Endometrial thickness (EMT) in the prediction of neonatal adverse outcomes in frozen cycles for singleton pregnancies

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Introduction

Previous studies suggest an association between endometrial thickness (EMT), as a categorical predictor, and adverse neonatal outcomes in IVF/ICSI frozen embryo transfers (FET). In this study, we aimed to investigate the continuous association of EMT before embryo transfer with adverse neonatal outcomes.

Method

We studied women undergoing IVF/ICSI with FET in a tertiary hospital. Outcomes included preterm delivery (PTD), small-for-gestational age (SGA), large-for-gestational age (LGA) and low birthweight (LBW). Multiple logistic spline regression was performed to assess the risk of these outcomes relative to EMT as a continuous variable. Area under receiver operating characteristic curve (AUC) was utilised to assess the best categorical cut-off points for EMT for multiple logistic regression analysis.

Figure 4: AUC for cut-off binarization for endometrial thickness

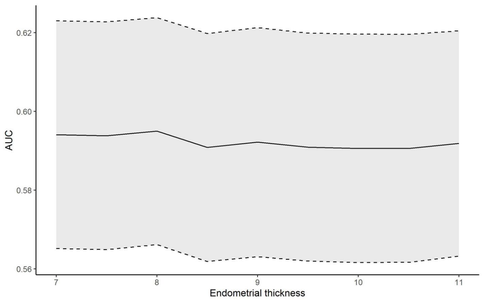


Table 1: Basic characteristics

	PTD	TD	P value	Not pregnant
Baseline variables				
Number of patients, n	566	5498		14065
Female age (years), mean (SD)	30.21 (4.17)	30.08 (4.06)	0.478	31.07 (4.87)
Male age (years), mean (SD)	31.45 (6.81)	31.84 (5.9)	0.139	32.85 (6.85)
Female BMI (Kg/m2), mean (SD)	22.12 (3.64)	21.73 (2.95)	0.004	21.87 (3.11)
Menarche (years), mean (SD)	13.69 (2.73)	13.9 (2.19)	0.029	13.85 (2.38)
Infertility (years), mean (SD)	3.82 (2.77)	3.65 (2.78)	0.185	4.01 (3.1)
Primary infertility, n (%)	266 (47)	2610 (47.47)	0.829	6171 (43.87)
Parity*			0.356	
0, n (%)	469 (82.86)	4638 (84.36)		11183 (79.51)
1, n (%)	59 (10.42)	572 (10.4)		1892 (13.45)
2+, n (%)	6 (1.06)	31 (0.56)		128 (0.91)
Unknown, n (%)	32 (5.65)	257 (4.67)		862 (6.13)
Gravidity*			0.807	
0, n (%)	254 (44.88)	2456 (44.67)		5692 (40.47)
1, n (%)	137 (24.2)	1353 (24.61)		3462 (24.61)
2, n (%)	73 (12.9)	772 (14.04)		2048 (14.56)
3+, n (%)	70 (12.37)	660 (12)		2001 (14.23)
Unknown, n (%)	32 (5.65)	257 (4.67)		862 (6.13)
Baseline bloods				
FSH (mIU/mL), median (IQR)*	6.17 (5.13 to 7.32)	6.21 (5.24 to 7.33)	0.695	6.35 (5.32 to 7.55)
LH (mIU/mL), median (IQR)*	4.94 (3.64 to 6.55)	5.06 (3.73 to 6.72)	0.291	4.8 (3.52 to 6.4)
E2/Oestradiol (pmol/L), median (IQR)*	106.3 (74.27 to 143.6)	110.8 (77.7 to 149.93)	0.043	112.6 (80.43 to 151.5)
Prolactin (ng/mL), median (IQR)*	16.5 (12.45 to 22.65)	16.4 (12 to 22.4)	0.777	15.9 (11.7 to 21.8)
Progesterone (nmol/L), median (IQR)*	1.7 (1.18 to 2.34)	1.74 (1.23 to 2.39)	0.517	1.7 (1.17 to 2.39)
Testosterone (nmol/L), median (IQR)*	0.9 (0.6 to 1.3)	0.8 (0.55 to 1.13)	0.018	0.8 (0.5 to 1.1)
AMH (ng/mL), median (IQR)*	3.75 (1.68 to 5.14)	3.12 (1.8 to 5.13)	0.906	2.98 (1.37 to 5.04)
Causes of infertility				
Ovulatory dysfunction, n (%)	64 (11.31)	469 (8.53)	0.026	1004 (7.14)
Tubal disease/factor, n (%)	319 (56.36)	3342 (60.79)	0.04	8598 (61.13)
Thyroid dysfunction, n (%)	19 (3.36)	236 (4.29)	0.291	583 (4.15)
Male causes, n (%)	179 (31.63)	1902 (34.59)	0.157	4707 (33.47)
Single ovarian removal, n (%)	1 (0.18)	9 (0.16)	1	17 (0.12)
Endometriosis/Adenomyosis, n (%)	57 (10.07)	488 (8.88)	0.344	1256 (8.93)
Hysteromyoma, n (%)	10 (1.77)	125 (2.27)	0.437	434 (3.09)
Chromosomal abnormalities, n (%)	19 (3.36)	173 (3.15)	0.786	399 (2.84)
Hyperprolactinoma, n (%)	2 (0.35)	30 (0.55)	0.764	57 (0.41)
IVF methods				
Follicle count, mean (SD)*	11.84 (3.84)	11.86 (3.65)	0.922	11.14 (3.84)
Number of oocytes collected, median (IQR)*	15 (11 to 21)	16 (11 to 21)	0.426	14 (9 to 20)
Number of embryos transferred, mean (SD)*	1.97 (0.6)	1.98 (0.59)	0.695	1.92 (0.65)
Embryo stage			0.410	
Blastocyst, n (%)	23 (4.06)	197 (3.58)		392 (2.79)
Cleavage, n (%)	542 (95.76)	5270 (95.85)		13573 (96.5)
Unknown, n (%)	1 (0.18)	31 (0.56)		100 (0.71)
Endometrium thickness*			<0.001	
≤8, n (%)	62 (10.95)	356 (6.48)		844 (6.00)
8-11, n (%)	291 (51.41)	3076 (55.95)		5265 (37.43)
>11, n (%)	126 (22.26)	1242 (22.59)		1904 (13.54)
Unknown, n (%)	87 (15.37)	824 (14.99)		6052 (43.03)
Fertilisation method*			0.319	
IVF, n (%)	335 (59.19)	3132 (56.97)		7504 (53.35)
ICSI, n (%)	110 (19.43)	1185 (21.55)		2852 (20.28)
Half ICSI, n (%)	2 (0.35)	51 (0.93)		90 (0.64)
Unknown, n (%)	119 (21.02)	1130 (20.55)		3619 (25.73)
Cycle method*			0.0317	
Hormone replacement cycle, n (%)	358 (63.25)	3165 (57.57)		8335 (59.26)
Natural cycle, n (%)	139 (24.56)	1672 (30.41)		4104 (29.18)
Ovulation promoting cycle, n (%)	58 (10.25)	547 (9.95)		1315 (9.35)
Unknown, n (%)	11 (1.94)	114 (2.07)		311 (2.21)
Freezing method*			0.350	
Slow freezing, n (%)	503 (88.87)	4855 (88.3)		8437 (59.99)
Vitrification, n (%)	32 (5.65)	267 (4.86)		456 (3.24)
Unknown, n (%)	31 (5.48)	376 (6.84)		5172 (36.77)

Figure 1: Cohort flowchart

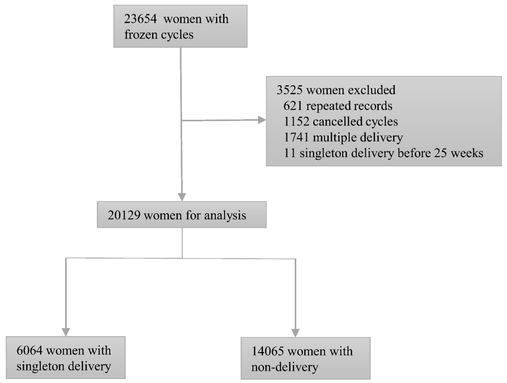


Figure 2: Predicted probability in pregnant women undergoing IVF/ICSI

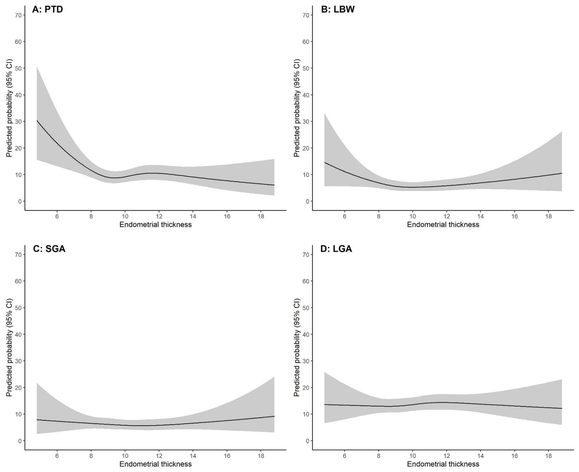
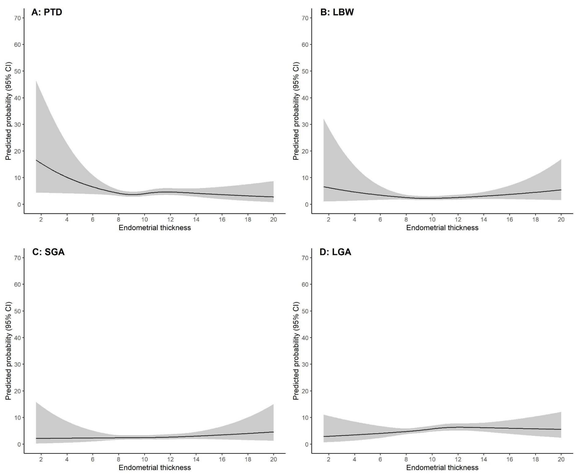


Figure 3: Predicted probability in all women undergoing IVF/ICSI



Results

We report on 20,129 FET cycles resulting in 6,064 singleton live births (Figure 1, Table 1)). Multiple spline regression visualisation showed that for every millimetre decrease in EMT less than 9 mm, there was an increasing risk of PTD and LBW (Figure 2-3). Using AUC, a cut-off of 8 mm was identified to categorise EMT (Figure 4). Compared to those with EMT greater than 8 mm, individuals with EMT less than 8 mm had an adjusted odds ratio of 1.69 (95% CI 1.28-2.21) for PTD, 1.65 (95% CI 1.18-2.30) for LBW, 1.30 (95% CI 0.91-1.88) for SGA and 0.96 (95% CI 0.74-1.24) for LGA.

Conclusion

Endometrial thickness can be used for prediction of PTD and LBW. In women with a thin endometrium, deferring FET to a subsequent cycle could be considered.

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