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## **REDEFINING ANEUPLOIDY RATES IN THE ERA OF MOSAICISM REPORTING: A LONGITUDINAL STUDY OF 24,341 EMBRYOS ANALYZED USING NEXT GENERATION SEQUENCING**

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### **OBJECTIVE:**

Our understanding of the relationship between female age and rate of embryonic aneuploidy has remained fairly consistent over the years.<sup>1</sup> The detection of embryo mosaicism in preimplantation genetic testing for aneuploidy (PGT-A) has introduced a third category into the possible options for embryo ploidy. The aim of this study is to determine how reporting of mosaicism in PGT-A alters the ratio of euploid and aneuploid embryos.

### **MATERIALS AND METHODS:**

This study included patients who underwent an IVF cycle at a single academic center with PGT-A from February 2016 through March 2021. Trophectoderm biopsies were analyzed using a modified FAST-SeqS NGS-based PGT method and bioinformatics pipeline. Patients were separated into groups based on availability of mosaic reporting (Group A: January 2020-March 2021, routine reporting included mosaicism; Group B: February 2016-December 2019, routine reporting did not include mosaicism). The proportion of embryos reported as euploid and aneuploid was compared among SART age groups. Embryos with both full aneuploidy and mosaicism were reported as aneuploid. Indeterminate results were excluded. Student's t-test and chi square were used for analysis, with multivariable logistic regression to adjust for confounders. Bonferroni correction was performed to control for multiple comparisons with a corrected p value of .004.

### **RESULTS:**

Of the 24,341 embryos from 4,407 patients identified in the study, 12,850 (52.8%) were reported as euploid and 10,450 (42.9%) were reported as aneuploid. The mean oocyte age was 35.2 years. The rate of embryonic euploidy was similar during the era of mosaic reporting compared to the period prior to mosaic reporting (51.8% vs. 53.5%,  $p=.02$ ) while the rate of aneuploidy decreased by 11.6% (35.1% vs. 46.7%,  $p<.0001$ ). No differences were seen in euploid rates between the study and control groups when stratified by SART age group. Aneuploidy rates were significantly lower in the era of mosaic reporting among age SART Group A (21.0% vs. 35.4%,  $p<.0001$ ), Group B (33.0% vs. 43.7%,  $p<.0001$ ), and Group C (46.7% vs. 56.5%,  $p<.001$ ) but not Group D (68.3% vs. 71.6%,  $p=.13$ ) or Group E (76.5% vs. 79.7%,  $p=.28$ ). Multivariable logistic regression controlling for oocyte age, high quality embryo, and day of biopsy revealed that mosaic reporting was significantly associated with a lower odds of aneuploid reports in Groups A, B, and C but not in D or E (Group A: OR 0.48, 95% CI 0.44-0.53,  $p<.0001$ ; Group B: OR 0.63, 95% CI 0.56-0.71,  $p<.0001$ ; Group C: OR 0.69, 95% CI 0.61-0.78,  $p<.0001$ ).

### **CONCLUSIONS:**

Mosaicism reporting alters the proportions of embryos interpreted as aneuploid, particularly among younger age groups. In older age groups, the predominance of meiotic errors resulting in full aneuploidy leads to a minimal shift in the proportions of embryos reported as euploid or aneuploid.



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**IMPACT STATEMENT:**

Reporting embryo mosaicism as a separate category from aneuploidy significantly modifies existing aneuploidy curves. This data may alter patient counseling regarding expected aneuploidy rates by age and the anticipated proportion of embryos with the potential for implantation.

**REFERENCES:**

1. Franasiak JM, Forman EJ, Hong KH, Werner MD, Upham KM, Treff NR, Scott RT Jr. The nature of aneuploidy with increasing age of the female partner: a review of 15,169 consecutive trophoctoderm biopsies evaluated with comprehensive chromosomal screening. *Fertil Steril*. 2014 Mar;101(3):656-663.e1. doi: 10.1016/j.fertnstert.2013.11.004.