EXPLORING THE REPRODUCTIVE POTENTIAL OF DELAYED DAY 7 BLASTULATION: AN INVESTIGATION OF 742 DAY 7 EUPLOID FROZEN EMBRYO TRANSFERS AND LIVEBIRTH OUTCOMES

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Background:
Extended embryo culture to the blastocyst stage of development is becoming more routine. However, pregnancy outcomes associated with embryos cultured past Day 5 or 6 are not well characterized as, historically, embryos not deemed suitable for transfer or cryopreservation by this time were discarded. It is difficult to determine whether poorer outcomes associated with Day 7 embryos are due to decreased embryo quality, increased aneuploidy associated with delayed blastulation, or endometrial and embryo asynchrony. Preliminary data which have suggested that there is potential for Day 7 embryos to result in a healthy pregnancy (1, 2).

Objective:
To characterize pregnancy outcomes of euploid frozen embryo transfers that developed to the blastocyst stage and underwent trophectoderm biopsy and vitrification on day 7.

Materials and Methods:
This was a retrospective cohort study from a multi-center private fertility network that included patients undergoing in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), trophectoderm biopsy with preimplantation genetic testing for aneuploidy (PGT-A), and frozen embryo transfer (FET) of a single, euploid embryo, per routine, from January 2018-December 2022. On the morning of day 5 of embryo development, embryos were evaluated based on expansion and cellularity of the inner cell mass (ICM) and trophectoderm (TE). Expanded blastocysts with a single cellular and compact ICM were biopsied and vitrified. If they did not meet these criteria, blastocysts remained in culture until the morning of day 6 for evaluation where the evaluation process was repeated and embryos meeting criteria were biopsied and vitrified. Those embryos that had not yet met criteria were kept in culture until the morning of day 7 when a final assessment was performed and embryos meeting criteria were biopsied and vitrified. Embryos not meeting criteria were considered arrested. Cycles were excluded if they utilized surgical sperm, PGT for monogenetic disorders or structural rearrangements or had endometrial insufficiency with a uterine lining <6mm at time of progesterone start.

Results:
Results from the 742 transfers that occurred during the study period are summarized in Table 1.
Table 2 describes the comparable demographic variables between the two live birth outcome groups.

Table 1: Pregnancy outcomes for day 7 euploid blastocyst FETs

Total embryo transfers	742
Mean age of patient at time of transfer	36.9 (±3.7)
Positive pregnancy test	380 (51%)
Clinical pregnancy with ultrasound findings	283 (38.1%)
Sustained Implantation	226 (30.5%)
Live birth	216 (29.1%)
Miscarriage	161 (21.7%)
Mean live birth weight	3301g

Table 2: Live birth versus no live birth demographic data

	Oocyte Age	Anti-Mullerian hormone (AMH)	Body mass index (BMI)	Endometrial thickness prior to progesterone initiation
Live Birth mean +/- SD	36.2 ± 3.8	2.9 ± 3.1	26.8 ± 5.9	9.3 ± 1.8

No Live Birth mean +/- SD	36.2 ± 3.8	2.9 ± 3.1	26.8 ± 5.9	9.3 ± 1.8
P value (<0.05=significant)	p=0.999	p=0.975	p=0.987	p=0.994

Conclusion:
This is the largest cohort of patients with outcome data from euploid FETs of embryos that blastulated on day 7. Culturing embryos to day 7 may increase the pool of embryos available for transfer in patients that may otherwise have no potentially usable embryos, however, live birth rates were 29% in this cohort. When compared to sustained implantation rate (SIR) data from the same center for embryos that reached the blastocyst stage on day 5 (68.9%) and day 6 (66.8%), there does appear to be significantly lower outcomes (Day 7 SIR 30.5%). Given the study controlled for aneuploidy with PGT-A and embryo and endometrial synchrony with an FET, we hypothesize that there is another metabolic factor responsible. However, for patients who would have otherwise not had an embryo available for transfer, culture of embryos to day 7 may represent a viable approach to care.

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References:
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