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# Factors influencing sperm retrieval rate by Microdissection Testicular Sperm Extraction (mTESE) in non-obstructive azoospermia cases: A literature review



I Made Nugraha Gunamanta Sabudi\*

## ABSTRACT

**Background:** Non-Obstructive Azoospermia (NOA) had dominating 60% of all azoospermia cases. Sperm Retrieval Techniques (SRT) continued with Intra-Cytoplasmic Sperm Injection (ICSI) are therapy modalities helping infertile azoospermia to be fertile. There are some options of SRT such as PESA, MESA, TESE, TESA and microdissection-TESE (mTESE) to collect sperm from azoospermia cases. This study aims to evaluate some factors influencing sperm retrieval rate by mTESE in non-obstructive azoospermia cases.

**Method:** The data collection for eligible articles were conducted from 2011 to 2019. Different database and manual search methods were used to find the topic-related articles, particularly in some factors influencing the sperm retrieval rate of mTESE in NOA cases. A total of 21 relevant kinds of literature were studied regarding some factors that might be increasing or decreasing of sperm retrieval rate by mTESE procedure. However, four literature were elaborated further due to a similar approach to get the results.

**Results:** A previous study from Saudi Arabia with 264 patients samples found significant different on testosterone level who had successful Sperm Retrieval Rate (SRR) 57.25%. SRR was related by several factors of testosterone, FSH, bilateral testis retrieval and seminiferous tubules diameter taken as the earliest study from India. Besides, taking bilateral testis sperm retrieval also had low SRR 14.4%, but serum FSH level was not influenced by increasing SRR. The previous study found a very weak correlation between FSH and SRR. A different study was conducted in Italy found that all NOA patient who undergone mTESE procedure found the Maturation Arrest (MA) has the significant higher success SRR until 67% after Sertoli Cell Only (SCO) syndrome and sclera-hyalinosis histology.

**Conclusion:** SRR depends on some factors those influencing by hormonal baseline preoperative such as testosterone level and FSH serum level, technique and how mTESE done by the operator in mTESE procedure.

**Keywords:** Sperm Retrieval Rate, mTESE, Non-Obstructive Azoospermia.

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General Practitioner, Faculty of Medicine, Universitas Udayana, Bali, Indonesia

## INTRODUCTION

Fifteen percent of couples seek medical service to help them with the inability of pregnant due to infertility in both male or female factors.<sup>1</sup> Fifty percent of infertile couples are associated together with an abnormal semen analysis.<sup>1</sup> In all infertile male, 15% of cases were found with azoospermia condition. By azoospermia condition, 60% contributes by Non-Obstructive Azoospermia (NOA).<sup>2,3</sup>

Azoospermia needs the intervention of taking sperm from the testis or epididymis.<sup>2,3</sup> This intervention called Sperm Retrieval Technique (SRT) to take the sperm and continued with Intra-Cytoplasmic Sperm Injection (ICSI) to transfer it into the ovum cell. Some of SRT technics are PESA, MESA, TESA, TESE, and mTESE (microdissection Testicular Sperm Extraction).<sup>3-5</sup> Each of SRT had good ability depend on cases, the expertise of the operator, and some factors influencing Sperm Retrieval Rate (SRR). One showed mTESE is the gold standard of SRT option to help NOA. This IVF SRT-ICSI

especially mTESE technique has some factors that need to consider for gaining high SRR.<sup>4-6</sup>

Based on those mentioned above, This literature review will elaborate further the several factors influencing sperm retrieval rate by mTESE in non-obstructive azoospermia cases.

## Testosterone Optimization on Preoperative mTESE

Hypogonadism is defined as a serum testosterone level below than 10 nmol/L. Forty-five until 47% of NOA patients who seek fertility clinic had low testosterone level or known as hypogonadism.<sup>2,7</sup> Here knew low of intratesticular testosterone (ITT) would decrease spermatogenesis process. Although mTESE one said the gold standard for NOA patient with high SRR, it also needs optimization of sperm quality by good spermatogenesis process.<sup>8</sup> Several studies have shown the optimization of testosterone level using clomiphene citrate or human chorionic gonadotropin increases SRR of NOA patients by mTESE.<sup>2,7-9</sup>

\*Correspondence to:  
I Made Nugraha Gunamanta Sabudi;  
General Practitioner, Faculty of  
Medicine, Universitas Udayana, Bali,  
Indonesia;  
[nugrahagunamanta@gmail.com](mailto:nugrahagunamanta@gmail.com)

A study held by Mehmood et al. in Saudi Arabia, 264 patients grouped into two with different level of serum testosterone level, the normal one ( $>10$  nmol/L) and the hypogonadism ( $<10$  nmol/L).<sup>2</sup> It revealed the SRR of the normal group was 57.25%, and the hypogonadism was 40.60%.<sup>2</sup> This SRR comparison by testosterone level was concluded the normal testosterone level gave better SRR. This study also proofed optimized preoperative testosterone before mTESE was optimal on histopathology findings of hypospermatogenesis and maturation arrest (MA).<sup>2</sup> Implicitly optimization of testosterone level as preoperative mTESE will be helpful for NOA patient with histopathology of hypospermatogenesis and MA.<sup>2</sup>

### Low FSH for High SRR on Debatable

Serum FSH level investigated as one of the predictive factors successful SR in TESE (conventional TESE and mTESE).<sup>10,11</sup> In general, serum FSH concentration is inversely related to SRR. Some of the studies showed low FSH level had high SRR outcome, but the other also revealed FSH had poor predictive value and weak correlation for SRR by using TESE SRT.<sup>10-12</sup>

A study held on India by Ashraf et al. compared between the successful and failed mTESE looking backwards to what factors indicate the successful of mTESE one was the low level of FSH.<sup>13</sup> FSH with mean value 16.3 mIU/ml and mean value 21.0 mIU/ml respectively 54.44% and 45.56% from 180 samples conclude by statistics analysis significant the lower FSH, the higher successful SRR.<sup>13</sup>

Other study held by Gnessi et al. also showed success SR happened on mean lower level FSH 15.70 with SRR 63.17% from total 486 samples.<sup>14</sup> Associated with the histopathology of testicular extraction, the previous study found the lower level of FSH progressively also followed by higher in testicular volume and improvement of histological appearance that conclude lower FSH had better SRR.<sup>14</sup>

Contrary study in India by Kalpana and Panda revealed there was not any strong correlation between FSH and SRR level.<sup>15</sup> In the study, Kalpana et al. grouped their samples into 4 groups according to the range of FSH level as group 1 ( $\leq 15$  mIU/ml), group 2 (15.1-30 mIU/ml), group 3 (30.1-45 mIU/ml) and group 4 ( $\geq 45.1$  mIU/ml).<sup>15</sup> By correlation coefficient ( $r$ ) in statistics found value 0.27 which means there is a very weak correlation between FSH and SRR.<sup>15</sup>

Two meta-analyses also revealed about FSH level in association with SRR. By the conclusion, two studies of meta-analysis both conclude that FSH couldn't include as the predictive factor of successful on SR. The first meta-analysis held by Li H et al.

explained that the FSH level would be inversely related to the number of germ cell in testicle which means low FSH level related to increasing number of germ cell.<sup>10</sup> However, the number of germ cells did not correlate with more advanced stages of spermatogenesis. Second, FSH only representative of global spermatogenesis function, not the local isolated area in a testis.<sup>10</sup> This discussion brings mTESE SRT privilege because mTESE might able to retrieve sperm even if global spermatogenesis function of the testis was low.<sup>10</sup> In the other hand by the second study of meta-analysis held by Yang Q et al. showed FSH still as a moderate factor of the independent predictor to SRR because FSH had different diagnostic value by the first country than the other one called as a different region.<sup>11</sup> Especially in the East Asia region and younger population, FSH had more valuable diagnostic to compare independently with SRR, some of the various factor found was serum and seminal leptin level but needed further investigation.<sup>11</sup> Based by region FSH interfere, FSH and SRR couldn't conclude as the only independent factor as directly predictive factor.<sup>11</sup>

### Bilateral Testis Retrieval and Seminiferous Tubules Taken by Operator

Testosterone and FSH are playing a role as a general predictive factor on the whole function of spermatogenesis influencing the high SRR. However, there also need to identify factors more locally or as isolated by SRT.<sup>13,16</sup> mTESE procedure was one of SRT could have high SRR because of its selective extraction on testicular tissues taken by operator.<sup>13,16,17</sup>

A prospective study held by Ashraf CM et al. in India serving data as the successful group of mTESE retrieval and the failed one.<sup>13</sup> The study showed successful bilateral testis retrieval group had low SRR, only 14.4% (14/98 samples), and a high rate for the failed group 95% (78/82 samples).<sup>13</sup> This study also identified the rate of SRR by the average maximum seminiferous tubules diameter taken. Successful retrieval group had higher size ( $241.2 \pm 77.4$  microns) than the failed one ( $188.3 \pm 73.5$  microns). Larger tubules had a higher probability of harbouring sperm production, but the size of extraction on mTESE also depend on operating microscope tool availability.<sup>13,18</sup>

Another study with the same interest of bilateral testis retrieval also held by Moein MR et al. and showed a similar result.<sup>19</sup> Moein MR et al. showed bilateral testis retrieval testicular as positive or negative per testicular in 165 samples.<sup>19</sup> For positive-positive result, only 9.1%, positive-negative result 13.3%, and the rest 77.6% was negative-negative.<sup>19</sup>

### Histopathology Pattern Improve SRR

Similar to bilateral testis retrieval, as well as the number of seminiferous taken on mTESE procedure, the histopathology pattern of testicular extraction also had a role of isolated/locally tissue taken in influencing SRR. Some studies had revealed some histopathology of testicular biopsy after mTESE which results in high SRR or normal.<sup>13,20</sup>

In a study of Ashraf CM, successful SR found most in histopathology of Hypospermatogenesis 100% (42 samples), Sertoli Cell Only (SCO) 41.3% (26 samples), and maturation arrest (MA) 40% (30 samples).<sup>13</sup> Although SCO and MA had low SRR, it still had the possibility to success on SR especially using mTESE technique.<sup>13</sup>

A study by Franco G et al. in Italy with the same interest for histopathology factor that influencing the SRR also had a similar result.<sup>21</sup> In Franco G et al. study, it differentiated the group histopathology into SCO, MA, and Sclera-hyalinosis.<sup>21</sup> Hypospermatogenesis was excluded from the study because it categorized as a mild form of NOA. In this study found 67% positive SR on MA (10/15 samples), 18.9% positive on SCO (7/37 samples) and 0.8% on sclera-hyalinosis (1/12 samples). Here on this study unfamiliar with other most studies which SCO had higher SRR than MA, it could because of the other study diagnosed an incomplete SCO into all of SCO cases which there were larger microtubule with spermatogenesis still can be easily identified with the optical magnification preferably those truly SCO.<sup>20,21</sup>

### CONCLUSION

Successful sperm retrieval depending on some factors that can be modified and unmodified. Some modified factors that are influencing the SRR are testosterone level, FSH serum level, and mTESE technique to get how large seminiferous tubules will be taken and consideration of taking a unilateral side. Those factors of hormonal can be modified preoperatively by hormonal medication, especially testosterone level, but still debatable for FSH. mTESE technique depends on operators and tools availability. Different from the last factor mentioned, histopathology factor was a factor that unmodified if found as MA, SCO or sclera-hyalinosis with low positive SRR. Those histopathologies were difficult to retrieve but still had a chance in percentage.

### Conflict Of Interest

The author declares there is no conflict of interest regarding all aspect of the study.

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None.

### AUTHOR CONTRIBUTION

IMNGS is responsible for the study from the literature search, data gathering, data analysis, until reporting the results of the study by a narrative form of literature review.

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