

EFFICACY OF SURGICAL SPERM RETRIEVAL IN AZOOSPERMIC PATIENT AND ITS CONTRIBUTION TO IN VITRO FERTILIZATION PROGRAM

¹I Putu Gde Sanjaya, ¹Ponco Birowo, ²Ivan Rizal Sini, ³Budi Wiweko, ¹Nur Rasyid.

¹Department of Urology, Faculty of Medicine/Indonesia University, Cipto Mangunkusumo General Hospital, Jakarta.

²Indonesian Reproductive Science Institute (IRSI) – Bunda Hospital, Jakarta.

³Indonesian Reproductive Medicine Research and Training Center (INA REPROD), Faculty of Medicine/Indonesia University, Cipto Mangunkusumo General Hospital, Jakarta.

ABSTRACT

Objectives: This study was made to evaluate efficacy and success rate of Percutaneous Epididymal Sperm Aspiration (PESA), Microsurgical Epididymal Sperm Aspiration (MESA), or Testicular Sperm Extraction (TESE) in azoospermic patients, and evaluate IVF program's pregnancy rate by comparing methods of sperm retrieval. **Material & method:** A descriptive retrospective study to azoospermic patients undergone PESA, MESA or TESE and IVF program in Bunda Hospital Jakarta and Cipto Mangunkusumo Hospital Jakarta in 2011–2012. The data were collected from patients' medical records and IVF program's database. **Results:** There were 146 azoospermic patients with mean age 38.97 ± 7.35 years. Viable sperm was found in 46 patients (31.5%) by PESA and 47 patients (32.2%) by MESA and TESE. The IVF program was followed by 72 patients. Sperm was retrieved by PESA in 43 patients (59.7%) and TESE in 29 patients (40.3%). Pregnancy was achieved in 18 patients in PESA group (25%) and 15 patients (20.8%) in TESE group. **Conclusion:** Sperm can be retrieved from azoospermic patients by PESA, MESA or TESE, and there was good success rate in pregnancy rate of IVF program by using surgically retrieved sperm.

Keywords: Azoospermia, Surgical sperm retrieval, PESA, MESA, TESE, IVF.

ABSTRAK

Tujuan: Penelitian ini dilakukan untuk mengevaluasi efektivitas dan keberhasilan cara pengambilan sperma dengan Percutaneous Epididymal Sperm Aspiration (PESA), Microsurgical Epididymal Sperm Aspiration (MESA), or Testicular Sperm Extraction (TESE) pada pasien azoospermia, dan untuk mengevaluasi angka kehamilan program IVF dengan berbagai cara pengambilan sperma. **Bahan & cara:** Penelitian deskriptif retrospektif pada pasien azoospermia yang menjalani PESA, MESA atau TESE dan program IVF di RS Bunda Jakarta dan RS Cipto Mangunkusumo pada tahun 2011–2012. Data diambil dari rekam medis pasien dan database program IVF. **Hasil:** Terdapat 146 pasien azoospermia dengan rerata usia 38.97 ± 7.35 tahun. Sperma baik didapat pada 46 pasien (31.5%) dengan PESA dan 47 pasien (33.2%) dengan MESA dan TESE. Program IVF diikuti oleh 72 pasien. Sperma diambil dengan PESA pada 43 pasien (59.7%) dan TESE pada 29 pasien (40.3%). Kehamilan terjadi pada 18 pasien pada grup PESA (25%) dan 15 pasien pada grup TESE (20.8%). **Simpulan:** Sperma dapat diambil pada pasien azoospermia dengan PESA, MESA atau TESE, dan terdapat angka keberhasilan yang baik di program IVF dengan menggunakan sperma yang diambil dengan pembedahan.

Kata kunci: Azoospermia, pengambilan sperma dengan pembedahan, PESA, MESA, TESE, IVF.

Correspondence: I Putu Gde Sanjaya, c/o: Department of Urology, Faculty of Medicine/Indonesia University, Cipto Mangunkusumo Hospital. Jl. Diponegoro No 71, Jakarta 10430. Phone: +62 21 3152892, Fax: +62 21 3145592. E-mail: gde.sanjaya@gmail.com.

INTRODUCTION

Infertility is a failure in reproductive system to achieve pregnancy, in couple with regular sexual intercourse and without contraception within 12 months or more.^{1,2} Currently, there are 72.4 couples with infertility in the world.^{1,3} About 50% of

infertility was caused by men, and 7% of all men in the world had infertility problem.^{4,6}

Infertility in men could be caused by defects in sperm's production or function and one of those are azoospermia.⁶ Azoospermia was found in 10% of male infertility causes and divided to obstructive and non-obstructive azoospermia. In obstructive

azoospermia, there was obstruction in male genital tract and normal spermatogenesis.^{5,7} Meanwhile, in non-obstructive azoospermia, there was defect in spermatogenesis and no obstruction in male genital tract.^{5,6,8}

In the last 2 decades, there were 2 milestones in treating infertility caused by azoospermia: *IntraCystoplasmic Sperm Injection* (ICSI) and surgical sperm retrieval.^{7,9} Sperm can be surgically retrieved from epididymis by *Percutaneous Epididymal Sperm Aspiration* (PESA) or *Microsurgical Epididymal Sperm Aspiration* (MESA), and from testis by *Testicular Sperm Extraction* (TESE).⁷⁻¹² Retrieved sperm can be used in fertilization process by ICSI, while the best procedure of surgical sperm retrieval is still debatable, and had good success rate.¹²⁻¹⁴

OBJECTIVE

The aim of the study is to evaluate efficacy and success rate of methods of surgical sperm retrieval (PESA, MESA or TESE), and to evaluate IVF program's pregnancy rate by comparing methods of sperm retrieval.

MATERIAL & METHOD

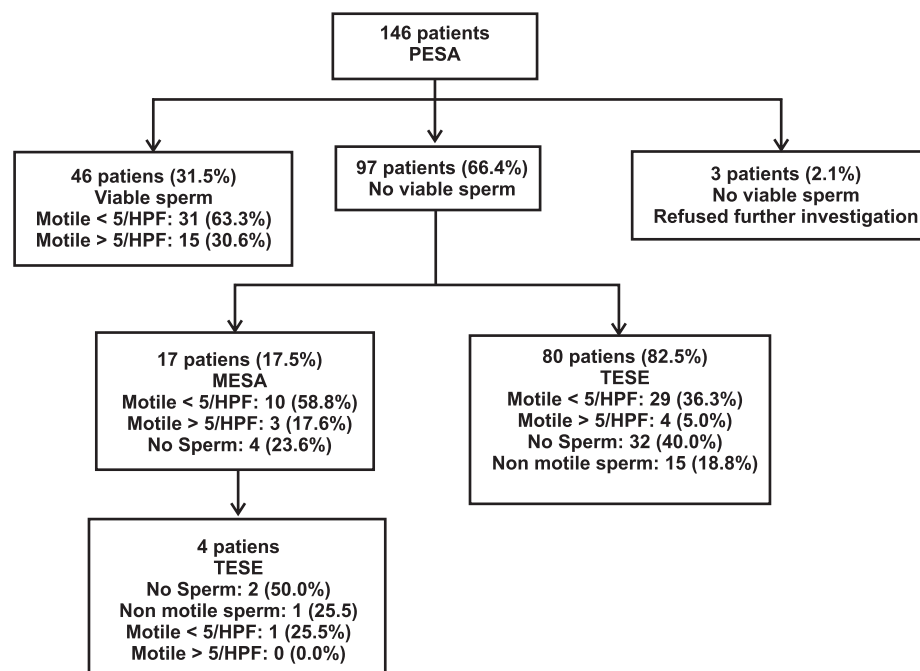
This study was a retrospective study of azoospermic patients who undergone surgical sperm

retrieval (PESA, MESA or TESE) and IVF program in Bunda Hospital and Cipto Mangunkusumo Hospital in 2011 – 2012. The data were collected from patients' medical records and IVF program's database. Azoospermia was diagnosed by sperm analysis. PESA was done in all azoospermic patients, if there was no sperm or there was only non-motile sperm in the specimen, then MESA or TESE was performed. Furthermore, if PESA and MESA was already performed but there was still no sperm or only non-motile sperm in specimen, then TESE was performed. The number and motility of sperm were evaluated intraoperative.

Retrieved sperm was used for ICSI in IVF program. The ICSI could be done directly after sperm retrieval or sometime after sperm retrieval. If the sperm retrieval was done at the same time with the ovum retrieval and ICSI, then it was called 'fresh sperm'. Meanwhile, if the ovum retrieval and ICSI was done sometime after sperm retrieval, then the retrieved sperm had to be frozen to be used in the future ('frozen sperm').

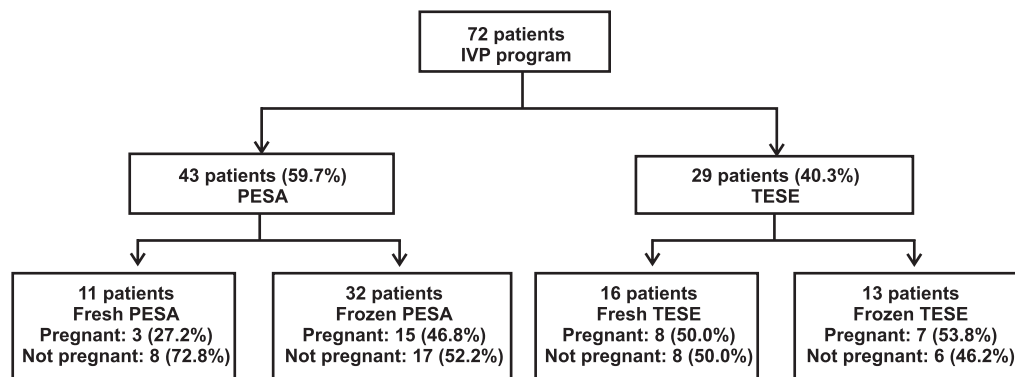
The data were analyzed using descriptive study in SPSS 17.0. Sperm retrieval results were compared between PESA, MESA, and TESE group. Pregnancy rate in IVF program was compared between methods of sperm retrieval. Both studies used Chi-Square test, $p < 0.05$ was considered significant.

RESULT



PESA: Percutaneous Epididymal Sperm Aspiration; MESA: Microsurgical Epididymal Sperm Aspiration; TESE: Testicular Sperm Extraction; HPF: High Power Field

Chart 1. Surgical sperm retrieval methods and the results.



IVF: In Vitro Fertilization; PESA: Percutaneous Epididymal Sperm Aspiration; TESE: Testicular Sperm Extraction

Chart 2. Methods of surgical sperm retrieval and IVF results.

There were 146 azoospermic patients undergone surgical sperm retrieval during 2011-2012 in Bunda hospital dan Cipto Mangunkusumo hospital Jakarta. The mean age of the patients and the spouse were 38.97 ± 7.35 years and 32.98 ± 4.74 years. PESA was done initially to all azoospermic patients and viable sperm was found in 46 patients (31.5%), 97 patients (66.4%) were performed more invasive surgical sperm retrieval (MESA and/or TESE) and most patients underwent TESE. Meanwhile, 3 patients (2.1%) refused to perform more invasive surgical procedure. There were still 50 patients (34.2%) with no sperm and motile sperm retrieved although MESA and TESE had already performed (chart 1).

From 146 azoospermic patients, 72 patients (49.3%) followed IVF program. Sperm was retrieved by PESA in 43 patients (59.7%) and from TESE in 29 patients (40.3%). Pregnancy was occurred in 33 couples (45.8%) (chart 2). There was no significant difference in pregnancy rate ($p > 0.05$) between sperm retrieved by PESA and TESE.

There were 3 patients (2 patients in Frozen PESA group and 1 patient in frozen TESE group) had to undergone same SSR procedure because their sperm were unviable after thawing. All sperm from those 3 patients were viable and all patients' spouses were clinically pregnant.

DISCUSSION

Sperm can be found in epididymis or testis in azoospermic patients through surgical intervention. Sperm retrieval by PESA, MESA and TESE had been developed since the last 2 decades and had good success rate.⁹

In this study, viable sperm can be retrieved by PESA, MESA and TESE. Study by Esteves et al

(2011) found that success rate in sperm retrieval was higher by MESA or TESE than by PESA.⁹ This study found similar result, viable sperm could be retrieved after failed in PESA by MESA in 13 patients (8.9%), and by TESE in 34 patients (23.2%) with $p < 0.05$. Higher success rate in sperm retrieval by MESA or TESE compared to PESA in this study could be due to several causes: higher proportion of non-obstructive azoospermic patients, technical difficulties in performing accurate PESA (hematoma or missed puncture site), and better sperm quality and quantity in testes. Although, MESA or TESE had better success rate in retrieving sperm than PESA, in our setting PESA still our first treatment of choice in retrieving sperm in azoospermic patients because of several reasons: high success rate in retrieving sperm (31.5%), minimal discomfort to the patients, lower complication rate compared to MESA or TESE, lower cost, easy to repeat in outpatient clinic and not requiring microscope.

There were several studies evaluating success rate of various methods of surgical sperm retrieval. Studies by Dohle et al (1998), Levine et al (2003) and Esteves et al (2011) showed success rate by PESA and TESA was higher in obstructive than non obstructive azoospermia patients, and TESE has higher success rate than PESA.^{7,9,12} It is possible that the proportion of non-obstructive azoospermic patients was higher in our study so that our success rate was similar to same group in study by Esteves et al (PESA group: 31.5% vs 35% and TESE group: 41.3% vs 50%)

This study also evaluated pregnancy rate in IVF program by comparing methods of sperm retrieval (PESA and TESE). There were different results of pregnancy rate by sperm retrieved by PESA or TESE. Study conducted by Pasqualotto et al (2002) and Semiao-Fransisco et al (2010) showed no

different in pregnancy rate between sperm retrieved by PESA or TESE. Furthermore, Cochrane review couldn't conclude whether there was correlation between methods of surgical sperm retrieval in pregnancy rate in IVF program, due to lack of evidences.¹³⁻¹⁵ Meanwhile, study by Mercan et al (2000)⁸ showed that pregnancy rate in IVF was higher with sperm retrieved by less invasive methods in non-obstructive azoospermic patients. Sperm quality had important role in success rate of pregnancy. Therefore, quality of sperm was associated with ease of sperm retrieval. Easier sperm retrieval was related to less invasive method to retrieve sperm and more concentration of retrieved sperm. Some studies showed that spermatogenetic impairment and chromosomal abnormalities were higher in patients with less concentration of sperm (difficult sperm retrieval) and with non-obstructive azoospermic patients.^{9,16,17} In our study, there was no statistically different in pregnancy rate between sperm retrieved by PESA or TESE ($p > 0.05$). This result could be due 2 biases: no differentiation between obstructive and non-obstructive azoospermic patients and high concentration of sperm retrieved in our patients. In our facility, the mortality rate of frozen sperm was around 40%, based on that experience we selectively chose patients with higher concentration of sperm to followed IVF program with frozen sperm. This could lead to indirectly include patients with more concentration of sperm, and consequently probably better sperm quality (less spermatogenetic impairment and chromosomal abnormalities). Furthermore, the success rate of pregnancy rate was also affected by spouse's (female) factors which not being investigated in this research.

The limitations of the study were no follow up of the pregnancy outcome of patients in IVF program, and no difference in etiology of azoospermic patients (obstructive and non-obstructive azoospermia).

CONCLUSION

Sperm can be retrieved from azoospermic patients by PESA, MESA or TESE, and there was good success rate in pregnancy rate of IVF program by using surgically retrieved sperm.

REFERENCES

1. Gurunath S, Pandian Z, Anderson RA. Defining infertility—a systematic review of prevalence studies. *Human Reproduction Update*. 2011; 17(5): 575-88.
2. Zegers-Hochschild F, Adamson GD, de Mouzon J. International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary of ART terminology, 2009. *Fertil Steril*. 2009; 92(5): 1520-4.
3. Boivin J, Bunting L, Collins JA. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. *Human Reproduction*. 2007; 22(6): 1506-12.
4. Hammarberg K, Baker HWG, Fisher JRW. Men's experiences of infertility and infertility treatment 5 years after diagnosis of male factor infertility: a retrospective cohort study. *Human Reproduction*. 2010; 25(11): 2815-20.
5. Dohle GR, Colpi GM, Hargreave TB. EAU guidelines on male infertility. *Eur Urol*. 2005; 48(5): 703-11.
6. Krausz C. Male infertility: pathogenesis and clinical diagnosis. *Best Pract Res Clin Endocrinol Metab*. 2011; 25(2): 271-85.
7. Dohle GR, Ramos L, Pieters MH. Surgical sperm retrieval and intracytoplasmic sperm injection as treatment of obstructive azoospermia. *Human Reproduction*. 1998; 13(3): 620-3.
8. Mercan R, Urman B, Alatas C. Outcome of testicular sperm retrieval procedures in non-obstructive azoospermia: percutaneous aspiration versus open biopsy. *Human Reproduction*. 2000; 15(7): 1548-51.
9. Esteves SC, Miyaoka R, Agarwal A. Sperm retrieval techniques for assisted reproduction. *Int Braz J Urol*. 2011; 37(5): 570-83.
10. Bromage SJ, Falconer DA, Lieberman BA. Sperm Retrieval Rates in Subgroups of Primary Azoospermic Males. *European Urology*. 2007; 51(2): 534-40.
11. Van Perperstraten AM, Proctor ML, Phillipson G. Techniques for surgical retrieval of sperm prior to ICSI for azoospermia. *Cochrane Database Syst Rev*. 2001; 4: CD002807.
12. Levine LA, Dimitriou RJ, Fakouri B. Testicular and epididymal percutaneous sperm aspiration in men with either obstructive or nonobstructive azoospermia. *Urology*. 2003; 62(2): 328-32.
13. Semiao-Francisco L, Braga DP, Figueira Rde C. Assisted reproductive technology outcomes in azoospermic men: 10 years of experience with surgical sperm retrieval. *Aging Male*. 2010; 13(1): 44-50.
14. Pasqualotto FF, Rossi-Ferragut LM, Rocha CC. Outcome of in vitro fertilization and intracytoplasmic injection of epididymal and testicular sperm obtained from patients with obstructive and nonobstructive azoospermia. *J Urol*. 2002; 167(4): 1753-6.
15. Van Peperstraten A, Proctor ML, Johnson NP. Techniques for surgical retrieval of sperm prior to intra-cytoplasmic sperm injection (ICSI) for

- azoospermia. Cochrane Database Syst Rev. 2008; 2: CD002807.
16. Hargreave TB. Genetic basis of male fertility. British Medical Bulletin. 2000; 56(3): 650-71.
17. Chandley AC. The genetic basis of male infertility. Reproductive Medicine Review. 1995; 4(01): 1-8.