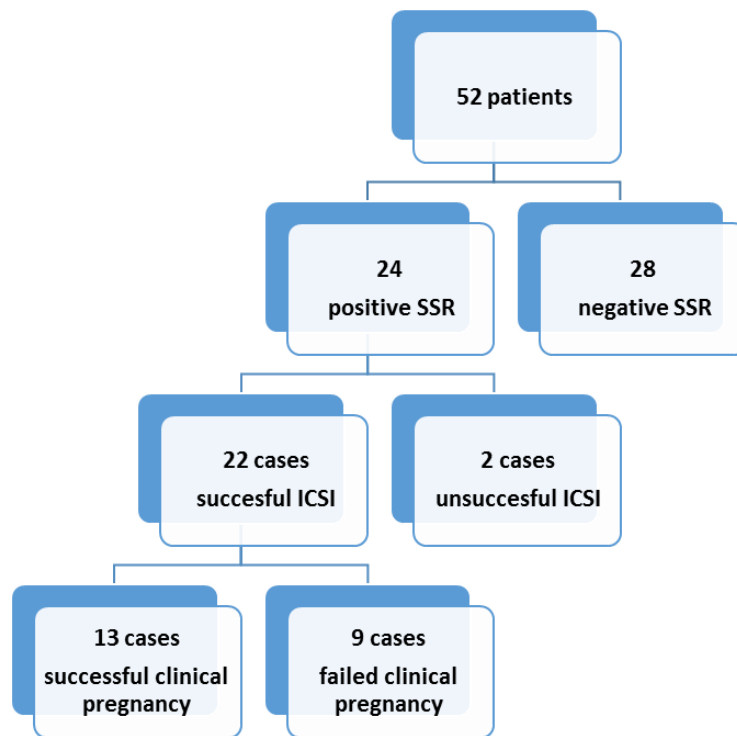
Variables		Negative SSR group	Positive SSR group	z.test	p.value
<b>FSH</b> (mIU/mL)	Range	2.5-47.0	3.5-73	0.439	0.660
	Mean ± SD	17.22±14.34	15.43±14.88		
	Median	11.6	12.8		
<b>LH</b> (mIU/mL)	Range	3.5-31.0	3-48.2	0.401	0.802
	Mean ± SD	10.26±8.01	9.65±9.42		
	Median	7.25	6.75		
<b>Testosterone</b> (ng/mL)	Range	0.9-11.3	1.8-11.1	0.698	0.485
	Mean ± SD	4.21±2.35	4.51±1.96		
	Median	3.9	4.5		
<b>Prolactin</b> (ng/mL)	Range	3.3-36.0	4.5-32.8	0.881	0.378
	Mean ± SD	11.67±6.73	11.40±7.57		
	Median	9.8	8.95		
<b>Estradiol</b> (pg/mL)	Range	2.5-48.3	6.8-65.0	0.835	0.485
	Mean ± SD	23.62±13.46	26.39±13.33		
	Median	22	27.35		

**Table 3. Testicular volume in relation to results of Micro-TESE**

testicular volume	Micro-TESE results	
	Negative	Positive
<b>Range (cm<sup>3</sup>)</b>	1.9-13.8	2.1-12.7
<b>Median (cm<sup>3</sup>)</b>	4.25	7.3
<b>Mean±SD (cm<sup>3</sup>)</b>	5.94±4.03	8.46±5.62
<b>Z</b>	1.736	
<b>p</b>	0.083	

**Table 4. Intraoperative size of seminiferous tubules in relation to results of Micro-TESE**

Large tubules	Negative		Positive	
	n	%	n	%
<b>Present</b>	2	7.1	21	87.5
<b>Absent</b>	26	92.9	3	12.5
<b>Total</b>	28	100.0	24	100.0
<b>χ<sup>2</sup></b>	30.650			
<b>p</b>	<0.001*			



**Fig. 2. Flowchart of included patients in the study and the pregnancy rate**

Similar results were obtained in a study done by Eken et al. 2018 [7], there was 145 men with NOA underwent micro-TESE. The patient's age, testicular volume, hormonal profile for FSH, LH, and testosterone, and testicular pathology were recorded. Testicular sperm retrieval rate was 65.5%. Levels of serum FSH and LH were high in all patients. There was no statistical difference in age, testicular volume or hormonal levels in the Micro-TESE positive and negative groups.

In a study conducted by Amer et al. [8], they evaluated the data of 1,395 consecutive patients who underwent micro-TESE. The evaluated data was patient's age, serum FSH, testicular volume, and duration of infertility. This study did not demonstrate any statistical significance between the mean age, the mean duration of infertility and finally, the mean of FSH levels of the patients with positive and negative Micro-TESE outcomes. Their results were similar to our study in age, duration of infertility, testicular volume and FSH.

As shown in Althakafi et al. [9], they performed Micro-TESE to 421 NOA patients. They evaluated patient's data as serum FSH, LH, estradiol, prolactin and testosterone level. Sperm were retrieved in 39.4% of Patients successfully. There was no significant between

serum testosterone level and the result of Micro-TESE as ( $P=0.820$ ). The others parameters were also insignificant. These results were analogous to the results of our study.

In a retrospectively study conducting by Caroppo, E. et al. [10], Data from 143 infertile NOA men undergoing Micro-TESE (222 testes) were evaluated. During Micro-TESE, if present, dilated tubules (DTs) were retrieved, otherwise tubules with slightly larger caliber (SDTs) than that of the surroundings were removed. When no DT or SDT were found, not dilated tubules (NDTs) were excised. They found that spermatozoa were retrieved in 95 of 222 testes (42.8%); sperm retrieval was successful in 90% of testes with DTs, in 47% of those with SDTs, and only in 7% of those with NDTs ( $p < 0.0001$ ). they concluded that The pattern of seminiferous tubules together with testis histology predicts sperm retrieval with an excellent diagnostic accuracy. These results were in accordance to our results regarding size of seminiferous tubules intraoperatively. This because, the method of sperm retrieval, the inclusion and exclusion criteria of this study were more or less similar to those of our study.

In this study, there were few limitations as the study was conducting in only fifty-two patients

and patients were not aware of infertility, its cause and the surgical treatment. Also the short follow up period was nearly one of the limitation.

From the study results it is recommended reperforming this interesting research in wide scale of patients and longer follow up period to consolidate our results. Good awareness of the patients with infertility, its causes and methods of treatment is also recommended to increase the number of patients participating in the study.

## 5. CONCLUSION

Micro-TESE is a safe option for treatment of NOA in men who present with infertility in normal female partner. The chances of sperm retrieval in men with NOA by Micro-TESE are not related to pre-operatively age, FSH, LH, estradiol, testosterone, prolactin and testicular volume as there was no significant between these factors and Micro-TESE outcomes. The detection of large seminiferous tubules intraoperatively is a good predictor for successful sperm retrieval with Micro-TESE as it was statistically significant.

## CONSENT AND ETHICAL APPROVAL

The study was done after approval from Ethical Committee and obtaining informed written consent.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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