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An Endometrial Thickness < 8 mm Was Associated With a Significantly Increased Risk of EP After Freeze-Thaw Transfer: An Analysis of 5,960 Pregnancy Cycles

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Introduction: Endometrium characteristics that are most likely to induce ectopic pregnancy were investigated on the basis of the data of 5,960 pregnant freeze-thaw cycles.

Methods: A total of 5,960 pregnancy cycles after freeze-thaw embryos transfer were included, with the number of intrauterine and ectopic pregnancies being 5,777 and 183, respectively. Ectopic pregnancy was the primary outcome. Endometrial thickness was the main measured variable. The risk factors of ectopic pregnancy were eventually determined based on univariate analysis and subsequent multiple-stepwise logistic regression analysis.

Results: 1. After adjusting for confounders, endometrial thickness could independently predict ectopic pregnancy. The adjusted odd ratios for women with endometrial thickness in the ranges of < 8 mm, 8–9.9 mm, and 10–11.9 mm were 3.270 [95% confidence interval (CI), 1.113–9.605, $P = 0.031$], 2.758 (95% CI, 0.987–7.707, $P = 0.053$), and 1.456 (95% CI, 0.502–4.225, $P = 0.489$), respectively, when compared with those having an endometrial thickness of 12–13.9 mm. 2. Endometrial type and preparation protocol were however not identified as risk factors for ectopic pregnancy.

Discussion: 1. After freeze-thaw embryo transfer, risks of ectopic pregnancy were significantly higher when the endometrial thickness was < 8 mm. 2. A thin endometrial thickness could be linked with abnormal endometrial peristaltic waves or abnormal endometrial receptivity. 3. Adequate attention should therefore be paid to patients with a thin endometrial thickness to prevent EP or to achieve early diagnosis during the peri-transplantation period.

Keywords: ectopic pregnancy, EMT, endometrial type, freeze-thaw cycles, cleavage stage embryo, blastocyst

BACKGROUND

Embryo implantation outside the uterine cavity represents an abnormal and dangerous form of pregnancy referred to as ectopic pregnancy (EP) (1), and according to reports, this condition is responsible for less than 1% of all maternal deaths in developing countries, with the figures rising to 5% for developed ones (2).

Assisted reproductive technology (ART) can theoretically decrease the incidence of EP, as both fertilization and embryo transfer (ET) do not involve the fallopian tubes. However, the rate of EP is around 1%–2% in spontaneous pregnancy as compared to 1.4%–5.4% in the case of ART (3, 4), and this can generally be attributed to risk factors such as low BMI (5), fresh ETs compared with freeze-thaw cycles (6–11), transfer of multiple embryos (12), and tubal factor infertility (TFI) (12–17). Similarly, the developmental stage of transferred embryos may be an important factor although its impact on EP incidence remains debatable (18–21).

In addition, few studies have also investigated the association between endometrial thickness (EMT) and EP occurrence after ART treatment, but there is no consensus on which EMT is applicable for EP prevention. Thus, identifying endometrial risk factors of EP and endometrial characteristics that could potentially predict EP after ART can be important.

METHODS

Definition of Clinical Outcomes

Intrauterine pregnancy (IUP), as confirmed by ultrasonic assessment, was defined as the condition when at least one gestational sac was present in the uterine cavity. In contrast, when the gestational sac/mass was observed on the outside of the uterine cavity after ultrasonography, it was considered as a case of EP. Finally heterotopic pregnancy (HP) was defined as the simultaneous occurrence of an intrauterine sac and EP. Twelve days after ET, all patients underwent blood tests to assess levels of β-human chorionic gonadotropin (β-hCG), with those having β-hCG levels below 5 IU/L and above 15 IU/L being considered as negative and positive for pregnancy, respectively. In addition, patients were classified as indeterminate if their blood β-hCG levels were in the range of 5–15 IU/L, but if the levels increased after 48 h, they were subsequently classified as positive. All positive women received transvaginal ultrasound examinations 4–5weeks after ET. As the primary purpose of this analysis was to investigate the endometrial variables associated with EP risks, heterotopic pregnancies were excluded.

Study Design and Patients

Between January 2014 and November 2021, the women underwent freeze-thaw ET at the Reproductive Medicine Centre of Xiangya hospital, Central South University (Changsha, China). Before ART procedure, ultrasonic examinations were performed at least twice at different periods of the menstrual cycles, with patients accepting further examination and treatment by hysteroscope if cavity abnormalities were found.

Patient data were collected from medical records. **Figure 1** presents a simplified selection process for IVF cycles. The following exclusion criteria was also applied: (1) non-pregnant cycles; (2) biochemical pregnancy; (3) HP; (4) cesarean scar pregnancy; (5) fresh embryos; (6) donor oocytes cycles; (7) presence of a known uterine anomaly; and (8) unrecorded endometrial data. As a result, from the initial 15,459 freeze-thaw ETs, 5,777 cycles were identified as IUP and 183 as EP.

EP was the primary outcome measured, whereas EMT was the main variables. Demographic data included patients age, previous history of EP, infertility type, infertility duration (years), etiology of infertility, parity, body mass index (BMI), number of embryos transferred, the developmental stage of the transferred embryos, and endometrial preparation protocol, as evaluated by the patient's treating doctor. Patients were considered as presenting TFI if they reported any of the following: previous EP, previous salpingectomy, hydrosalpinx, or tubal scarring including occlusion. Similarly, women were diagnosed with polycystic ovary syndrome if they presented any two of the following characteristics: PCOM, ovulatory dysfunction, and clinical and/or biochemical hyperandrogenism. Finally, diminished ovarian reserve was diagnosed when women returned an abnormal ovarian reserve test (i.e., AMH < 0.5–1.1 ng/ml or antral follicular count (AFC) < 5–7 follicles) or presented any of the risk factors for POR. The follow-up rate was 100% in this study.

Assessment of Primary Exposure

On the day of hCG administration for the natural and induced ovulation cycles, EMTs were monitored by transvaginal ultrasound scans. On the other hand, when providing hormone replacement cycle (HRT) and HRT combined with downregulation, EMT was measured when the last ultrasound exam was performed before progesterone (P) administration

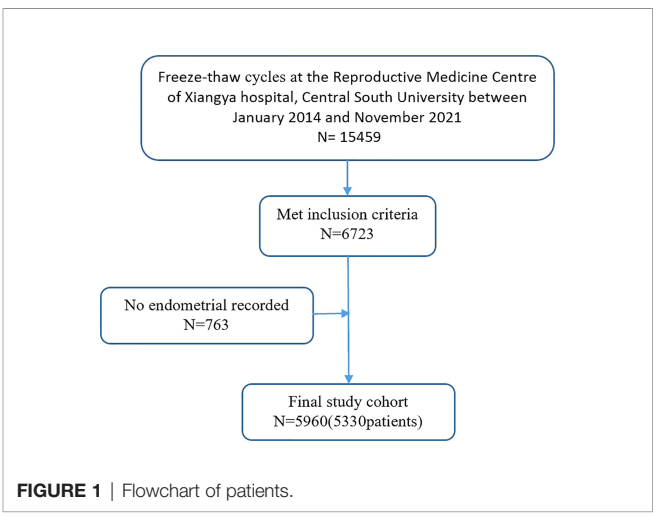

FIGURE 1 | Flowchart of patients.

starting. EMT was measured on sagittal view, with the maximal anteroposterior thickness used by transvaginal sonography (22). According to the Gonen system (23), the endometrial morphology can be classified into three types: type A, trilaminar pattern (a triple-line pattern) that consist of hypoechoic inner layers, hyperechoic middle and outer layers, and evident echo at the intrauterine center line; type B, the echo of the endometrium is relatively homogeneous and hyperechoic, with a clear interface between muscular layers and the endometrium but unclear endometrial layers and obscure intrauterine center line echo; type C, the echo of the endometrium is homogeneous hyperechoic without intrauterine center line. EMTs were measured by six physicians who had received standardized training.

Endometrial Preparation Protocol

Four protocols were available to prepare the endometrium for freeze-thaw transfer (FET): natural cycles, induced ovulation cycles, hormone replacement therapy cycles, and HRT after downregulation cycles. Natural cycles were used for patients who had regular ovulation cycles, whereas the other three were used for those without regular ovulation cycles.

In an induced ovulation cycle, follicular growth was induced as from the third day of menstruation by orally administering 2.5 mg of letrozole daily for 5 days. Then, as from the 10th day, transvaginal ultrasound exams were performed while monitoring the level of serum estrogen. In this case, if the diameter of the dominant follicle was found to be < 10 mm, then a daily injection of 37.5–75 IU of hMG was performed until the follicle's diameter ≥ 17 mm. However, no injection was given if the follicle diameter was > 14 mm. In both natural and induced ovulation cycles, once the dominant follicle's average diameter was > 17 mm and, at the same time, other conditions such as an EMT of >7 mm, P of < 1 ng/ml, and E_2 of > 150 pg/ml were met, two types of treatment was administered based on LH levels in the serum. In cases where LH levels were < 20 mIU/ml, a night injection of 10,000 IU of hCG was provided, with P subsequently administered after 3 days. Embryos at the cleavage stage were then transferred 5 days after hCG had been administered, whereas for blastocysts, transfer was made after 7 days. When LH levels were > 20 mIU/ml, hCG was injected in the afternoon, with P administered after 2 days. Transfer of embryos at the cleavage stage was then performed 4 days after hCG injection, whereas for blastocysts, transfer was made after 6 days. For the HRT cycle, a dose of 4-6 mg of E_2 was administered daily as from the third day of the period. Transvaginal ultrasound scans were then performed after 6 and 12 days. In this case, if an EMT >7 mm was observed along with the absence of ovulation signs or a main follicle, then the luteal phase was supported with a dose of 200 mg of oral progesterone capsules (Qining) once a day, accompanied with a 200-mg dose of vaginal micronized progesterone (Utrogestan) three times per day for 75 days. The course of E_2 treatment did not last for less than 12 days or more than 21 days as it was previously shown that extended exposure to E_2 could decrease the rates of live birth and clinical pregnancy (24). Finally, cleavage-stage ETs or blastocysts transfer were performed on the third or the fifth day, respectively. HRT after downregulation cycles differed from HRT in the use of one to two doses of 3.75 mg of GnRH-a during the early follicular phase before using E_2.

Statistical Analyses

Variables for EP were selected based on previous literature (25–27) and availability of data. SPSS version 23 (IBM) was used for data analysis and for quantitative data, the median (quartile interval), and mean ± SD were used to, respectively, describe normal and non-normal distributions. In the case of categorical data, the proportion of cases was presented as percentages.

For univariate comparisons, Pearson chi-square test and Mann–Whitney U test were used for categorical variables and non-normal distribution respectively. The risk factors linked with EP were then determined on the basis of stepwise multiple logistic regression analysis, with a receiver operating characteristic (ROC) curve generated for the predictors of EP. Finally, area under curve (AUC)–based validation of the model was performed. For analysis, differences with *P*-values < 0.05 were considered to be of statistical significance.

RESULTS

Figure 1 shows the flowchart for cycle admission. This study included a total of 5,960 freeze-thaw cycles, including 5,777 IUP and 183 EP cycles.

The baseline characteristics were as shown in **Table 1**. The women's age, BMI, infertility type and duration, endometrial type, male factor infertility, polycystic ovary syndrome, diminished ovarian reserve, intrauterine adhesions, scarred uterus, and endometrial preparation regime were not significantly different between two groups. Significant differences were, however, found for previous history of EP, the developmental stage of the transferred embryos, the number of embryos transferred, gravidity, TFI, and endometriosis (P < 0.05).

EMTs of women with EP were significantly thinner in comparison with IUP patients (*P* <0.001). In addition, the EP rate in women with EMT < 8 mm (5.2%) was significantly higher than for those with an EMT of 8–9.9 mm (3.9%), 10–11.9 mm (1.5%), 12–13.9 mm (0.9%), and ≥ 14 mm (0%) (*P* < 0.001). In fact, none of the patients with an EMT of ≥ 14 mm developed EP in subsequent analysis and as such, those with EMT of 12–13.9 mm were selected as the reference group.

Table 2 shows the results of the univariate analysis. Compared with an EMT of 12–13.9 mm as the reference, the risk of EP in patients with an EMT of < 8 mm was fivefold (OR, 6.084; 95% CI 2.154–17.189; *P* = 0.001), with the risk decreasing to threefold in the case of those with an EMT of 8–9.9 mm (OR, 4.530; 95% CI, 1.663–12.337; *P* = 0.003). However, the EP risk for women with an EMT of 10–11.9 mm was not statistically different from that of the reference group (i.e., 12–13.9 mm) (OR, 1.738; 95% CI, 0.605–4.994; P = 0.304).

The risk factors for EP were a small BMI, an EP history, TFI, multiple embryos transfer, and transfer of embryos at the

TABLE 1 | Comparison of the baseline data of two groups patients.

Variables	Intrauterine pregnancy, n = 5,777	Ectopic pregnancy, n = 183	*P* value
Age (years)	31 (28,34)	30 (27,34)	0.059
Body mass index (kg/m^2)	21.48 (19.70,23.63)	20.93 (19.55,23.41)	0.175
Infertility type			0.135
Primary sterility	2913 (50.4%)	82 (44.8%)	
Secondary sterility	2864 (49.6%)	101 (55.2%)	
Infertility duration (years)	4 (2,6)	4 (2,7)	0.479
Previous history of ectopic pregnancy			0.000*
=0	4905 (84.9%)	137 (74.9%)	
≥1	866 (15.1%)	46 (25.1%)	
Gravidity			0.014*
=0	3022 (52.3%)	79 (43.2%)	
≥1	2750 (47.7%)	104 (56.8%)	
Tubal factor infertility			0.001*
Yes	4860 (84.1%)	171 (93.4%)	
No	917 (15.9%)	12 (6.6%)	
Male factor infertility			0.327
Yes	1807 (31.3%)	51 (27.9%)	
No	3970 (68.7%)	132 (72.1%)	
Endometriosis			0.019*
Yes	279 (4.8%)	2 (1.1%)	
No	5498 (95.2%)	181 (98.9%)	
Polycystic ovary syndrome			0.962
Yes	828 (14.3%)	26 (14.2%)	
No	4949 (85.7%)	157 (85.8%)	
Diminished ovarian reserve			0.455
Yes	467 (8.1%)	12 (6.6%)	
No	5310 (91.9%)	171 (93.4%)	
IUA			0.222
Yes	229 (4.0%)	4 (2.2%)	
No	5548 (96.0%)	179 (97.8%)	
Scarred uterus			0.147
Yes	452 (7.8%)	9 (4.9%)	
No	5325 (92.2%)	174 (95.1%)	
No. of embryos transferred			0.000*
1	1717 (29.7%)	31 (16.9%)	
2	4047 (70.1%)	150 (82.0%)	
3	13 (0.2%)	2 (1.1%)	
Endometrial thickness (mm)	9.50 (8.50,10.70)	8.60 (8.10,9.60)	0.000*
Endometrial thickness (mm)			0.000*
<8	675 (11.7%)	37 (20.2%)	
8–9.9	2818 (48.8%)	115 (62.8%)	
10–11.9	1724 (29.8%)	27 (14.8%)	
12–13.9	444 (7.7%)	4 (2.2%)	
≥14	116 (2.0%)	0 (0%)	
Endometrial type			0.396
A	1974 (34.2%)	70 (38.3%)	
B	3270 (56.6%)	100 (54.6%)	
C	533 (9.2%)	13 (7.1%)	
Endometrial Preparation Regime			0.309
Hormone replacement therapy	3130 (54.2%)	111 (60.7%)	
Hormone replacement therapy after downregulation	407 (7.0%)	9 (4.9%)	
Induced ovulation cycle	333 (5.8%)	8 (4.4%)	
Natural cycle	1907 (33.0%)	55 (30.1%)	
Embryo stage			0.000*
Cleavage stage embryo	3301 (57.1%)	147 (80.3%)	
Blastocyst	2476 (42.9%)	36 (19.7%)	

*EP, ectopic pregnancy; IUP, intrauterine pregnancy; BMI, body mass index. *The difference is significant between groups.*

TABLE 2 | Factors related to ectopic pregnancy based on univariate analysis.

Predictor variables	Odds ratio	95% confidence interval	*P* value
Age (years)	0.974	0.943, 1.007	0.121
BMI (kg/m^2)	1.001	1.000, 1.002	0.043*
Infertility type			
Primary infertile	1	——	——
Secondary sterility	1.253	0.932, 1.684	0.135
Infertility duration (years)	1.009	0.967, 1.052	0.680
Previous history of ectopic pregnancy			
=0	1	——	——
≥1	1.902	1.351, 2.676	0.000*
Gravidity			
=0	1	——	——
≥1	0.691	0.514, 0.930	0.015*
Tubal factor infertility			
Yes	2.689	1.491, 4.848	0.001*
No	1	——	——
Male factor infertility			0.327
Yes	0.849	0.612, 1.178	
No	1	——	——
Endometriosis			0.033*
Yes	0.218	0.054, 0.882	
No	1	——	——
Polycystic ovary syndrome			0.962
Yes	0.990	0.649, 1.509	
No	1	——	——
Diminished ovarian reserve			0.456
Yes	0.798	0.441, 1.444	
No	1	——	——
IUA			0.229
Yes	0.541	0.199, 1.471	
No	1	——	——
Scarred uterus			0.151
Yes	0.609	0.310, 1.199	
No	1	——	——
No. of embryos transferred			0.000*
=1	1	——	——
=2	2.053	1.389, 3.034	0.000*
=3	8.521	1.844, 39.371	0.006*
Embryo stage			
Cleavage stage embryo	1	——	——
Blastocyst	0.326	0.226, 0.472	0.000*
Endometrial thickness (mm)	0.700	0.629, 0.779	0.000*
Endometrial thickness (mm)			0.000*
12-13.9	1	——	——
<8	6.084	2.154, 17.189	0.001*
8–9.9	4.530	1.663, 12.337	0.003*
10–11.9	1.738	0.605, 4.994	0.304
≥14	0.000	0.000, 0.000	0.996
Endometrial type			0.398
A	1	——	——
B	0.862	0.632, 1.176	0.350
C	0.688	0.378, 1.253	0.221
Ovarian stimulation protocol			0.314
Hormone replacement therapy	1	——	——
Hormone replacement therapy after downregulation	0.624	0.314, 1.240	0.178
Induced ovulation cycle	0.677	0.328, 1.401	0.293
Natural cycle	0.813	0.586, 1.129	0.217

**The difference is significant between the two groups.*

cleavage stage. In contrast, history of IUP and endometriosis infertility was protective against EP, whereas endometrial preparation regime was not identified as a risk factor for EP.

For multivariate stepwise regression analysis, all variables with a P-value of < 0.1 during univariate analysis were included, with the results shown in **Table 3**.

A small BMI (aOR, 1.001; 95% CI, 1.000–1.002; P = 0.034) and blastocyst transfer (aOR, 0.451; 95% CI, 0.297–0.683; $P < 0.001$) were protective factors against EP after FET cycles. On the other hand, TFI (aOR, 2.221; 95% CI, 1.191–4.144; P = 0.012), a previous history of EP (aOR, 1.573; 95% CI, 1.102–2.243; P = 0.012) and an EMT of < 8 mm (aOR, 3.270; 95% CI, 1.113–9.605; P = 0.031) before P administration were found to independently predict EP. An EMT of 8–9.9 mm (aOR, 2.758; 95% CI, 0.987–7.707; P = 0.053) and 10–11.9 mm (aOR, 1.456; 95% CI, 0.502–4.225; P = 0.489) was not significantly linked with EP occurrence.

Figure 2 shows the prediction model for EP, with the embryo stage, BMI, previous history of EP, and TFI as the variables. The suitability of the model was assessed with an ROC curve for which the area under the curve was 0.651 (95% CI 0.612–0.689, $P < 0.001$). After including EMT as one of the variables of the model, the AUC increased to 0.686 (95% CI 0.650–0.722, $P < 0.001$) (**Figure 3**).

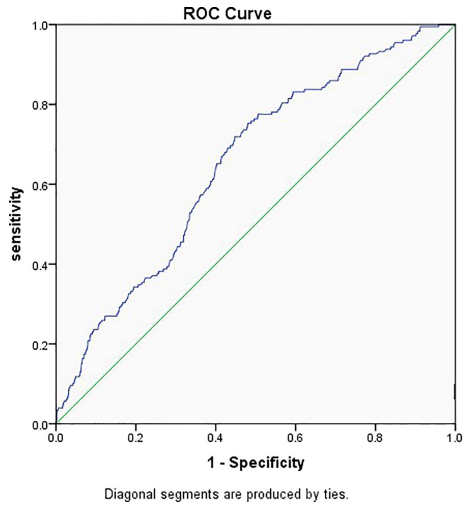

FIGURE 2 | Receiver operator characteristic curve of the embryo stage, BMI, previous history of ectopic pregnancy, and tubal factor infertility. Diagonal segments were produced by ties and the area under the curve was 0.651.

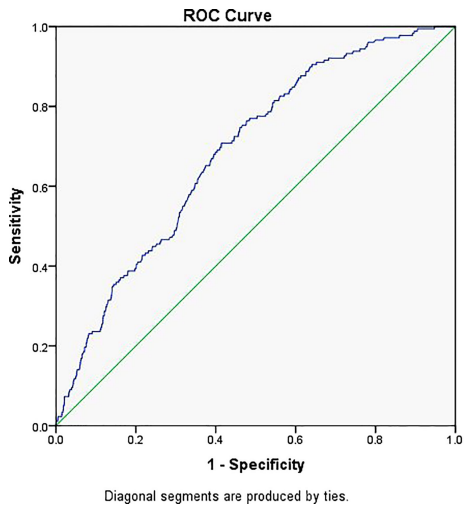

FIGURE 3 | Receiver operator characteristic curve of the embryo stage, BMI, tubal factor infertility, previous history of ectopic pregnancy, and EMT. Diagonal segments were produced by ties and the area under the curve was 0.686.

DISCUSSION

This retrospective analysis of frozen ET cycles sought to investigate the possible link between EMT and EP after freeze-thaw transfer.

In this study, TFI increased the risk of EP by more than twofold, with the results supported by previous studies (12, 13, 15, 26, 28–31). Similarly, women with low BMI were more likely to develop EP after ART, with this outcome being consistent with a previous research (5). As for multiple embryos transfer, although some studies (26, 28, 32) reported that it was risk factor for EP, another one considered that it actually had no impact (29). In fact, previous history of EP (29, 33) is similarly debatable. In the present work, multiple embryos transfer was not identified as a risk factor.

Consistent with some previous studies (34–37), transferring embryos at cleavage stage was a risk factor of EP in the current study. Embryos at this stage could be more prone to "traveling

TABLE 3 | Factors associated with ectopic pregnancy based on stepwise multiple regression analysis.

Predictor variables	Odds ratio	95% confidence interval	*P* value
Previous history of ectopic pregnancy			
=0	1	——	——
≥1	1.573	1.102, 2,243	0.012*
BMI (kg/m^2)	1.001	1.000, 1.002	0.034*
Tubal factor infertility			
Yes	2.221	1.191, 4.144	0.012*
No	1	——	——
Embryo stage			
Cleavage stage embryo	1	——	——
Blastocyst	0.451	0.297, 0.683	0.000*
Endometrial thickness (mm)			0.021*
12–13.9	1	——	——
<8	3.270	1.113, 9.605	0.031*
8–9.9	2.758	0.987, 7.707	0.053
10–11.9	1.456	0.502, 4.225	0.489
≥14	0.000	0.000, 0.000	0.996

** The difference is significant between groups.*

around", unlike blastocysts that tend to immediately seek contact and attachment. Furthermore, a study has shown that decreased uterine contractions on the fifth day could also lower EP rate after blastocysts transfer (19). However, some studies (19, 38–41) do suggest that EP occurrence was not influenced by the stage of embryos. In fact, some reports even suggest that blastocysts transfer could actually heighten EP risks due to potentially higher implantation rates of each blastocyst (20, 25).

These inconsistencies could be the result of variations between studies, especially in terms of patients' age, sample sizes, evaluation system for embryos, and differences in blastocysts culture techniques between reproductive centers.

Few studies have examined the suitability of EMT during ART therapy for predicting EP, but the currently applicable cutoff value that link EMT and EP is controversial. One study in which fresh or frozen embryo cycles were not separately analyzed suggested that, prior to ET, an EMT > 12 mm protected against EP (29). In the same vein, another study reported increased risks of EP when the EMT was < 12 mm in the frozen embryo cycle (28). The current study indicated that an EMT of < 8 mm significantly increased risks of EP. Because it is clinically impractical to perform ET only if the EMT is greater than 12mm, it would therefore be more clinically meaningful to select an EMT of < 8 mm rather than 12 mm as the threshold for being considered a risk factor for EP.

It remains unclear why a thin endometrium increases risks of EP rates, with the reason likely to be complex. Many researchers have suggested that there is a relationship between EMT and uterine receptivity (42–47), and, as such, it is generally believed that thinner EMTs may lead to a poorer endometrial receptivity.

Differences in oxygen concentrations could also explain the link between a thin endometrium and EP. Indeed, a thin EMT would bring embryos quite close to the spiral arteries in the basal endometrium layer, thereby exposing them to high oxygen concentrations which are known to inhibit embryonic development (48).

Uterine peristalsis could be another factor that links EP incidence with a thin endometrium. Previous studies have reported that, compared with IUP, women diagnosed with EP experienced higher uterine peristaltic wave frequencies, but these differences were not statistically significant due to uneven distribution of the sample size (49). A previous research further showed the EMT thickness was positively associated with risks of placenta previa (50). In this case, the authors hypothesized that high EMTs were an indication of the amplitude and/or frequency of uterine peristalsis waves, which can push the embryos downward, dislodging them from their transferred location. Another study (51) found that, compared with natural cycles, controlled ovarian hyperstimulation cycles showed increased uterine waves from the cervix to the fundus but reduced ones from the fundus to the cervix. Therefore, although the results of that study suggest that the direction of uterine peristalsis could influence EP occurrence, yet this link would need to be confirmed through additional studies. Altogether, this study's findings point out that uterine peristalsis from the fundus to the cervix is more likely to occur when the endometrium is thicker as the embryos are more easily implanted in the lower segment of the uterine cavity, resulting in a higher incidence of placenta previa (50) and, correspondingly, a lower incidence of EP. Future studies will focus on how different EMT are associated with the frequency, amplitude, and direction of endometrial peristalsis waves, including the correlation between EP occurrence and the presence of different types of endometrial peristalsis at the time of ET.

As EP risks were higher for patients with an EMT of < 8 mm, especially when the transferred embryos were in the cleavage stage or when multiple embryos were transferred, such patients should be given clear advice. Furthermore, it should be carefully decided whether frozen ET should be performed in the current cycle while routinely examining the endometrial peristaltic wave (49, 52) and providing appropriate treatments such as phloroglucinol (53) and atosiban (54) when necessary as these would help in preventing EP or diagnosing the condition at an early stage.

This study was not without limitations, with the first one being that it was a retrospective study. Chromosomal abnormalities of embryos as a potential risk factor for EP were also not included as not all embryos were tested for chromosomes before transfer, but it was previously reported (55, 56) that chromosomal abnormalities in embryos were not actively involved in the etiology of EP. In addition, the study contained a high rate of multiple embryos transfer. Some researchers (26, 28) believe that multiple embryos transfer is an independent risk factor for EP as well as HP, but this study did not find this variable to be an independent risk factor after multivariate regression analysis, consistent with a previous study (32). This could have been due to the exclusion of HP in the present research.

In short, the results can be very meaningful in the absence of a consensus about the optimal EMT, which can predict or prevent EP after ART.

CONCLUSION

An EMT < 8 mm on the day of endometrial transformation was found to independently predict EP after freeze-thaw ET. Efforts to increase the EMT may reduce EP risks. It may also be necessary to perform endometrial peristaltic wave examination, endometrial receptivity testing as well as provide corresponding treatment in the peri-transfer period for patients with risk factors.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by YZ. The first draft of the manuscript was written by YZ, and all authors commented on previous versions of the manuscript. All authors contributed to the article and approved the submitted version.

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