OUTCOMES OF NATURAL VERSUS PROGRAMMED CYCLES AMONG WOMEN OVER 40

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ABSTRACT (430/500)

Background: Choice of endometrial preparation prior to frozen embryo transfer (FET) is a key consideration in optimizing pregnancy outcomes after pursuing in vitro fertilization. Prior studies suggest equivalent pregnancy outcomes between natural cycles, in which a corpus luteum exists, and medicated cycles, in which exogenous estrogen and progesterone are given for endometrial preparation and luteal hormone replacement.[1,2] However, limited data exists for women of very advanced maternal age (≥ 40 years) in which ovulation may be irregular and the corpus luteum potentially less reliable.

Objective: To compare pregnancy outcomes in patients with very advanced maternal age after single euploid FET based on type of endometrial preparation.

Material and Methods: This is a retrospective cohort study of all single euploid FETs performed in patients 40 years and older at HRC Fertility from January 2015 to September 2024. Embryo transfer cycles were classified as natural versus programmed based on the presence or absence of a corpus luteum. Donor and surrogate cycles were excluded. The primary outcomes were clinical pregnancy rate (hCG >= 5mIU/mL) per embryo transfer, miscarriage rate, and live birth rate. Secondary outcomes included cycle cancellation rate and reason for cancellation. Logistic regression was used for analysis of primary outcomes adjusting for patient age, embryo quality, day of embryo biopsy, and BMI.

Results: A total of 687 single euploid FET cycles were included in the analysis, consisting of 47 (6.8%) natural cycles and 640 (93.2%) programmed cycles. All primary outcomes are shown in Table 1. There were no statistically significant differences in clinical pregnancy rate, live birth rate, or miscarriage rate in multivariable logistic regression analyses (P>0.05, all). The cancellation rate per initiated FET was significantly higher in the natural cycle group compared to the programmed cycle group—26% (19/73) versus 16% (440/2698) respectively [OR 1.81; 95% CI 1.06-3.08; p=0.028]. The most common reasons for cancellation were anovulation in natural cycles, and inadequate endometrial thickness in programmed cycles.

Table 1: Pregnancy outcomes for natural vs. programmed FET cycles

	Natural cycle FETs (N=47)	Programmed FETs (N=640)	Adjusted odds ratio [95% confidence interval], P-value*
Clinical pregnancy rate (hCG >= 5mIU/mL)	70.2%	65.6%	1.142 [0.591-2.206] P=0.693
Miscarriage rate (per positive hCG)	15.2%	24.5%	0.526 [0.194-1.424] P=0.206
Live birth rate (per embryo transfer)	59.6%	48.8%	1.512 [0.815-2.806] P=0.190

*Obtained in multivariable logistic regression model adjusting for age, embryo morphologic grade, day of embryo biopsy, and patient BMI.

Conclusions:

Natural cycle FETs are a viable option for women over 40, though they carry a significantly higher risk of cycle cancellation, most commonly due to anovulation. While natural cycles trended toward improved pregnancy outcomes compared to medicated cycles, no statistically significant differences were observed which may be attributed to low numbers of natural cycles performed in this age group.

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References

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