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Title

IN AN ERA OF EUPLOID SINGLE EMBRYO TRANSFERS: DOES OOCYTE AGE MATTER?

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Objective

It is well established that women of advanced age have an increased likelihood of embryonic aneuploidy. The use of pre-implantation genetic testing (PGT) during IVF cycles has optimized selection of embryos for transfer and has been demonstrated to enhance pregnancy outcomes of women of advancing age. However it remains to be determined if advanced maternal age affects reproductive competence beyond chromosomal screening. This study sought to evaluate if advancing oocyte age decreases the implantation potential of a single, euploid embryo.

Design

Retrospective cohort study

Materials and Methods

The study included patients who underwent autologous IVF cycles and subsequent single, euploid frozen embryo transfer (FET) between 2012 and 2017. Trophectoderm biopsy and PGT was performed on all embryos. Clinical pregnancy (CP) was confirmed by presence of fetal cardiac activity on ultrasound. A mixed effect logistic regression model was used for analysis of all clinical variables based on age. A random intercept term was added to account for subjects



that contributed >1 embryo. Age was categorized by SART age groups (A: <35 years (y), B: 35-27 y, C: 38-40 y, D: 41-42 y, E: >42 y) for additional analysis.

## Results

A total of 982 patients underwent 1,117 single, euploid FETs. Age groups were evenly distributed and patient age ranged from 22 to 45 years (y) (mean  $36.7 \pm 3.7$  y). Younger patients had a lower BMI, gravidity and parity and were more likely to undergo a Day 5 FET compared to older patients [Table 1]. Endometrial thickness did not significantly differ among groups. After adjusting for all possible confounders, including embryo morphologic grade, age was not found to have an effect on clinical pregnancy rate (CPR) (OR 1.03, 95% CI 0.98-1.08,  $p=0.56$ ), ongoing pregnancy rate (OPR) (OR 0.99, 95% CI 0.96-1.01,  $p=0.29$ ) or clinical pregnancy loss (CPL) rate (OR 1.01, 95% CI 0.96-1.05,  $p=0.31$ ). Pregnancy rates were also not significantly different when comparing SART age groups [Table 1].

## Conclusion

Despite the significant effect of aging on oocyte quality and rates of embryonic aneuploidy, advanced oocyte age does not deter a successful IVF outcome following transfer of a single euploid embryo. The use of PGT combined with an FET protocol continues to compensate for the age-related decline in reproductive competence. While it still remains unclear why some euploid embryos fail to implant, age is not likely to be a contributor to this outcome.

## Support

None.

Table 1.

Cycle parameters and pregnancy outcomes based on SART Age Group

	A (n=606)	B (n=426)	C (n=452)	D (n=66)	E (n=81)	P Value
BMI (kg/m <sup>2</sup> )	22.6 ± 3.7	23.6 ± 4.3	23.6 ± 4.3	24.2 ± 4.1	24.6 ± 4.2	<0.01
Gravidity	1.02 ± 1.3	1.26 ± 1.4	1.78 ± 1.7	1.45 ± 1.8	1.26 ± 1.5	<0.01
Parity	0.38 ± 0.66	0.42 ± 0.72	0.57 ± 0.76	0.35 ± 0.57	0.49 ± 0.76	<0.01
Day 5 ET	69.3%*† (420/606)	65.7% (280/426)	60.6%* (274/452)	54.5%‡ (36/66)	55.6% <sup>γ</sup> (45/81)	≤0.01*† <sup>γ</sup>
Endometria l Thickness at Transfer	9.22 ± 2.1	9.14 ± 2.0	9.20 ± 1.9	9.83 ± 3.0	9.05 ± 1.9	NS



(mm)						
Clinical Pregnancy Rate	55.6% (337/606)	55.4% (236/426)	54.9% (248/452)	62.1% (41/66)	55.6% (45/81)	NS
Ongoing Pregnancy Rate	49.3% (299/606)	48.6% (207/426)	46.7% (211/452)	51.5% (34/66)	50.6% (41/81)	NS
Clinical Pregnancy Loss	9.7% (59/606)	10.8% (46/426)	11.7% (53/452)	6.0% (4/66)	8.6% (7/81)	NS