



PD25-01: Does the Use of Testicular Sperm Improve Outcomes in Nonazoospermic Couples with Previous In-Vitro Fertilization (IVF) Failure Using Ejaculated Sperm?

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Disclosures

- None

Introduction

- Recommendations for couples after repeat IVF failures can be frustrating
- Use of testicular sperm for intracytoplasmic sperm injection (ICSI) may lead to higher implantation rates, clinical pregnancy rates, and live birth rates for couples with a history of prior IVF failure(s) using ejaculated sperm¹⁻³
- Mechanism unknown
- Sperm DNA fragmentation (SDF) may play a role

1. Ben-Ami I, et al. Fertil Steril 2013;99:1867-71.

2. Esteves SC, et al. Fertil Steril 2015; 104:1398-405.

3. Negri L, et al. Gynecol Endocrinol 2014;30:48-52.

Introduction

- Sperm DNA fragmentation (SDF):
 - Percentage of sperm in a sample with damaged DNA chromatin¹
 - This damaged DNA becomes incorporated into the embryonic genome and may negatively affect fertility outcomes²
- Elevated SDF has been associated with lower rates of clinical pregnancy³

1. Evgeni E, et al. Eur J Obstet Gynecol Reprod Biol 2015;188:17-23.

2. Parikh FR, et al. Fertil Steril 2019;111:672-3.

3. Simon L, et al. Asian J Androl 2017;19:80-90.

Introduction

- Testicular sperm has a lower SDF vs. ejaculated sperm¹
- Some providers offer testicular sperm for ICSI in the setting of elevated SDF²⁻⁵
- Studies using testicular sperm for this indication are conflicting
 - Higher clinical pregnancy and live birth rates⁶
 - No improvement in fertilization or pregnancy rates⁷⁻⁹
- Currently, there is insufficient evidence to routinely recommend that patients with high SDF undergo ICSI with testicular sperm vs. ejaculated sperm¹⁰

1. Zini A, et al. Hum Reprod 2008;23:2663-8.

2. Simon L, et al. Asian J Androl 2017;19:80-90.

3. Majzoub A, et al. Transl Androl Urol 2017;6:S710-S9.

4. Esteves SC, et al. Fertil Steril 2017;108:456-67 e1.

5. Esteves SC. Int Braz J Urol 2018;44:667-75.

6. McQueen DB, et al. Fertil Steril 2019; 112: 54-60.

7. Esteves SC, et al. Fertil Steril 2015;104:1398-405.

8. Abhyankar N, et al. Fertil Steril 2016;105:1469-75 e1.

9. Bradley CK, et al. Andrology 2016;4:903-10.

10. Practice Committee of the American Society for Reproductive M. Fertil Steril 2013;99:673-7.

Introduction

- While there is early evidence to suggest that the use of testicular sperm is associated with better outcomes compared to ejaculated sperm for couples with a history of previous IVF failure(s), many argue that performing a testicular sperm extraction for this purpose is an invasive surgical procedure without clear benefit¹

1. Halpern JA, et al. Eur Urol Focus 2018;4:299-300

Objective

- Evaluate IVF-ICSI cycles using testicular sperm in non-azoospermic couples with a history of prior IVF failure(s) using ejaculated sperm

Methods

- Single center, retrospective cohort
- Underwent a testicular sperm extraction (TESE) or testicular sperm aspiration (TESA) from January 2015 to October 2019
- Inclusion criteria:
 - Underwent sperm retrieval procedure for history of ≥ 1 prior IVF failure using ejaculated sperm
 - No significant erectile or ejaculatory dysfunction
- Exclusion criteria:
 - Azoospermia

Methods

- ICSI cycles using testicular sperm were compared to the couples' prior cycle(s) using ejaculated sperm
- Primary outcomes:
 - Clinical pregnancy rate (CPR)
 - Live birth rate (LBR)
- Secondary outcomes:
 - Fertilization rate
 - Blastocyst conversion rate
- Subgroup analyses
 - Elevated SDF (>25%)
 - ≥2 failed cycles using ejaculated sperm

Demographics

- 112 couples met criteria
- Mean male partner age: 40.4 years
- Mean female partner age: 36.4 years
- Abnormal semen parameters: 74.1%
(Table 1)

Table 1: Abnormal Semen Parameters (WHO Criteria)¹

Semen Analysis Diagnosis:	Percentage of Men:
Oligospermia	12.6% (14/112)
Asthenospermia	7.1% (8/112)
Teratospermia	13.4% (15/112)
Oligoasthenospermia	21.4% (24/112)
Oligasthenoteratospermia	19.6% (22/112)
Total	74.1% (83/112)

1. Cooper TG, et al. Hum Reprod Update 2010;16:231-45.

Demographics

- Mean and interquartile ranges (IQR) for semen parameters, FSH, and testosterone levels were evaluated (Table 2)
- Sperm DNA fragmentation:
 - Mean SDF (n=105): 32%
 - Range: 0%-90%
 - IQR: 0%-53%
 - Mean Elevated SDF (>25%; n=66): 49%

Table 2: Semen Parameters & Hormone Levels

Parameter	Mean (IQR)
Sperm concentration (million/mL)	29.9 (3.0-39.5)
Sperm motility (%)	40.7 (26.0-55.5)
Total Motile Sperm Count (million)	51.6 (1.5-57.5)
Sperm morphology (%)	1.9 (1.0-3.0)
Ejaculate volume (mL)	3.0 (2.0-3.8)
Testosterone, total (ng/dL)	398.3 (275.0-451.0)
Male FSH (IU/mL)	9.8 (4.1-10.7)

Results

- Couples underwent an average of 2.3 (range 1-8) prior failed IVF cycles using ejaculated sperm before using testicular sperm
- 157 ICSI cycles were performed using testicular sperm
 - Fresh testicular sperm cycles: n=133
 - Frozen testicular sperm cycles: n=24
- Of these 157 cycles, there were 101 embryo transfers
- All prior failed cycles were performed using fresh ejaculated sperm

Results

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M2 oocytes (n)	11.0 (6.0-15.0)	11.2 (7.0-14.0)	0.81	10.9 (6.0-14.0)	9.6 (7.0-14.0)	0.31
M2's fertilized (%)	69.7% (50.0-80.0)	57.9% (30.1-80.8%)	0.02	76.1 (50.0-80.0)	58.6 (30.0-83.3)	0.17
Cycles without blastocyst development	51/157 (32.5%)	73/112 (65.2%)	<0.001	27/66 (40.9%)	48/66 (72.7%)	<0.001
Blastocyst conversion	66.9%	34.8%	<0.001	59.1%	27.1%	<0.001
Embryos transferred (n)	1.9 (0.0-2.0)	0.9 (0.0-1.0)	0.83	1.0 (0.0-2.0)	2.0 (0.0-1.0)	0.30
Blastocysts vitrified (n)	1.6 (0.0-2.0)	0.7 (0.0-1.0)	<0.001	1.6 (0.0-2.0)	0.9 (0.0-1.0)	0.03
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Results

Subset analysis of couples with ≥ 2 prior failed IVF cycles using ejaculated sperm:

- No difference:
 - Number of oocytes retrieved (16.1 vs 15.6, $p=0.91$)
 - Number of mature oocytes (10.7 vs 11.3, $p=0.39$)
 - Fertilization rates (73.2% vs 61.9%, $p=0.25$)
- TESE cycles with significantly improved:
 - Blastocyst conversion rates (64.9% vs 36.4%, $p<0.001$)
 - Number of blastocysts available for vitrification (1.6 vs 0.7, $p=0.03$)
- Clinical pregnancy rate: 41.7% (vs 43.6% in entire TESE-ICSI cohort)
- Live birth rate: 33.3% (vs 31.7% in entire TESE-ICSI cohort)

Strengths and Limitations

Strengths:

- Large patient cohort
- Limited evaluation to patients undergoing sperm extraction due to prior IVF failure

Limitations:

- Subset of patients with SDF available to compare differences between normal vs elevated SDF outcomes
- Retrospective, observational study without matched control
- Combined fresh and frozen testicular sperm, as well as fresh and frozen embryo transfers, in the final analysis

Conclusions

- Among nonazoospermic couples with previous IVF failures, testicular sperm may:
 - Improve blastocyst development
 - Increase the number of blastocysts available for vitrification
 - Improve clinical pregnancy rates
 - Improve live birth rates
- Testicular sperm may avoid the adverse effects of elevated SDF
- Additional large-scale, randomized controlled trials are needed to determine the true benefit of using testicular sperm in this setting

A landscape photograph showing Georgetown University's historic architecture. In the foreground, there are dense green trees. Behind them, several buildings are visible, including a large red brick building on the left and a prominent grey stone building with two tall, ornate towers on the right, identified as Healy Hall. The sky is a clear, pale blue with a few wispy clouds.

Thank you