

Original Article

Association of uterine artery Doppler parameters and coagulation function indicators with endometrial morphology and frozen-thawed embryo transfer outcomes

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Abstract: Objective: To analyze the associations of uterine artery Doppler parameters and peripheral blood coagulation function indicators with endometrial morphological measures and clinical pregnancy outcomes following frozen-thawed embryo transfer (FET), and to explore the discriminative ability of a combined indicator model for pregnancy outcomes. Methods: A total of 97 patients undergoing FET were retrospectively enrolled. Patients were divided into pregnant and non-pregnant groups according to the presence of clinical pregnancy confirmed 28-30 days after embryo transfer. Differences in uterine artery Doppler parameters, coagulation function indicators, and endometrial morphological parameters were compared between the two groups. Logistic regression analysis and receiver operating characteristic (ROC) curve analysis were performed to screen independent influencing factors and evaluate the predictive efficacy of the combined model. Results: The non-pregnant group presented significantly lower levels of progesterone (P) on the endometrial transformation day, endometrial thickness (EMT), endometrial volume (EV), end-diastolic velocity (EDV), activated partial thromboplastin time (APTT), prothrombin time (PT), and D-dimer (D-D), as well as significantly higher pulsatility index (PI), resistance index (RI), systolic/diastolic velocity ratio (S/D), and peak systolic velocity (PSV). $RI > 0.89$, $PI > 2.78$, $PT < 10.20$ s, and $D-D < 0.20$ mg/L were identified as independent risk factors for adverse FET pregnancy outcomes. The area under the curve (AUC) of the combined prediction model was 0.927. Conclusion: Uterine artery Doppler parameters and coagulation function indicators are associated with FET clinical pregnancy outcomes. The combined model demonstrated high apparent discriminative ability in this study sample.

Keywords: Uterine artery Doppler parameters, coagulation function, endometrial receptivity, frozen-thawed embryo transfer

Introduction

Infertility is a reproductive disorder with multiple etiologies, affecting approximately 15% of couples of childbearing age worldwide [1, 2]. Assisted reproductive technology (ART), particularly in vitro fertilization-embryo transfer (IVF-ET), has become a primary treatment for infertility. With the continuous optimization and widespread application of embryo cryopreservation technology, frozen-thawed embryo transfer (FET) has been increasingly applied in clinical ART practice [3-5]. Compared with fresh embryo transfer, FET has unique advantages in reducing the risk of ovarian hyperstimulation

syndrome, optimizing endometrial preparation protocols, and facilitating preimplantation genetic testing, thereby providing a more flexible fertility treatment option for infertile patients [6-8].

Nevertheless, embryo transfer success is affected by multiple confounding factors, among which endometrial receptivity (ER) is recognized as one of the core determinants of implantation and subsequent pregnancy outcomes. ER refers to the capacity of the endometrium to accept embryo implantation and support early embryonic development within a specific implantation window. Accurate evaluation of ER

is of great clinical significance for predicting embryo transfer outcomes and improving the clinical pregnancy rate of ART [9]. At present, clinical evaluation of ER mainly relies on transvaginal ultrasound morphological indicators, with endometrial thickness (EMT) and endometrial volume (EV) being the most widely used indices. It is generally believed that an EMT $\geq$ 7-8 mm on transfer day is a prerequisite for favorable pregnancy outcomes; however, embryo implantation failure still occurs in some patients even with satisfactory EMT [10]. In recent years, the predictive value of uterine artery hemodynamics for ER has attracted growing research attention [11].

Uterine artery Doppler parameters reflecting uterine perfusion status are closely correlated with endometrial blood supply and nutritional support, and thus strongly associated with ER [12]. Meanwhile, the balance between the coagulation and fibrinolysis systems plays a critical role in embryo implantation. Physiological coagulation homeostasis stabilizes the local microenvironment at the implantation site, regulates local hemorrhage, and promotes the establishment of placental vascular networks. In contrast, systemic or local hypercoagulability may induce placental microthrombosis, impair maternal-fetal blood perfusion and substance exchange, and further increase the risks of implantation failure and early spontaneous abortion [13].

Most previous studies have separately explored the correlations of uterine artery Doppler parameters or coagulation indicators with embryo transfer outcomes, while few studies have focused on their combined application in evaluating ER and predicting FET outcomes [11-13]. Accordingly, this study aimed to analyze the relationships between uterine artery Doppler parameters, peripheral blood coagulation indicators, endometrial morphological measures, and FET clinical pregnancy outcomes, and to explore the potential value of combined indicators in identifying pregnancy outcome risks, thereby providing a basis for future prospective, multicenter studies.

Materials and methods

Study subjects

This retrospective observational study enrolled 97 infertile patients who underwent FET with

hormone replacement therapy (HRT) cycles at Beijing United Family Hospital from January 2024 to December 2025. The study protocol was approved by the Ethics Committee of Beijing United Family Hospital.

Inclusion and exclusion criteria

Inclusion criteria: (1) Aged 20-40 years; (2) Infertility caused by tubal factors or unexplained infertility, with scheduled FET treatment; (3) Endometrial preparation performed via a standard HRT protocol; (4) Availability of high-quality embryos for transfer; (5) First embryo transfer cycle; (6) Complete clinical data and follow-up records.

Exclusion criteria: (1) Organic uterine diseases; (2) Concurrent endocrine and metabolic disorders, autoimmune diseases, or infectious diseases; (3) Documented history of coagulation disorders, thrombotic diseases, or other hematological disorders; (4) Transfer of $\geq$ 3 embryos per cycle; (5) Chromosomal abnormalities in either partner.

Treatment protocol

All patients received standard HRT for endometrial preparation. Oral estradiol valerate (Bayer Healthcare, Guangzhou, China) was initiated at a daily dose of 4-6 mg on days 2-3 of the menstrual cycle, with individual dosage adjustment guided by serial ultrasonic monitoring and a maximum daily dose capped at 12 mg. When EMT reached the standard for embryo transfer and luteal phase support was clinically indicated, 20 mg/d dydrogesterone (Abbott Biologicals B.V., Netherlands) was administered to induce endometrial transformation. The day of progesterone initiation was defined as the P+0 day (endometrial transformation day). Cleavage-stage embryos were transferred on day 3 after transformation, and blastocyst-stage embryos were transferred on day 5 according to embryonic developmental stage.

Outcome measures

Endometrial morphological and uterine artery Doppler parameters: On the endometrial transformation day, transvaginal ultrasound examination was performed by two senior sonographers following unified operating standards using a Samsung XW80A ultrasonic diagnostic

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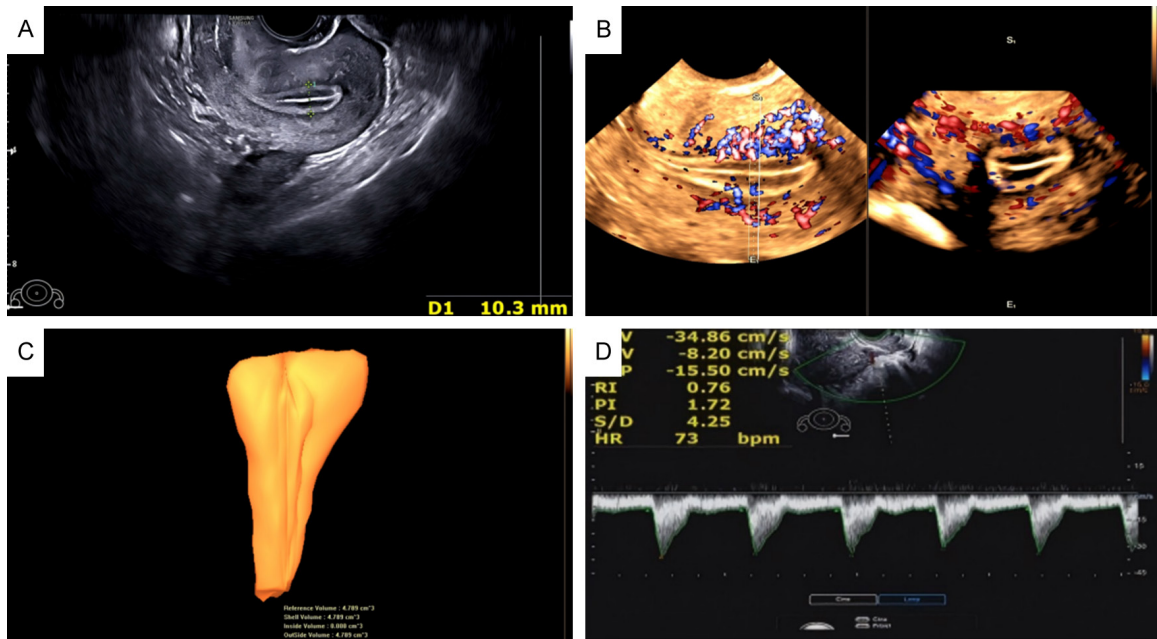


Figure 1. Ultrasound images of the endometrium in the pregnant group. A. Endometrial thickness. B. Endometrial blood flow. C. Endometrial volume. D. Uterine artery. PSV, Peak systolic velocity; EDV, end-diastolic velocity; RI, resistance index; PI, pulsatility index; S/D, systolic/diastolic ratio; TAP, time-averaged mean velocity; HR, heart rate.

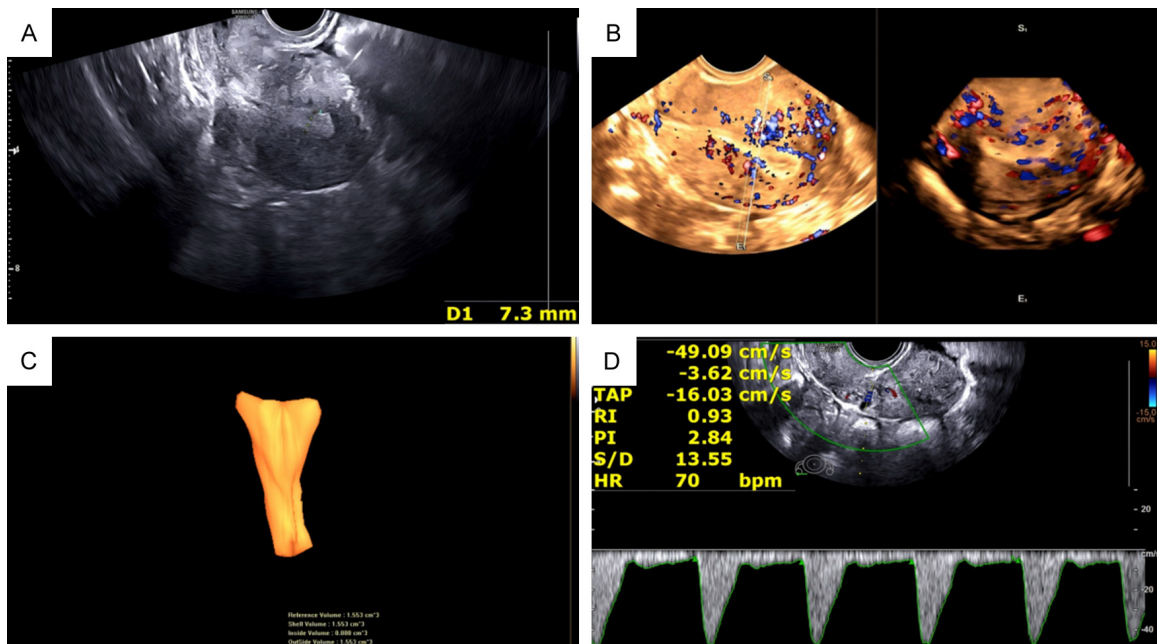


Figure 2. Ultrasound images of the endometrium in the non-pregnant group. A. Endometrial thickness. B. Endometrial blood flow. C. Endometrial volume. D. Uterine artery. PSV, Peak systolic velocity; EDV, end-diastolic velocity; RI, resistance index; PI, pulsatility index; S/D, systolic/diastolic ratio; TAP, time-averaged mean velocity; HR, heart rate.

instrument equipped with a 7.5 MHz transvaginal probe. The detected indicators included EMT, EV, and uterine artery Doppler parameters. EMT was measured as the maximum

thickness of the anterior and posterior endometrial layers on the uterine sagittal plane, excluding uterine cavity effusion (Figures 1 and 2).

After clear visualization of the bilateral main uterine arteries at the cervical internal os, pulsed-wave Doppler mode was activated with a 2 mm sampling gate, and the angle between the ultrasound beam and blood flow was corrected to less than 30°. At least three stable and clear Doppler spectral waveforms were acquired to record peak systolic velocity (PSV) and end-diastolic velocity (EDV). Resistance index (RI) = (PSV-EDV)/PSV; pulsatility index (PI) = (PSV-EDV)/mean velocity; systolic/diastolic ratio (S/D) = PSV/EDV. The average values of bilateral uterine arteries were used for statistical analysis (**Figures 1 and 2**).

Coagulation function indicators: Fasting peripheral venous blood (3 mL) was collected on the morning of the endometrial transformation day. An automatic coagulation analyzer was used to detect prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT), fibrinogen (FIB), and D-dimer (D-D). All specimens were tested by the clinical laboratory of Beijing United Family Hospital in accordance with standard operating procedures with strict internal quality control.

Baseline sex hormones and transformation-day progesterone (P): Baseline serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E₂), and P on menstrual cycle days 2-4 were recorded. Venous blood samples (3 mL) were collected on the endometrial transformation day, and serum P levels were measured via chemiluminescence assay.

Grouping by pregnancy outcome

Transvaginal ultrasonography was performed 28-30 days after embryo transfer. Clinical pregnancy was defined as the presence of an intra-uterine gestational sac (with or without fetal cardiac activity). All patients were divided into the clinical pregnancy group (65 cases) and the non-pregnant group (32 cases) accordingly.

Statistical analysis

SPSS 22.0 software was used for statistical analysis. Normally distributed measurement data were expressed as mean $\pm$ standard deviation ($\bar{x} \pm s$), and independent-samples t-test was applied for intergroup comparisons. Enumeration data were presented as case numbers and percentages, and compared via the

Chi-square test. Pearson correlation analysis was used to assess linear correlations between each indicator and EMT or EV. The Benjamini-Hochberg method was applied to control the false discovery rate (FDR) for multiple testing.

Variables with statistically significant differences in univariate analysis were included in a binary Logistic regression model to screen independent influencing factors of pregnancy outcomes. In the Logistic regression analysis, pregnancy outcome was set as the dependent variable, with assignments of 1 for non-pregnancy and 0 for clinical pregnancy. All candidate predictive variables were converted into binary indicator variables based on optimal threshold values and assigned 0 or 1 scores: variables reaching the risk threshold were scored 1, and those not reaching the threshold were scored 0. The specific assignment criteria were as follows: transformation-day P < 0.23 ng/mL, RI > 0.89, PI > 2.78, S/D > 6.21, PSV > 51.09 cm/s, EDV < 8.23 cm/s, APTT < 29.65 s, PT < 10.20 s, and D-D < 0.20 mg/L were each assigned 1; all other conditions were assigned 0. All variables included in the model were binary 0/1 indicators, and no multi-level categorical variables were incorporated in this study. The receiver operating characteristic (ROC) curve was used to assess the discriminative ability of the model for pregnancy outcomes, and the area under the curve (AUC) together with its 95% confidence interval (CI) were calculated. The Hosmer-Lemeshow goodness-of-fit test and calibration curves were adopted to evaluate the consistency between the predicted probabilities of the model and the actual observed results. P < 0.05 was considered statistically significant

Results

Comparison of baseline clinical data

No significant differences in baseline clinical characteristics were observed between the pregnant and non-pregnant groups (all P > 0.05) (**Table 1**).

Comparison of EMT and EV

EMT and EV in the non-pregnant group were significantly lower than those in the pregnant group (both P < 0.05) (**Table 2**).

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Table 1. Comparison of clinical data between the pregnant group and the non-pregnant group

Group	Average age (years)	Infertility duration (years)	Body mass index (kg/m ²)	Average number of embryos transplanted
Pregnant group (n = 65)	32.32±4.12	3.72±1.54	22.56±2.63	1.78±0.41
Non-pregnant group (n = 32)	31.97±4.97	3.24±1.32	22.87±2.64	1.88±0.34
<i>t</i>	0.372	1.494	0.550	1.072
<i>P</i>	0.711	0.138	0.583	0.286

Table 2. Comparison of EMT and EV levels between the pregnant group and the non-pregnant group

Group	EMT	EV (mm ³)
Pregnant group (n = 65)	9.57±1.12	3.74±0.45
Non-pregnant group (n = 32)	8.64±1.06	3.05±0.51
<i>t</i>	3.900	6.797
<i>P</i>	< 0.001	< 0.001

Note: EMT, Endometrial thickness; EV, endometrial volume.

Comparison of sex hormone levels

Baseline serum P, LH, FSH and E₂ levels showed no significant differences between the two groups (all *P* > 0.05). The transformation-day serum P level in the non-pregnant group was significantly decreased (*P* < 0.05) (**Table 3**).

Comparison of uterine artery Doppler parameters

The non-pregnant group had significantly higher PI, RI, S/D, and PSV than the pregnant group, while EDV was significantly lower (all *P* < 0.05) (**Table 4**).

Comparison of coagulation function indicators

APTT, PT and D-D levels in the non-pregnant group were significantly lower than those in the pregnant group (all *P* < 0.05) (**Table 5**).

Correlation analysis of EMT, EV with related indicators

Correlation analysis showed that EMT and EV were positively correlated with P levels on the day of endometrial transformation, EDV, APTT, PT, and D-D, and negatively correlated with RI, PI, S/D, and PSV. Following FDR correction via the Benjamini-Hochberg procedure, the correlations retained statistical significance (all *P* < 0.05, **Table 6**). It should be noted that correla-

tion analysis reflects only linear associations and does not imply causation.

Logistic regression analysis

Pregnancy outcome was set as the dependent variable, and all indicators with significant inter-group differences in univariate analysis were included as candidate variables in the binary Logistic regression model. The results demonstrated that RI > 0.89, PI > 2.78, PT < 10.20 s and D-D < 0.20 mg/L were independent risk factors for FET pregnancy outcomes. After multivariate adjustment, transformation-day P, S/D, PSV, EDV, and APTT showed no independent statistical significance. Notably, all variables incorporated into the Logistic regression model were binary 0/1 indicator variables rather than continuous variables. To avoid confusion between model parameters and continuous variable names, each predictor was denoted as X_Plow, X_RI, X_PI, X_SD, X_PSV, X_EDVlow, X_APTTlow, X_PTlow, and X_DDlow, respectively. The combined prediction model was established as $P = e^y / (1 + e^y)$, where $y = -3.232 - 1.380 \times X_Plow + 2.048 \times X_RI + 1.983 \times X_PI + 0.662 \times X_SD + 0.726 \times X_PSV + 0.029 \times X_EDVlow - 0.180 \times X_APTTlow + 2.877 \times X_PTlow + 3.702 \times X_DDlow$.

Among these variables, X_Plow indicates transformation-day P < 0.23 ng/mL, X_RI indicates RI > 0.89, X_PI indicates PI > 2.78, X_SD indicates S/D > 6.21, X_PSV indicates PSV > 51.09 cm/s, X_EDVlow indicates EDV < 8.23 cm/s, X_APTTlow indicates APTT < 29.65 s, X_PTlow indicates PT < 10.20 s, and X_DDlow indicates D-D < 0.20 mg/L. Each variable was assigned a score of 1 when the corresponding threshold was met and 0 otherwise (**Table 7**).

ROC curve analysis

ROC curve analysis showed that the exploratory combined model, based on predicted probabilities from the multivariate Logistic regres-

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Table 3. Comparison of sex hormone levels between the pregnant group and the non-pregnant group

Group	P (ng/mL)	LH (mU/mL)	FSH (mU/mL)	E ₂ (pg/mL)	Transformation-day P (ng/mL)
Pregnant group (n = 65)	0.59±0.19	4.78±1.14	6.61±2.03	38.03±13.37	0.27±0.05
Non-pregnant group (n = 32)	0.51±0.21	4.59±1.28	7.09±2.25	38.79±12.47	0.23±0.06
<i>t</i>	1.880	0.741	1.058	0.269	3.546
<i>P</i>	0.063	0.460	0.293	0.788	< 0.001

Note: FSH, Follicle-stimulating hormone; LH, luteinizing hormone; E₂, estradiol; P, progesterone.

Table 4. Comparison of uterine artery blood flow spectrum parameters between the pregnant group and the non-pregnant group

Group	Uterine artery PI	Uterine artery RI	S/D	PSV (cm/s)	EDV (cm/s)
Pregnant group (n = 65)	2.29±0.45	0.78±0.11	5.77±0.82	50.26±1.17	8.71±1.09
Non-pregnant group (n = 32)	2.78±0.41	0.89±0.09	6.21±0.94	51.09±1.45	8.23±1.04
<i>t</i>	5.193	4.908	2.361	3.031	2.067
<i>P</i>	< 0.001	< 0.001	0.020	0.003	0.041

Note: PSV, Peak systolic velocity; EDV, end-diastolic velocity; RI, resistance index; PI, pulsatility index; S/D, systolic/diastolic ratio.

Table 5. Comparison of coagulation function indicators between the pregnant group and the non-pregnant group

Group	APTT (s)	TT (s)	PT (s)	D-D (mg/L)	FIB (g/L)
Pregnant group (n = 65)	31.14±2.28	17.21±1.42	11.61±0.73	0.37±0.09	3.54±0.72
Non-pregnant group (n = 32)	29.65±2.41	17.45±1.52	10.19±0.65	0.20±0.07	3.33±0.82
<i>t</i>	2.981	0.756	9.236	9.340	1.294
<i>P</i>	0.004	0.452	< 0.001	< 0.001	0.199

Note: PT, Prothrombin time; APTT, activated partial thromboplastin time; TT, thrombin time; FIB, fibrinogen; D-D, D-dimer.

Table 6. Correlation between EMT and EV levels of patients and various indicators

Indicators	Statistical value	Transformation-day P (ng/mL)	RI	PI	S/D	PSV	EDV	APTT	PT	D-D
EMT	<i>r</i>	0.451	-0.533	-0.477	-0.343	-0.437	0.210	0.512	0.540	0.488
	<i>P</i>	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.039	< 0.001	< 0.001	< 0.001
EV	<i>r</i>	0.554	-0.459	-0.568	-0.416	-0.429	0.330	0.466	0.597	0.599
	<i>P</i>	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

Note: Given the exploratory nature of the correlation analyses without correction for multiple comparisons, these findings warrant cautious interpretation. EMT, Endometrial thickness; EV, endometrial volume.

sion model in **Table 7**, yielded an apparent AUC of 0.927 (95% CI: 0.862-0.992) in the current development sample. At the optimal cutoff, sensitivity was 0.875 and specificity was 0.908, suggesting that the model has discriminative potential in this study sample. However, since model development, cutoff selection, and performance evaluation were all conducted in the same cohort, these results may be subject to optimistic bias.

The Hosmer-Lemeshow goodness-of-fit test yielded $\chi^2 = 10.596$ ($P = 0.226$), indicating no

significant discrepancy between predicted probabilities and observed outcomes; the calibration curve showed overall agreement. Nevertheless, the Hosmer-Lemeshow test is influenced by sample size and grouping method and should not be interpreted alone as definitive evidence of good calibration. The calibration curve demonstrated that the model's predicted probabilities were generally consistent with the actual observed probabilities.

It should be acknowledged that this study had a limited sample size and lacked external valida-

Table 7. Results of logistic regression analysis for the training group

Indicators	β	SE	Wald	P	OR	95% CI
Constant	-3.232	0.791	16.700	< 0.001	0.039	0.01-0.19
Transformation-day P (< 2.03 ng/mL)	-1.380	0.864	2.549	0.110	0.252	0.05-1.37
RI > 0.89	2.048	0.891	5.280	0.022	7.756	1.35-44.51
PI > 2.78	1.983	0.844	5.522	0.019	7.265	1.39-37.99
S/D > 6.21	0.662	0.708	0.874	0.350	1.938	0.48-7.76
PSV > 51.09	0.726	0.861	0.710	0.399	2.067	0.38-11.18
EDV < 8.23	0.029	0.712	0.002	0.967	1.030	0.26-4.15
APTT < 29.65	-0.180	0.845	0.045	0.831	0.835	0.16-4.38
PT < 10.20	2.877	1.291	4.965	0.026	17.762	1.41-223.12
D-D < 0.20	3.702	1.000	13.719	< 0.001	40.536	5.72-287.51

Note: PSV, Peak systolic velocity; EDV, end-diastolic velocity; RI, resistance index; PI, pulsatility index; S/D, systolic/diastolic ratio; PT, prothrombin time; APTT, activated partial thromboplastin time; TT, thrombin time; FIB, fibrinogen; D-D, D-dimer. The variable assignment is defined as non-pregnancy = 1 and clinical pregnancy = 0. All predictive variables were incorporated into the Logistic regression model as binary 0/1 indicator variables. Values reaching the risk thresholds shown in the table were assigned 1, while those failing to reach the thresholds were assigned 0. All categorical variables included in the model of this study are binary variables, so one 0/1 indicator variable was set for each variable; multi-level categorical variables were not included. The regression coefficients for PT < 10.20 s and D-D < 0.20 mg/L are positive, which indicates that low PT and low D-D levels are associated with an elevated risk of non-pregnancy, rather than implying that rising continuous PT or D-D levels will increase the risk of non-pregnancy.

tion and decision curve analysis. Therefore, the model only presents preliminary predictive potential, and its clinical practicability requires further verification (**Figures 3 and 4**).

Discussion

Successful embryo implantation is predominantly determined by embryo quality and endometrial receptivity [14]. Despite continuous advances in ART, the clinical pregnancy rate of FET cycles remains only 40%-60%. Accordingly, accurate evaluation of endometrial receptivity is crucial for improving FET success rates [15]. At present, clinical assessment of ER mainly relies on ultrasonic morphological indicators such as EMT, which have inherent limitations in predictive efficacy. Therefore, exploring objective and quantitative biomarkers reflecting endometrial functional status has become a research hotspot in reproductive medicine.

Uterine artery Doppler parameters are non-invasive indices for evaluating uteroplacental perfusion, and their close correlation with embryo implantation outcomes has been well validated [16, 17]. PI and RI are core indicators reflecting the vascular resistance of the distal uterine arterial bed. During the implantation window, progesterone dominates the transformation of the endometrium from the proliferative to the secretory phase, accompanied by

physiological remodeling of uterine spiral arteries. This process reduces the contractile reactivity of vascular smooth muscle, remodels vascular wall structure, and decreases vascular resistance, ensuring sufficient and sustained diastolic perfusion of the endometrium and constructing a favorable microenvironment for embryo implantation [18, 19]. Reduced PI and RI reflect arteriolar diastole, luminal dilation, and decreased blood flow resistance.

Consistent with previous studies, this study found that the non-pregnant group had elevated PI, RI, S/D, and PSV, as well as reduced EDV. These findings suggest insufficient physiological remodeling of uterine spiral arteries, increased vascular tension, and inadequate endometrial perfusion, which ultimately impair endometrial receptivity [20]. Correlation analysis further confirmed that EMT and EV were negatively correlated with RI, PI, S/D, and PSV, and positively correlated with EDV, verifying that adequate uterine perfusion is essential for normal endometrial proliferation and volume maintenance. Clinically, the combination of hemodynamic parameters can screen patients with satisfactory EMT but insufficient endometrial perfusion, providing evidence for early clinical intervention.

Embryo implantation is a physiological process accompanied by local vascular remodeling and

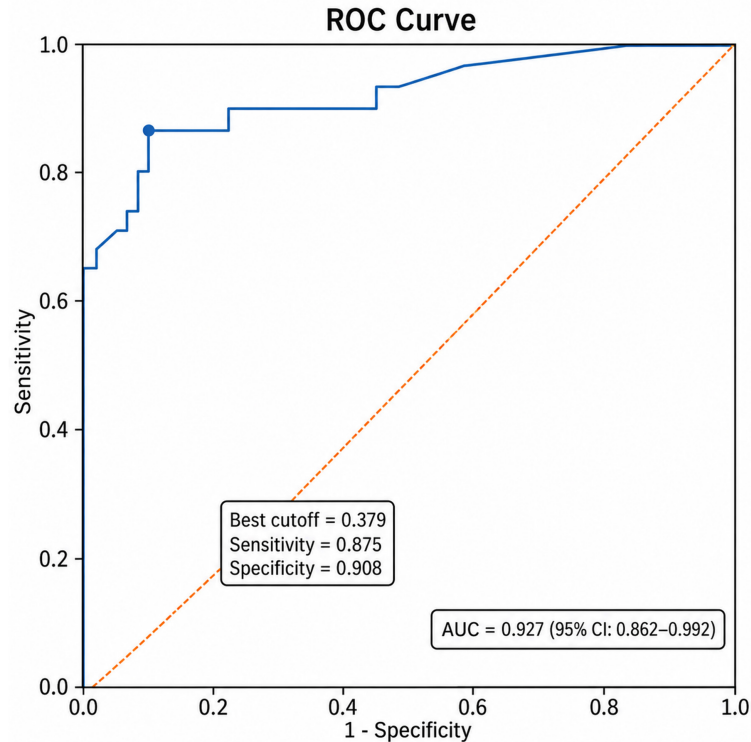


Figure 3. ROC Curve of the combined prediction model. Note: The combined prediction model is constructed based on the predicted probabilities of the multivariate Logistic regression model in Table 7, with all predictive variables incorporated into the model as 0/1 binary indicator variables. AUC = 0.927, 95% CI: 0.862-0.992; the optimal cut-off value corresponds to a sensitivity of 0.875 and a specificity of 0.908.

tissue repair, which is tightly regulated by the dynamic balance of the coagulation and fibrinolysis systems [21, 22]. Systemic hypercoagulability has been recognized as a key risk factor for implantation failure [23]. PT reflects the function of the extrinsic coagulation pathway, and shortened PT indicates enhanced activity of coagulation factor VII and a potential hypercoagulable state [24]. Moderate physiological coagulation activation is indispensable for successful implantation. Blastocyst apposition, adhesion, and invasion disrupt the integrity of local microvessels, and exposed subendothelial tissue factors initiate the coagulation cascade. The formed fibrin network not only maintains hemostasis and tissue stability but also provides a scaffold for trophoblast migration and placental angiogenesis. Moreover, thrombin regulates the proliferation, differentiation, and inflammatory cytokine secretion of endometrial epithelial and stromal cells via protease-activated receptors, participating in the construction of the local implantation microenvironment [25].

The present study identified shorter APTT and PT in the non-pregnant group, along with positive correlations of EMT or EV with both APTT and PT. These findings indicate a hyperactive baseline coagulation state in patients experiencing embryo implantation failure. Excessively premature or excessive coagulation activation within the implantation window may disrupt normal embryonic invasion and subsequent implantation. Meanwhile, timely activation of the fibrinolytic system is essential for the degradation and remodeling of fibrin deposits at the endometrial implantation site. D-Dis is a specific degradation product of cross-linked fibrin, which serves as a reliable biomarker reflecting the activation status of the fibrinolytic system [26]. The significantly reduced peripheral D-D levels observed in the non-pregnant group, as well as its positive correlation with EMT and EV, demonstrate insufficient fibrinolytic activity.

Such impaired fibrinolysis fails to eliminate and remodel local fibrin deposits in a timely manner, thereby hindering successful implantation.

Previous relevant studies have predominantly focused on the independent predictive value of either uterine hemodynamic parameters or coagulation indicators, while few investigations have explored their combined predictive efficacy [27]. Besides, multivariate Logistic regression analysis identified that $RI > 0.89$, $PI > 2.78$, $PT < 10.20$ s, and $D-D < 0.20$ mg/L were identified as independent influencing factors for predicting FET pregnancy outcomes. Notably, PT and D-D were incorporated into the model as binary variables representing low PT and low D-D statuses, respectively. Although parameters such as systolic/diastolic ratio (S/D), EDV, APTT and transformation-day P exhibited significant differences in intergroup comparisons and univariate analyses, they failed to serve as independent predictive factors after multivariate adjustment. This suggests that their predictive effects may be confounded and influ-

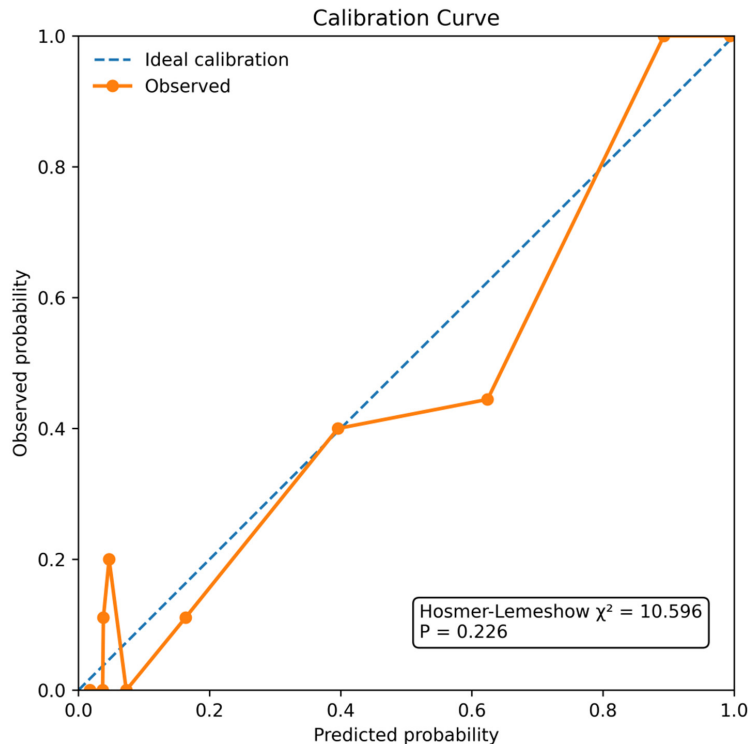


Figure 4. Calibration curve of the combined prediction model. Note: The calibration curve is used to evaluate the consistency between the predicted probabilities and the actual observed probabilities of the multivariate Logistic regression model in Table 7. The Hosmer-Lemeshow goodness-of-fit test yielded $\chi^2 = 10.596$ and $P = 0.226$, indicating no statistically significant difference between the model-predicted probabilities and actual observed outcomes, and the model had acceptable calibration.

enced by blood flow resistance indicators (including RI, PI, PT, D-D) and other clinical variables. In this study, the model yielded an AUC of 0.927, indicating excellent discriminative power for FET pregnancy outcomes. Hosmer-Lemeshow goodness-of-fit test and calibration curve analysis further verified that the model's predicted probabilities were well consistent with the actual observed values, with acceptable calibration performance. The exploratory combined model in this study achieved an apparent AUC of 0.927 in the development sample, suggesting discriminative potential for the selected indicator combination in the current cohort. However, the model has not been externally validated in an independent cohort, nor has DCA been performed. Its stability, generalizability, and net clinical benefit across different institutions and patient populations remain unclear. Therefore, the current findings are insufficient to support the development of a stratified or individualized clinical screening tool.

Limitations

First, this was a single-center retrospective study with a sample size of only 97 cases, which may introduce selection bias. The limited number of non-pregnancy events may also affect parameter estimation and apparent performance due to overfitting. Second, model development, cutoff selection, and performance evaluation were all based on the same cohort; only the Hosmer-Lemeshow test and calibration curve were performed, without external validation in independent multicenter cohorts or DCA. Thus, the net clinical benefit and practical translational value of the model cannot be determined. Third, this study did not include stratified subgroup analyses based on endometrial type (A/B/C) or repeated implantation failure populations, and the current sample size is insufficient to support stable subgroup modeling. Fourth, although ultrasound examinations were performed by

two senior physicians following a standardized protocol, complete data from independent duplicate measurements by both physicians for the same case were not retained, preventing assessment of inter-observer agreement. The reproducibility of flow and endometrial measurements requires further verification. Finally, while FDR correction was applied to the multiple correlation analyses, both the correlation results and the combined model remain exploratory. Future multicenter, prospective, large-sample studies with standardized repeated measurements, external validation, DCA, and subgroup analyses in specific populations are needed to further confirm these findings.

Conclusion

Uterine artery Doppler parameters and peripheral blood coagulation indicators are associated with FET clinical pregnancy outcomes. In this study sample, $RI > 0.89$, $PI > 2.78$, $PT < 10.20$ s, and $D-D < 0.20$ mg/L were associated

with an increased risk of non-pregnancy. The exploratory combined model showed discriminative potential. However, given the single-center, small-sample retrospective design and the lack of external validation, DCA, and subgroup analyses, the current results should be interpreted as exploratory and are not suitable for direct application in individualized screening or clinical decision-making.

Disclosure of conflict of interest

None.

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