

COMPARING HCG-TRIGGERED AND SPONTANEOUS NATURAL-CYCLE FROZEN EMBRYO TRANSFERS USING SINGLE EUPLOID BLASTOCYSTS

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Background

- NC-FET offers physiologic endometrial preparation and may reduce obstetric risk
- Spontaneous ovulation timing is unpredictable; hCG trigger is often used to optimize scheduling
- Prior studies show similar outcomes [1], but none have focused on single euploid transfers
- The role of follicle size at trigger is unclear [2]

Objectives

To compare reproductive outcomes between hCG-triggered and spontaneous NC-FET of single euploid blastocysts and to assess whether follicle size at trigger is associated with outcomes

Primary Outcome:

- Good perinatal outcome, defined as a singleton live birth, ≥37 weeks gestation, and birth weight 2500–4000g

Secondary Outcomes:

- Live birth, clinical pregnancy, spontaneous abortion (SAB)

Methods

Design: Retrospective cohort, single academic center

Period: 1/2021–12/2023

Cycles: 232 NC-FET cycles (206 patients)

- Spontaneous: n = 197; hCG-Triggered: n = 35

Analysis:

- Kruskal–Wallis & χ^2 tests
- Multivariable logistic regression adjusted for age, BMI, race, endometrial thickness (EMT)
- Cluster-robust standard errors for repeated patients
- Post-hoc power analysis: 38.3% power to detect the observed difference in good perinatal outcome between triggered and spontaneous NC-FET cycles

Results

Table 1: Baseline Characteristics

Variable	Spontaneous (n = 197)	Triggered (n = 35)	p
Age, median (IQR)	37 (35, 39)	36 (32, 38)	0.017
BMI, median (IQR)	23.9 (21.6, 26.1)	25.8 (23.0, 29.3)	0.005
White race (%)	57.4	82.9	0.045
EMT, mean (mm)	9.5	9.7	0.749
EMT n (%)			0.392
<7 mm	13 (6.6)	1 (2.9)	
≥ 7 mm	184 (93.4)	34 (97.1)	

Table 2: Reproductive Outcomes by NC-FET Type

Outcome	Spontaneous (n = 197)	Triggered (n = 35)	p
Good perinatal outcome, n (%)	105 (53.3)	24 (68.6)	0.094
Live birth, n (%)	129 (65.5)	25 (71.4)	0.493
Clinical pregnancy, n (%)	139 (70.6)	27 (77.1)	0.426
Spontaneous abortion, n (%)	66 (33.5)	10 (28.6)	0.567

Table 3: Adjusted Reproductive Outcomes - hCG-Triggered vs Spontaneous NC-FET

Outcome	aOR (95% CI)
Good perinatal outcome	2.08 (0.91 – 4.76)
Live birth rate	1.22 (0.54 – 2.77)
Clinical pregnancy rate	1.27 (0.54 – 3.00)
Spontaneous abortion rate	0.90 (0.39 – 2.06)

*Adjusted for maternal age category, BMI category, race/ethnicity, and endometrial thickness category

*Odds ratios >1 indicate higher odds with hCG-triggered NC-FET compared with spontaneous NC-FET

Results

- Patients undergoing hCG-triggered NC-FET were slightly younger, had a higher BMI, and were more likely to be White compared with spontaneous cycles; endometrial thickness did not differ
- Good perinatal outcome occurred in 68.6% of triggered cycles vs 53.3% of spontaneous cycles, representing a non-significant trend favoring trigger
- Live birth, clinical pregnancy, and spontaneous abortion rates were similar between groups
- On multivariable analysis, hCG trigger remained associated with higher odds of good perinatal outcome, but this did not reach statistical significance
- Among hCG-triggered cycles with follicle size data (n = 34), pregnancy outcomes did not differ by follicle size at trigger (<18 mm vs ≥18 mm)

Conclusions

- hCG-triggered NC-FET resulted in similar reproductive outcomes compared with spontaneous NC-FET in single euploid transfers
- A non-significant trend toward a higher good perinatal outcome was observed with hCG trigger on multivariable analysis
- Follicle size at trigger was not associated with pregnancy outcomes among triggered cycles
- These findings are hypothesis-generating and support the flexibility of hCG trigger use in natural-cycle FET planning
- Larger studies are needed

References

1. Ranisavljevic N, Vidal A, Siaud P, et al. Ovulation trigger versus spontaneous luteinizing hormone surge on live birth rate after frozen embryo transfer in a natural cycle: a randomized controlled trial. *Fertil Steril.* 2025; 123(4): 718–720.
2. Alonso-Mayo C, Kohls G, Santos-Ribeiro S, Soares SR, Garcia-Velasco JA. Modified natural cycle allows a window of 7 days for frozen embryo transfer planning. *Reprod Biomed Online.* 2024 Jul;49(1):103774. doi: 10.1016/j.rbmo.2023.10377