ONGOING CLINICAL PREGNANCY OUTCOMES FOLLOWING A CHANGE IN ENDOMETRIAL PREPARATION AFTER A FAILED FROZEN EMBRYO TRANSFER CYCLE

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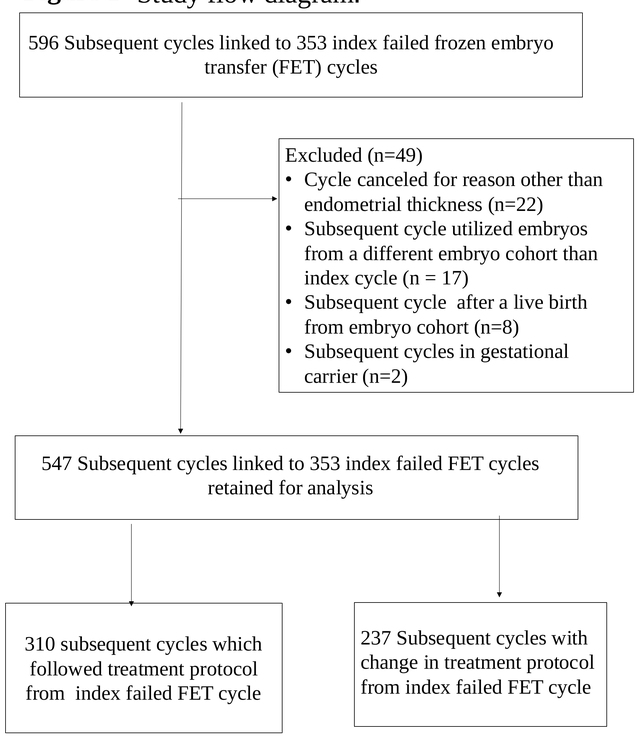
Introduction

- Frozen embryo transfer (FET) is the primary method of embryo transfer in the United States (1). Most recently FET has accounted for 83% of all embryo transfers (2).
- Endometrial preparation is critical in ensuring successful outcomes following an FET cycle (3) and is one of the main driving factors in successful ongoing intrauterine pregnancy and live birth rates (4).
- In this study, we evaluated a cohort of women who had at least one failed FET, to determine whether a change in endometrial preparation impacts live birth rate in a subsequent frozen cycle.

Methods

- This retrospective analysis was performed using IVF clinic data collected by the University of Iowa Hospitals and Clinics.
- The data set included patients who underwent subsequent FET cycles following an initial failed FET cycle between January 2017 and August 2023.
- The primary outcome was live birth rate defined as delivery of one or more live born infants at or beyond 28 weeks gestation.
- The institutional review board of the University of Iowa exempted this project from review
- Generalized estimating equations used to calculate relative risk (RR) and rate ratios (RR) for change compared to no change.

Figure 1 Study flow diagram.



Results

There is no significant difference in endometrial thickness between an initial failed FET cycle and a subsequent FET cycle, despite a change in endometrial preparation.

After a failed FET cycle, a change in the endometrial preparation for the subsequent FET cycle did not increase chance of live birth.

Table 1 Types of Protocol Changes

	Cycle with change from index failed cycle (n=237)	
Change in Preparation Utilized	125 (52.7%)	
	Added	Stopped
Natural Preparation	33 (13.9%)	4 (1.7%)
Estrogen	14 (5.9%)	79 (33.3%)
GnRH agonist	17 (7.2%)	2 (0.8%)
GnRH antagonist	9 (3.8%)	2 (0.8%)
FSH	46 (19.4%)	11 (4.6%)
Ovidrel (hCG trigger)	79 (33.3%)	5 (2.1%)
Letrozole	19 (8.0%)	16 (6.8%)
Tamoxifen	31 (13.1%)	1 (0.4%)
Sildenafil	3 (1.3%)	0 (0.0%)
Change in Estrogen Route	117 (n=49.4%)	
	Added	Stopped
Patch	10 (8.1%)	0 (0%)
Oral	1 (0.8%)	11 (8.9%)
Vaginal	4 (3.2%)	4 (3.2%)
Change in Continuous Progesterone	132 (55.7%)	
	Added	Stopped
IM 50 mg PIO	7 (3.2%)	101 (47.3%)
IM 75 mg PIO	103 (46.4%)	5 (2.3%)
Vaginal	8 (3.6%)	0 (0%)
None	2 (0.9%)	3 (1.4%)
Number of Protocol changes:		
1	127 (53.6%)	
2	83 (35.0%)	
3	27 (11.4%)	

Table 2 Cycle Outcomes by Protocol Change from Index Cycle

	Change in Treatment from initial cycle (n=237)	No Change in Treatment from initial cycle (n=310)	RR (95% CI)	ARR (95% CI)
Live Birth	87 (36.7%)	134 (43.2%)	0.85 (0.67 – 1.07)	0.87 (0.69 – 1.10)
Endometrial Thickness	8.54 ± 2.15	9.12 ± 2.13	0.78 (0.56 – 1.08)[1]	0.77 (0.55 – 1.07)[1]
Cycle Canceled for endometrial lining	6 (2.5%)	8 (2.6%)	0.98 (0.35 – 2.76)	1.05 (0.39 – 2.84)[2]
Miscarriage	17/105 (16.2%)	36/171 (21.1%)	0.77 (0.46 – 1.30)	0.68 (0.41 – 1.13)
Biochemical	33 (13.9%)	33 (10.6%)	1.31 (0.84 – 2.05)	1.36 (0.86 – 2.14)
Ectopic	2 (0.8%)	1 (0.3%)	2.62 (0.24 – 28.42)	2.59 (0.22 – 30.50)

[1]RR for endometrial thickness in subsequent cycle adjusted for endometrial thickness in initial cycle. ARR for endometrial thickness in subsequent cycle adjusted for endometrial thickness in initial cycle, age and BMI.
[2]ARR for cycle cancelation in subsequent cycle adjusted for age and BMI.

Discussion

- This retrospective cohort study did not find evidence that a change in endometrial preparation in subsequent FET cycles following an initial failed FET cycle affects live birth rate outcomes.
- Several previous studies investigated the optimal protocol for endometrial preparation prior to embryo transfer.
- These preparation methods can broadly be grouped by the following: a natural cycle, a stimulated cycle and a programmed cycle.
- If a patient demonstrated a clear clinical need for change in endometrial preparation protocol, they would be part of the change in protocol group.
- Further studies are needed to translate these results to cumulative live birth rates.
- Our study found that there was no significant difference in endometrial thickness between an initial failed FET cycle and a subsequent FET cycle, despite changing endometrial preparation.
- Based on our findings, patients can be reassured about chance of success when using the same protocol for a subsequent FET after a failed FET

Conclusion

- Our data show that there is no evidence that a change in endometrial preparation protocol between a failed FET cycle and subsequent FET cycle increases the chance of live birth rate.
- The decision to change treatment protocol for subsequent FET cycles after an initial failed FET cycle should continue to be a shared conversation.

References

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