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Title

CLINICAL FACTORS ASSOCIATED WITH POOR EMBRYO DEVELOPMENT AND CYCLE CANCELLATION IN IVF/PGT CYCLES

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Objective:

Pre-implantation genetic treatment (PGT) in good-prognosis patients increases clinical pregnancy rates and improves embryo selection. Unfortunately, some patients with diminished ovarian reserve do not produce enough biological material to realize the advantages of PGT. The aim of this study is to analyze clinical factors associated with impaired and poor blastocyst development and ultimately result in IVF/PGT cycle cancellation.

Design:

Retrospective cohort analysis

Materials and Methods:

The study included patients who underwent IVF and PGT between January 2012 and February 2017. Egg donation and/or single gene disorder screening cycles were excluded. Patients were segregated into two groups (Group A: IVF cycles with ≥ 1 blastocyst for trophoctoderm (TE) biopsy; Group B: Cancelled IVF cycles due to suboptimal blastocyst expansion and TE biopsy ineligibility (Gardner's classification $< 4CC$). Data was analyzed by student's t-test, Kruskal-Wallis and Wald chi-square, with significance set at $p < 0.05$. Multivariate logistic regression analysis was performed to observe variability in clinical factors and blastulation rates.

Results:

Of the 3255 IVF cycles analyzed, 2764 cycles (75%) had ≥ 1 embryo biopsied while 491 cycles (15%) were cancelled due to suboptimal blastocyst expansion. Each study group's cycle demographics, stimulation protocols, laboratory parameters and embryology metrics are shown in Table 1. Increasing age was most associated to cycle cancellation (OR 1.10 CI95% 1.07 –



1.17, $p < 0.0001$). Patients having a low AMH level (OR 1.07 CI95% 1.00 – 1.16 $p < 0.04$) and total mature (MII) oocyte count (OR 0.7 CI95% 0.6 – 0.7, $p < 0.0001$) were shown to yield the highest proportions of blastocysts with suboptimal expansion and were at greatest risk for cycle cancellation ($p < 0.05$). The logistic regression used for this study's model was best fitted (AUC 0.88) and adjusted for critical metrics including: age, day 3 FSH, BAFC, Estradiol level the day of the surge, the surge day, the number of eggs retrieved, mature oocytes and fertilized eggs. (Table 2)

Conclusions:

Patients of advanced age with low ovarian reserves are at the greatest risk of having suboptimal blastocyst expansion and high rates of IVF/PGT cycle cancellation. Our analysis demonstrated that for every additional year of age there is an 11% increased likelihood of cycle cancellation. Maternal age and ovarian reserve markers are the most important predictors of having embryos available for trophectoderm biopsy.

Support:

None.

Table 1.

Table 1: Demographic characteristics and embryological data by group			
Variable	Group A. (n=2764) IVF cycles with ≥ 1 blastocyst biopsy	Group B. (n=491) Cancelled IVF cycles	Comparison P value
Age (n=3253)	37.5 (± 4.1)	40.1 (± 3.9)	<0.0001
Day 3 FSH (n=2691)	6.4 (± 3.4)	7.3 (± 4.1)	<0.0001
AMH (n=2366)	2.8 (± 3.5)	1.4 (± 2.03)	<0.0001
BMI (n=3130)	23.5 (± 4.33)	23.62 (± 4.1)	NS
Day 3 LH (n=2691)	4.3 (± 2.66)	4.2 (± 2.7)	NS
Srg E2 (n=3245)	2133 (± 1113.4)	1396 (± 891)	<0.0001
Srg Day (n=3253)	12.1 (± 1.55)	12.6 (± 1.88)	<0.0001
BAFC (n=2917)	11 (± 5)	7.5 (± 4)	<0.0001
Eggs retrieved	13.6 (± 8.5)	6.7 (± 4.8)	<0.0001
Mature eggs	10.4 (± 6.8)	4.5 (± 3.5)	<0.0001

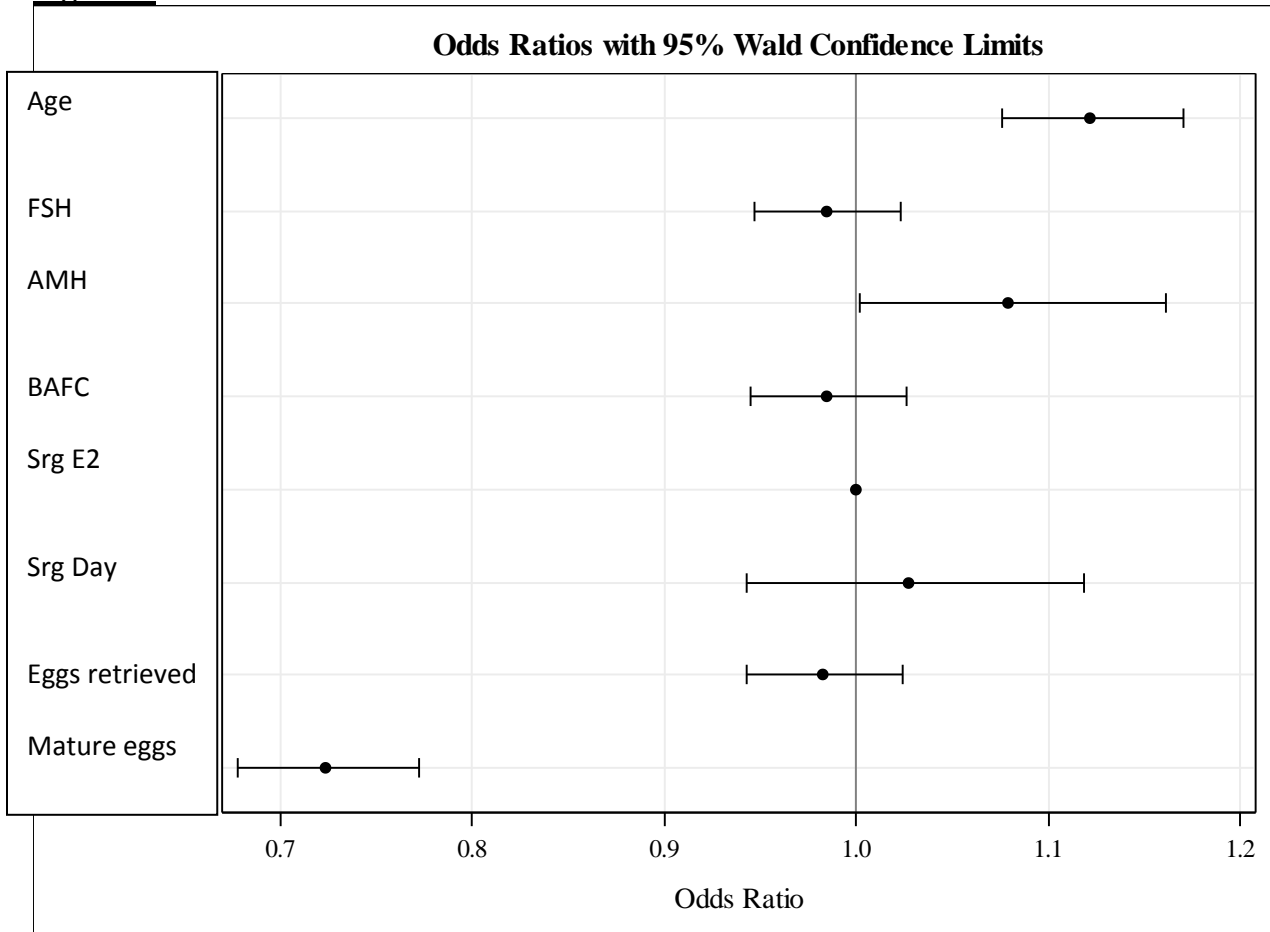


(M2)			
Fertilized eggs	8.4 (± 5.8)	2.6 (±2.6)	<0.0001
Cleavage ongoing	8.1 (± 5.6)	2.2 (± 2.2)	<0.0001
Total expanded blastocysts	3.1 (± 3.3)	0.0 (±0.1)	<0.0001

Table 2.

Analysis of maximum likelihood estimates of cycle cancellation.			
Variable	Odds ratio estimates	95% Wald confidence limits	P value
Age (n= 3253)	1.122	1.07 – 1.17	<0.0001
Day 3 FSH (n=2691)	0.98	0.94 – 1.02	NS
AMH (n=2366)	1.079	1.02 – 1.16	<0.044
Srg E2 (n=3245)	1.00	1.0 – 1.0	NS
Srg Day (n=3253)	1.027	0.9 – 1.19	NS
BAFC (n=2917)	0.985	0.94 – 1.02	NS
Eggs retrieved	0.983	0.94 – 1.02	NS
Mature eggs (M2)	0.723	0.67 – 0.77	<0.0001

Figure 1.



(Odds ratios of cycle cancellation: age (1.12 CI95% 1.07 – 1.17); FSH (0.98 CI95% 0.94 – 1.02), AMH (1.07 CI95% 1.02 – 1.16); Surge E2 (1.00 CI95% 1.00 – 1.00); Surge day (1.02 CI95% 0.99 – 1.09); BAFC (0.98 CI95% 0.94 – 1.02); Eggs retrieved (0.98 CI95% 0.94 – 1.02); Mature eggs (0.72 CI95% 0.67 – 0.77).