THE CANADIAN FERTILITY AND ANDROLOGY SOCIETY'S 71ST ANNUAL MEETING

September 18 - 20, 2025
Centre des Congrès de Québec, Quebec City

#51 - Segmental Aneuploidy in IVF: The Hidden Role of Sperm DNA Fragmentation and Selection Strategies

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INTRODUCTION

- The growing trend toward delayed parenthood has led to an increase in parental age at conception[1].
- **Paternal age plays a role in the occurrence of segmental aneuploidy**: involves paternally inherited chromosomes[2], no reported correlation with maternal age[3], associated with higher levels of sperm DNA fragmentation index (DFI[2] – which correlates with increased paternal age[4]).
- ZyMot and testicular sperm aspiration (TESA) have shown promise in selecting morphologically normal, highly motile sperm with low levels of DFI[5,6].

AIMS

- Evaluate the association between sperm DFI and the incidence of segmental aneuploidy in embryos analyzed via PGT-A.
- Assess whether sperm selection techniques—ZyMot and TESA—reduce segmental aneuploidies in cases of elevated DFI.
- Explore the contribution of maternal and paternal age to segmental aneuploidy rates.

METHOD

- Retrospective chart review of **2052 embryos from 614 IVF cycles** who underwent PGT-A analysis between November 2020 and February 2025
- Couples who used a sperm donation, with a maternal age superior to 43, with known karyotype anomalies, or without a DFI analysis within one year of the IVF cycle were **excluded**.
- DFI was classified as **elevated (>30%), normal (≤16.8%), or intermediate,** according to clinical standards.
- Data distribution was assessed to determine normality, and parametric or non-parametric tests were applied accordingly. Proportions were compared using Chi-square or Fisher's exact tests. When multiples comparisons were performed, p-values were adjusted using Holm method to control for type I error. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Table 1. Comparison of parental age, embryo characteristics, and incidence of segmental aneuploidy (SA), across the three sperm DNA fragmentation index (DFI) groups

Variable	All Participants	DFI ≤ 16.8%	DFI 16.8-30%	DFI > 30%	P-value
Maternal age (years)	38.1 ± 3.4 39.0 (37.0, 40.0)	37.9 ± 3.6 39.0 (36.0, 40.0)	38.3 ± 3.2 39.0 (37.0, 40.0)	38.4 ± 3.2 39.0 (37.0, 40.7)	NS
Paternal age (years)	40.1 ± 5.8 40.0 (36.0, 43.0)	39.2 ± 5.4 39.2 (36.0, 42.0)	40.5 ± 5.9 40.0 (37.0, 44.0)	42.6 ± 6.1 42.0 (38.0, 46.0)	≤16.8 vs >30: **<0.001** 16.8-30 vs >30: **0.01**
Biopsied embryos (n)	2052 (100%)	1154 (100%)	594 (100%)	304 (100%)	
SA embryos (n)	65 (3.2%)	38 (3.3%)	13 (2.2%)	14 (4.6%)	0.56
SA + whole aneuploid embryos (n)	38 (1.8%)	22 (1.9%)	11 (1.8%)	5 (1.6%)	0.96
SA +/- whole aneuploid embryos (n)	103 (5.0%)	60 (5.2%)	24 (4.0%)	19 (6.3%)	0.66
Cycles (n)	614 (100%)	332 (100%)	189 (100%)	93 (100%)	
Cycles with at least 1 SA embryo (n)	91 (14.8%)	57 (17.2%)	22 (11.6%)	12 (12.9%)	0.21

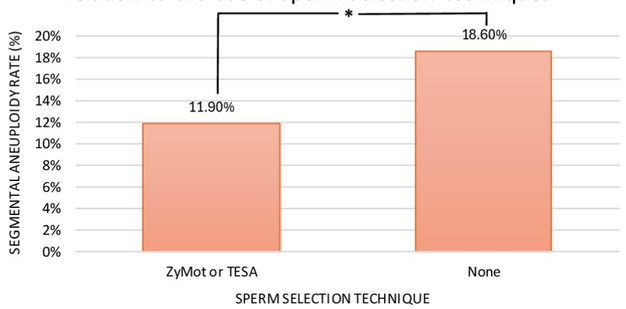
- Paternal age was significantly higher in cycles with **elevated DFI**
- Although the proportion of cycles with segmental aneuploidy **did not differ significantly** across DFI groups, the absolute frequency was higher in the low DFI group.

Table 2. Analysis of parental age in relation with the presence of segmental aneuploidy (SA)

Variable	Cycles without SA n=523	Cycles with SA n=56	Cycles with SA + whole aneuploidy n=36	P-value
Maternal age (years)	38.2 ± 3.4 39.0 (37.0, 40.0)	36.5 ± 4.0 38.0 (35.0, 39.0)	38.5 ± 3.2 39.0 (37.0, 40.7)	No SA vs SA : **0.002** SA vs SA + whole : **0.03**
Paternal age (years)	40.3 ± 5.7 40.0 (36.0, 43.0)	39.2 ± 6.4 39.0 (35.0, 43.7)	39.3 ± 5.5 39.0 (35.2, 42.0)	NS

- Maternal age was significantly higher in cycles with both segmental and whole aneuploidies compared to cycle with only segmental aneuploidies

Figure 1. Incidence of segmental aneuploidy in relation to the use of sperm selection techniques



- Sperm selection techniques were least used in cycles with low DFI ($p < 0.001$), yet their use (ZyMot or TESA) was associated with a significantly **reduced rate of segmental aneuploidies ($p = 0.02$)**

CONCLUSION

We present evidence consistent with the current understanding that **advancing paternal age is associated with increased sperm DNA fragmentation**, which in turn may contribute to segmental chromosomal abnormalities in embryos. Given the silent nature of DNA fragmentation and its prevalence in older men, paternal age should serve as a clinical trigger to explore DFI levels or to proactively use sperm selection techniques. Our findings **support the integration of ZyMot or TESA in IVF protocols for men of advanced age as it mitigates the risks of segmental aneuploidy**, even when DFI testing is unavailable or borderline. Still, there is a need to elucidate the impact of other DFI reducing treatments, such as oral antioxidants therapy, on the incidence of segmental aneuploidy.

REFERENCES

1 Cedars, M.I. Introduction: Childhood implications of parental aging. Fertil. Steril. 2015, Jun; 103(6):1379–1380. **2 Gao, J., et al.** The effect of sperm DNA fragmentation on the incidence and origin of whole and segmental chromosomal aneuploidies in human embryos. Reproduction. 2023, Aug; 166(2):117-124. 3 **Rodrigo, L., et al.** New tools for embryo selection: comprehensive chromosome screening by array comparative genomic hybridization. Biomed Res Int. 2014, Apr; 517125. **4 Petersen, C. G., et al.** The effects of male age on sperm DNA damage: an evaluation of 2,178 semen samples. JBRA Assist Reprod. 2018, Nov; 22(4):323-330. **5 Esteves, S. C., et al.** Comparison of reproductive outcome in oligozoospermic men with high sperm DNA fragmentation undergoing intracytoplasmic sperm injection with ejaculated and testicular sperm. Fertil Steril. 2015, Dec; 104(6):1398-1405. **6 Zaha, I., et al.** Comparative Study of Sperm Selection Techniques for Pregnancy Rates in an Unselected IVF-ICSI Population. J Pers Med. 2023, Mar; 13(4).

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