MORPHOLOGIC PARAMETERS OF EUPLOID BLASTOCYSTS THAT PREDICT PROGRESSION TO CLINICAL PREGNANCY

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OBJECTIVE:
Pregnancy loss after a single euploid embryo transfer remains one of the greatest conundrums in the field of assisted reproduction. Expansion (Exp), inner cell mass (ICM) grade, and trophectoderm (TE) grade all are associated with ongoing pregnancy/live birth (OP/LB) rate, but the factors that govern initial implantation vs. progression to ongoing pregnancy are less clear.[1] Our study aims to determine which morphologic parameters are associated with progression to clinical pregnancy once implantation has begun.

MATERIALS AND METHODS:
This study included all single euploid frozen-thawed embryo transfer (FET) cycles from September 2016-February 2021. Pregnancy was defined as serum HCG ≥2.5 IU/L. Pregnancies that progressed to clinical pregnancy (presence of a gestational sac (GS) on ultrasound) were compared to those that resulted in biochemical pregnancy only (down-trending HCG with no GS visualized). The association of embryo morphologic parameters per modified Gardner's criteria with pregnancy and with progression to clinical vs. biochemical pregnancy were analyzed. Student's t-test, Chi-square test, and multivariable logistic regression were used for analysis.

RESULTS:
A total of 6952 single euploid FET cycles were identified and included in the study, of which 5173 (74.4%) resulted in pregnancy. Of these, 4330 (83.7%) progressed to clinical pregnancy and 843 (16.3%) resulted in biochemical pregnancy. Baseline demographics were similar between the groups. Cycles that progressed to clinical pregnancy had a significantly higher proportion of ICM grade A and lower proportion of grades B and C compared to those that resulted in biochemical pregnancy (A: 73.4% vs. 64.4%; B: 21.1% vs. 26.6%; C: 5.5% vs. 9.0%; p<.001). No significant differences were seen in Exp (4: 53.1% vs. 49.6%; 6: 37.3% vs. 41.4%; 6: 9.6% vs. 10.6%; p=.30) or TE grade (A: 43.8% vs. 43.5%; B: 40.3% vs. 38.0%; C: 15.9% vs. 9.0%; p=.14). Controlling for endometrial thickness and day of biopsy, ICM grade was significantly associated with increased odds of progression to clinical pregnancy (A vs. C: aOR 1.65, 95% CI 1.25-2.19, p=.0005). In contrast, all three criteria were significantly associated with establishment of pregnancy on adjusted analysis (Exp 4 vs. 6: aOR 1.43, 95% CI 1.18-1.74, p=.0003; 5 vs. 6: aOR 1.38, 95% CI 1.14-1.66, p=.0009; ICM A vs. C: aOR 1.52, 95% CI 1.24-1.87, p<.0001; TE A vs. C: aOR 1.56, 95% CI 1.32-1.84, p<.0001; B vs. C: aOR 1.35, 95% CI 1.15-1.57, p=.0002).

CONCLUSIONS:
Exp, ICM, and TE are all associated with establishment of pregnancy following single euploid FET; however, once implantation has begun, ICM grade is the morphologic parameter most associated with increased odds of progression to clinical pregnancy.

IMPACT STATEMENT:

While degree of expansion and quality of the ICM and TE all play a role in initiating successful apposition, adhesion, and implantation, it appears that it is the quality of the ICM that drives successful growth and continued development of a pregnancy. This data helps explain the mechanism underlying prior findings that, among the morphologic parameters, ICM is the strongest predictor of OP/LB.

REFERENCES:

1. Nazem TG, Sekhon L, Lee JA, Overbey J, Pan S, Duke M, Briton-Jones C, Whitehouse M, Copperman AB, Stein DE. The correlation between morphology and implantation of euploid human blastocysts. Reprod Biomed Online. 2019 Feb;38(2):169-176. doi: 10.1016/j.rbmo.2018.10.007. Epub 2018 Dec 7. PMID: 30579820.