ARE YOU THE ONE? SELECTING THE BEST EMBRYO FOR FROZEN EMBRYO TRANSFER

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Background:
Prior studies have determined that embryos with a good morphological grade have higher live birth rates than those with fair or poor morphology.[1] To date, most studies have not demonstrated an improvement in live birth per embryo transfer for women aged 25-40 years utilizing preimplantation genetic testing for aneuploidy (PGT-A) compared to morphology alone,[2] while some studies have concluded that PGT-A improves clinical outcomes following first embryo transfer.[3]

Objective:
To elucidate the differences in reproductive and obstetrical outcomes of the first frozen embryo transfer (FET) based on morphological grading and PGT-A.

Materials and Methods:
We queried data from a network of fertility practices across the United States for single FET cycles between 2017 and 2022. We excluded cancelled transfers, fresh embryo transfers, oocyte thaws, donor oocyte or embryos, gestational carriers, and transfers of day 2, 3, or 4 embryos. Only the first FET was included to prevent duplication of patient data.
Embryos with good morphology were either labeled “good” by the embryologist or had an embryology grade (inner cell mass/trophectoderm) of AA, AB, or BA. Embryos with fair morphology were assigned “fair” or a grade of BB. Finally, embryos with a poor morphology were assigned “poor” or a grade of CB, BC, CC. All transferred embryos that underwent PGT-A were reported as euploid.
We first assessed the impact of embryo grade on live birth and secondary outcomes, including clinical pregnancy, good birth outcome (defined as term, singleton, with appropriate weight for gestational age), biochemical pregnancy, and spontaneous abortion. Next, within each embryo grade strata we evaluated whether having PGT-A testing further improved outcomes from the first FET.

Results:
Our study cohort included 15,316 FET cycles (Table 1). Among all transfers, embryos classified as having good morphology exhibited the highest rates of clinical pregnancy (63%), live birth (51%), and good birth outcomes (39%) (Table 2). There were no differences once the data were restricted to those who achieved clinical pregnancy. Among embryos with good morphology, those that underwent PGT-A had a significantly higher probability of resulting in a live birth compared to those without PGT-A (RR = 1.24, 95% CI: 1.20–1.29, $p < 0.001$). A similar difference was observed within the fair morphology group, where PGT-A testing also conferred a significant increase in live birth proportion (RR = 1.22, 95% CI: 1.10–1.34, $p < 0.001$). Due to the limited number of poor morphology embryos in our sample, we were unable to adequately evaluate the interaction between morphological grade and PGT-A testing in this subset.

Conclusions:

Our findings demonstrate that euploid embryos with good or fair morphology have a significantly higher likelihood of achieving a live birth compared to PGT-A untested embryos of the same morphological grade. Looking ahead, we aspire to develop a user-friendly comprehensive model that incorporates additional factors, such as the day of embryo vitrification, to further optimize embryo selection and provide even more nuanced guidance to both providers and patients.

Table 1:

Characteristic	All	Good (n=13050)	Fair (n=2232)	Poor (n=34)
Age, years (SD)	35.2 (4.0)	35.2 (4.0)	35.4 (4.2)	36.0 (3.4)
BMI, kg/m^2 (SD)	26.5 (5.8)	26.5 (5.8)	26.4 (6.2)	28.8 (6.8)
Infertility diagnosis				
Ovarian Reserve	2387 (16%)	1863 (14%)	518 (23%)	6 (18%)
Endometriosis	775 (5%)	646 (5%)	126 (6%)	3 (9%)
PCOS	2642 (17%)	2217 (17%)	419 (19%)	6 (18%)
Uterine Factor	513 (3%)	437 (3%)	74 (3%)	2 (6%)
Male infertility	4755 (31%)	3957 (30%)	787 (35%)	11 (32%)
Other	5997 (39%)	5365 (41%)	621 (28%)	11 (32%)
ICSI	13707 (89%)	11847 (91%)	1829 (82%)	31 (91%)
PGT-A				
Yes	9210 (60%)	7926 (61%)	1264 (57%)	20 (59%)
No	6106 (40%)	5124 (39%)	968 (43%)	14 (41%)
Day of Freeze				
5	9826 (64%)	8591 (66%)	1226 (55%)	9 (26%)
6	5129 (33%)	4174 (32%)	935 (42%)	20 (59%)
7	361 (2%)	285 (2%)	71 (3%)	5 (15%)

Table 2. Clinical outcomes by embryo grade

Characteristic	All	Good (n=13050)	Fair (n=2232)	Poor (n=34)	p-value
Clinical Pregnancy	9493 (62%)	8241 (63%)	1238 (55%)	14 (41%)	< 0.001
Live birth	7625 (50%)	6645 (51%)	968 (43%)	12 (35%)	<0.001
Biochemical	1394 (9%)	1171 (9%)	222 (10%)	1 (3%)	0.154
Good birth outcome	5879 (38%)	5119 (39%)	750 (34%)	10 (29%)	<0.001
Among clinical pregnancies					
Livebirth	7625 (80%)	6645 (81%)	968 (78%)	12 (86%)	0.115
Spontaneous abortion	1663 (18%)	1413 (17%)	248 (20%)	2 (14%)	0.043
Good birth outcome	5879 (62%)	5119 (62%)	750 (61%)	10 (71%)	0.447

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References:

1. Awadalla M, Kim A, Vestal N, Ho J, Bendikson K. Effect of Age and Embryo Morphology on Live Birth Rate After Transfer of Unbiopsied Blastocysts. JBRA Assist Reprod. 2021 Jul 21;25(3):373-382. doi: 10.5935/1518-0557.20200101
2. Munné S, Kaplan B, Frattarelli JL, et al. Preimplantation genetic testing for aneuploidy versus morphology as selection criteria for single frozen-thawed embryo transfer in good-prognosis patients: a multicenter randomized clinical trial. *Fertil Steril*. 2019;112(6):1071-1079.e7. doi:10.1016/j.fertnstert.2019.07.1346
3. Kasaven LS, Marcus D, Theodorou E, et al. Systematic review and meta-analysis: does pre-implantation genetic testing for aneuploidy at the blastocyst stage improve live birth rate?. *J Assist Reprod Genet*. 2023;40(10):2297-2316. doi:10.1007/s10815-023-02866-0
4. Rubio C, Bellver J, Rodrigo L, et al. In vitro fertilization with preimplantation genetic diagnosis for aneuploidies in advanced maternal age: a randomized, controlled study. *Fertil Steril*. 2017;107(5):1122-1129. doi:10.1016/j.fertnstert.2017.03.011