IVF OUTCOMES USING SPERM RETRIEVED VIA EXTENDED SPERM SEARCH (ESSM) VERSUS MICROSURGICAL TESTICULAR SPERM EXTRACTION (mTESE) AMONG PATIENTS WITH NON-OBSTRUCTIVE AZOOSPERMIA

Email for corresponding author:
Claudia.Durbin@nyulangone.org

Claudia Durbin[1], Emily Weidenbaum MD[2], Caroline McCaffery PHD, HCLD[2], Bobby Najari MD[3]

[1]NYU Grossman School of Medicine, New York, NY, [2]NYU Langone Prelude Fertility Center, New York, NY, [3]Department of Urology, NYU Grossman School of Medicine, New York, NY

NYU Langone Prelude Fertility Center

INTRODUCTION

- Male factor accounts for 20-30% of infertility cases but can contribute to 50% of cases overall[1].
  - Non-obstructive azoospermia (NOA) is the most severe form of male infertility[2].
  - Cryptozoospermia is impaired spermatogenesis in which sperm observed after centrifugation.
- Current sperm retrieval options for in-vitro fertilization (IVF) include mTESE and ESSM.
- mTESE sperm retrieval rate (SRR) is 52% with unclear positive predictive factors and surgical morbidity[3].
- ESSM is a non-invasive alternative that uses laboratory techniques to identify sperm in ejaculate.
- There is no consensus for the efficacy of testicular versus ejaculated sperm to achieve fertilization.
- **Study Objectives:**
  1. **Describe the incrementally increased SRR among patients with NOA or cryptoozospermia who undergo ESSM before mTESE versus mTESE alone.**
  2. **Compare IVF outcomes using testicular versus ejaculated sperm.**

MATERIALS & METHODS

- **Retrospective cohort study** (NYU IRB #13-00389) of male patients with NOA or cryptozoospermia who underwent mTESE or ESSM at a single university-affiliated center from 2018-2024.
- Inclusion criteria: (1) diagnosis of NOA or cryptozoospermia on two semen analyses, (2) underwent mTESE at our center, (3) referred to ESSM from our center.
- Exclusion criteria: (1) found to have obstructive azoospermia or severe OAT (2) mTESE performed at an outside center.
- Patients were categorized according to the intervention they pursued first: “mTESE first” or “ESSM first”; if ESSM first failed, patients were referred to mTESE and categorized as “mTESE after ESSM”.
- Statistical analysis: Chi-squared test and multiple logistic regression, an alpha error of 0.05 as significant

RESULTS: OVERVIEW

- **73** patients were included
  - **NOA:** 46 patients (63%)
  - **Cryptozoospermia:** 27 patients (37%)
- **45** pursued **ESSM first** | **28** pursued **mTESE first** | **12** pursued **mTESE after ESSM**
  - **ESSM First SRR:** 64% (29/45)
  - **mTESE First SRR:** 54% (15/28)
  - **mTESE after ESSM SRR:** 42% (5/12)
- **55** IVF cycles using ejaculated sperm from ESSM or testicular sperm from mTESE were included
  - **IVF cycle using ejaculated sperm:** 42% (23/55)
  - **IVF cycle using testicular sperm:** 58% (32/55)
  - Average age female partner: 35 years (Range: 24-45)
  - Average age male partner: 40 years (Range: 28-58)

TABLE 1: DEMOGRAPHIC OF MEN UNDERGOING MTESE VS ESSM FIRST

	Age	Diagnosis		Biopsy		Hormone		Prior Therapy		Exam	
		NOA	Crypto	SCO	Hypo/ Mat Arrest	Eu-gonadal	Hypo-gonadal	Medical	Varicocel-ectomy	Testes Vol	Varicolele
ESSM First N = 45	35.3 (33.2, 40.5)	26 (58)	19 (42)	6 (50)	6 (50)	38 (84)	7 (16)	15 (33)	4 (9)	9.6 L, 10 R	22 (49)
mTESE First N = 28	36.3 (32.5, 29.8)	20 (72)	8 (28)	13 (48)	14 (52)	23 (82)	5 (18)	10 (35)	7 (25)	8.6 L, 8.8 R	17 (61)

Notes: (1) Data presented as Median (IQR) or Number (%); **n.s. difference between groups**; (2) Abbreviations: NOA, Non-obstructive azoospermia; Crypto, cryptozoospermia; SCO, Sertoli Cell Only; Hypo/Mat Arrest = Hypospermatogenesis/Maturation Arrest

FIGURE 1: PROPOSED PROTOCOL STUDY FLOW

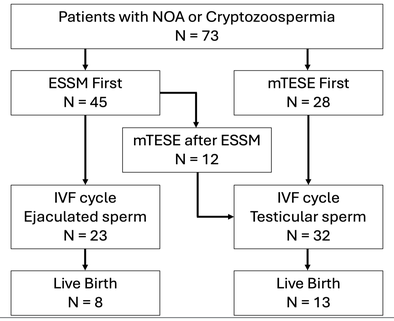

FIGURE 2: FERTILIZATION AND TRANSER OUTCOMES FOR TESTCULAR VS EJACULATED SPERM

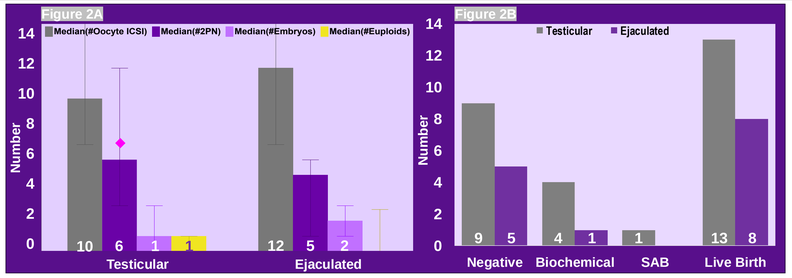

Figure 2A. Median oocyte, embryo, euploids using testicular vs ejaculated sperm **Notes:** (1) Data presented as Median, error bar = IQR; (2) ◆ = significantly more 2PN with testicular sperm (p = 0.05); **Figure 2B.** FET outcomes using ejaculated vs testicular sperm; n.s. difference (p = 0.77).

OBJECTIVE 1: SPERM RETRIEVAL RATE ESSM VS mTESE

- **Patients who underwent ESSM before mTESE had a significantly higher SRR than patients who underwent mTESE alone (76% vs. 54%; p = 0.05).**
  - 64% (29/45) of patients overall retrieved sperm on ESSM without mTESE
  - mTESE after failed ESSM had similar SRR to mTESE first (42% vs. 54%; p = 0.49)
- **No significant difference in total motile sperm number retrieved from successful ESSM vs mTESE (26 vs. 76; p = 0.18).**
  - **ONE** successful ESSM yielded an average of **ONE** IVF cycle.
  - **ONE** successful mTESE yielded an average of **TWO** IVF cycles.

OBJECTIVE 2: IVF OUTCOMES FOR TESTICULAR VS EJACULATED SPERM

- **See Figure 2A for median number of oocytes fertilized, embryos, and euploids using testicular versus ejaculated spermatozoa for ICSI**
- **IVF cycles using ejaculated sperm had no significant difference in fertilization rate, higher blastulation rate, and no significant difference in euploidy rate compared to testicular sperm**
  - *Fertilization rate* (2PN/total oocytes) = 42% ejaculated sperm **SIMILAR** 48% testicular sperm (p = 0.15)
  - *Blastulation rate* (embryo/2PN) = 50% ejaculated sperm **HIGHER** 20% testicular sperm (p = 0.002)
  - *Euploid rate* (euploid/embryo) = 40% ejaculated sperm **SIMILAR** 67% ejaculated sperm (0.07)
- **See Figure 2B for frozen embryo transfer (FET) outcomes using testicular versus ejaculated spermatozoa for ICSI**
- **No significant difference in FET outcomes between cycles using ejaculated versus testicular sperm**
  - *Live Birth Rate per FET* = 57% ejaculated sperm **SIMILAR** 48% testicular sperm
  - *Live Birth Rate per IVF cycle* = 34% ejaculated sperm **HIGHER** 40% testicular sperm

CONCLUSIONS

- Evidence-based recommendations for pursuing ESSM versus mTESE are essential, as both interventions are associated with cost and potential delay in IVF cycles.
- The proposed protocol of pursuing ESSM before mTESE has an incrementally increased sperm retrieval rate of 76%, compared to 54% among men who undergo mTESE alone (p = 0.05).
- No difference in IVF outcomes using ejaculated versus testicular sperm, with a live birth rate of 57% for cycles using ejaculated spermatozoa and 48% for testicular spermatozoa (p = 0.77).
- More studies with larger sample sizes are needed to evaluate outcomes

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