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Title:

THE ASSOCIATION BETWEEN ANEUPLOIDY AND THE RATE OF BLASTOCYST DEVELOPMENT IS AGE DEPENDENT

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Objective:

Modern preimplantation genetic testing (PGT) requires extended culture of embryos to the blastocyst stage to facilitate trophectoderm biopsy. While PGT to select euploid blastocysts for transfer have increased implantation and pregnancy rates, failed or slow development to the blastocyst stage may preclude biopsy of embryos at the appropriate stage. We hypothesize that embryos with a normal chromosomal complement are more likely to cavitate quickly. Alternatively, some have proposed that very rapid cleavage may indicate embryonic dysfunction. This study sought to evaluate the relationship between blastocyst development and the incidence of chromosomal abnormalities in patients undergoing PGT with targeted NGS.

Design:

Retrospective, observational study

Materials and Methods:

The study included women that underwent IVF with trophectoderm biopsy for PGT, on day 5 and/or 6 of blastocyst development, from February 2016 to April 2017. Aneuploidy screening by targeted NGS was performed. Embryos were cultured to the expanded blastocyst stage and evaluated for potential day 5 biopsy based on morphological grading and development

(morphological grading criteria: ≥4BC). Embryos deemed unsuitable for biopsy on day 5 were kept in culture and reevaluated for potential biopsy on day 6. The rate of aneuploidy was compared according to maternal age (stratified by <38 vs. ≥38 years) and the day of embryo development (stratified by day 5 vs. day 6 of embryo development). Chi square and linear regression were used for analysis.

Results:

The rates of aneuploidy detected by targeted NGS were compared among blastocysts that underwent trophectoderm biopsy on day 5 (n=1131) and 6 (n=525). The aneuploidy rate increased significantly with increasing maternal age (□=0.036 p<0.0001). Overall, embryos biopsied on day 6 had a higher rate of aneuploidy than those biopsied on day 5 (53.5% vs. 48.8%, p=0.07). This difference was more pronounced and statistically significant in patients aged ≥38 years (74.0% vs. 66.2%, p<0.05) (Table 1).

Conclusion:

The association between slower embryo development and aneuploidy is more pronounced with advancing age. This finding is consistent with prior studies that used lower resolution techniques to interrogate chromosome copy number, but this is the first and largest study to demonstrate this association using targeted NGS. While differences in the incidence of aneuploidy at discrete checkpoints of blastocyst development were observed, the use of time-lapse imaging in future studies may advance clinical understanding of the exact point in time at which embryos become amenable to trophectoderm biopsy and the developmental threshold beyond which embryos are more likely to be aneuploid. Clinical studies should aim to determine whether the implantation potential of euploid embryos is impacted by their rate of development.

Support:

None

Table 1:

The rate of aneuploidy stratified by day of embryo development at time of trophectoderm biopsy and patient age.

Age	Day 5 Biopsy	Day 6 Biopsy	P Value
All patients	48.8% (552/1131)	53.5% (281/525)	0.07
<38	38.1% (267/701)	40.0% (127/317)	NS
≥38	66.3% (285/430)	74.0% (154/208)	<0.05