

Original Article

Correlation between insulin resistance-related index and recurrent spontaneous abortion: a retrospective study

Shan Zheng^{1*}, Bei Gan^{1*}, Chunyan Huang², Yihong Chen², Jinhuan Chen¹

¹Department of Obstetrics and Gynecology, The First Affiliated Hospital of Fujian Medical University, Fuzhou 350005, Fujian, China; ²Department of Ultrasound, The First Affiliated Hospital of Fujian Medical University, Fuzhou 350005, Fujian, China. *Equal contributors.

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Abstract: Objective: To investigate the changes and clinical significance of uterine artery blood flow parameters, insulin resistance index, and the triglyceride-glucose (TyG) index in patients with recurrent spontaneous abortion (RSA). Methods: A total of 72 pregnant women with a history of recurrent spontaneous abortion were enrolled as the RSA group, and 82 pregnant women without a history of abnormal pregnancy during the same period were selected as the normal pregnancy group. Fasting insulin (FINS), fasting blood glucose (FBG), insulin resistance index (HOMA-IR), uterine artery pulsatility index (PI), resistance index (RI), the ratio of uterine artery systolic maximum blood flow velocity to end-diastolic blood flow velocity (S/D) and TyG index were compared between the two groups at 6-10 weeks of gestation. Multivariate analysis was performed to identify independent risk factors for RSA. Receiver operating characteristic (ROC) curves were used to evaluate the predictive performance of individual and combined indicators. Results: There were significant differences in age, FINS, HOMA-IR, uterine artery PI and RI, S/D ratio, and TyG index between the RSA group and the control group (all $P < 0.05$). Multivariate analysis identified these variables as independent risk factors for RSA. The combined predictive model yielded an AUC of 0.881. Conclusion: There is a direct correlation between the insulin resistance and the occurrence of recurrent spontaneous abortion. A combination of multiple metabolic and hemodynamic parameters may improve the predictive accuracy for RSA.

Keywords: Recurrent spontaneous abortion, uterine artery blood flow parameters, insulin resistance, triglyceride glucose product index, outcome prediction

Introduction

Recurrent spontaneous abortion (RSA) is a common complication in women of reproductive age, defined as two or more consecutive spontaneous pregnancy losses with the same partner. Its incidence ranges from 1% to 5% among women of reproductive age [1, 2]. The etiology of RSA is complex, involving genetic factors, anatomical abnormalities, endocrine disorders, immune dysfunction, infections, and prethrombotic states [3, 4]. RSA not only adversely affects the mental health of patients but also imposes a substantial economic burden. Therefore, early identification of high-risk population and timely intervention are of great clinical significance for improving pregnancy outcomes.

In recent years, increasing evidence has highlighted the potential role of abnormal uterine

artery hemodynamics in the pathogenesis of RSA [5]. Elevated uterine artery resistance can lead to inadequate placental perfusion, thereby contributing to pregnancy loss. In addition, metabolic disorders can also lead to RSA. Insulin resistance (IR), a core feature of metabolic syndrome, has attracted growing attention in the investigation of RSA [6]. Previous studies have suggested that IR is a potential risk factor for unexplained RSA [7, 8]. As a simple and reliable surrogate marker of IR, triglyceride-glucose (TyG) index has been widely applied in studies of cardiovascular and metabolic diseases. Emerging evidence has reported altered TyG index levels in RSA patients and their relationship with uterine artery blood flow parameters and IR-related indicators; however, systematic evidence remains limited [9].

Based on these considerations, this study aimed to analyze uterine artery blood flow param-

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ters, IR-related indices, and TyG index in pregnant women with RSA, and to explore their expression patterns and clinical significance, in order to provide new insights into early identification and clinical intervention in RSA.

Materials and methods

Study population

The clinical data of 154 pregnant women who visited the First Affiliated Hospital of Fujian Medical University from January 2022 to December 2024 were retrospectively analyzed. According to the predefined inclusion criteria, a total of 72 pregnant women with a history of RSA were assigned to the RSA group, while 82 pregnant women without abnormal pregnancy history were selected as the normal pregnancy group. This study was approved by the Ethics Committee of the First Affiliated Hospital of Fujian Medical University.

Inclusion criteria

1. Age between 20 and 45 years;
2. Pregnant women in the RSA group were defined as having two or more consecutive spontaneous abortions with the same partner;
3. Normal pregnancy group: no history of spontaneous abortion and at least one previous full-term delivery;
4. Singleton pregnancy with a gestational age of 6-10 weeks;
5. Completion of all relevant prenatal examination and laboratory tests at our hospital;
6. Availability of complete clinical data.

Exclusion criteria

1. Multiple pregnancy;
2. Presence with uterine anatomical abnormalities (e.g., uterine septum, uterine fibroids, intrauterine adhesions);
3. Chromosomal karyotype abnormalities in either partner;
4. Endocrine disorders, including thyroid dysfunction, diabetes, and polycystic ovary syndrome;
5. Autoimmune diseases (e.g., antiphospholipid syndrome, systemic lupus erythematosus);
6. Acute or chronic infectious diseases, or a history of infection within the preceding 2 weeks;
7. Severe dysfunction of the heart, liver, or kidneys;
8. Incomplete clinical data.

Data collection

General demographic and clinical data of all participants were collected from the hospital

electronic medical record system, including age, gestational age, gravidity, parity, number of spontaneous abortions, body mass index (BMI), systolic blood pressure, and diastolic blood pressure.

Laboratory measurements

At 6-10 weeks of gestation, 5 mL of fasting venous blood was collected from all participants. Blood samples were placed in serum separator tubes and allowed to stand for 30 minutes. The samples were centrifuged at 3000 r/min for 10 minutes. The supernatant serum was separated and stored at -80°C until analysis.

Fasting blood glucose (FBG) was detected using an automatic biochemical analyzer (Cobas c702; Roche; Germany), and fasting insulin (FINS) levels were determined by fully automatic electrochemiluminescence immunoassay (Cobas e601; Roche, Germany) using the Elecsys insulin test kit. The intra-assay and inter-assay coefficients of variation were 2.8% and 4.2%, respectively, indicating good precision and repeatability. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the following formula: $HOMA-IR = FINS (\mu U/mL) \times FBG (mmol/L) / 22.5$. Triglyceride (TG) levels were detected using the same automatic biochemical analyzer (Cobas c702; Roche). The triglyceride-glucose (TyG) index was calculated using the following formula: $TyG \text{ index} = \ln [TG (mmol/L) \times FBG (mmol/L) / 2]$. All laboratory procedures were performed in strict accordance with the manufacturers' standard operating protocols.

Uterine artery hemodynamic assessment

Uterine artery blood flow parameters were assessed using a color Doppler ultrasound system (Voluson E10; GE), equipped with RAB6-D convex array probe (frequency 2-8 MHz). All examinations were performed with the patient in the supine position and with an empty bladder. A routine obstetric ultrasound was first conducted to confirm fetal viability and gestational age. The uterine artery pulsatility index (PI), resistance index (RI), and the ratio of maximum systolic blood flow velocity to end-diastolic blood flow velocity (S/D) were measured. Each uterine artery was assessed three times, and the average value was calculated for analysis.

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Outcome measures

The primary outcomes included insulin resistance-related indices (FBG, FINS, HOMA-IR), uterine artery blood flow parameters (PI, RI, S/D) and TyG index between the RSA group and the normal pregnancy group. Multivariate Logistic regression analysis was performed to identify independent risk factors for RSA. Receiver operating characteristic (ROC) curves were constructed to evaluate the predictive performance of individual indicators and their combination, and the area under the curve (AUC) was calculated.

Secondary outcomes

A calibration curve of the combined predictive model for RSA was generated to evaluate model's goodness-of-fit and predictive performance.

Statistical analysis

All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed data were expressed as mean \pm standard deviation ($\bar{x} \pm sd$), and comparisons between groups were conducted using the independent-samples t-test. Non-normally distributed data were expressed as median (interquartile range) [M (P25, P75)], and comparisons between groups were performed using the Mann-Whitney U test. Categorical data were presented as counts and percentages [n (%)], and group comparisons were performed using the Chi-square test or Fisher's exact test (when the expected frequency was < 5).

Binary logistic regression analysis (forward stepwise method) was used to identify independent risk factors for RSA. Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were calculated. Variables with $P < 0.05$ in univariate analysis were entered into the multivariate regression model. Collinearity diagnostics were performed before regression analysis, with a variance inflation factor (VIF) < 5 or tolerance > 0.2 indicating no significant collinearity.

A combined prediction model was constructed based on the independent risk factors identified in the multivariate analysis. The predicted

probability (P) was calculated for each patient using the following formula: $\text{Logit}(P) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \dots + \beta_k X_k$.

The predicted probability was then used to plot the ROC curve. The AUC was calculated to evaluate the discriminative ability of the model. The Hosmer-Lemeshow goodness-of-fit test was used to assess model calibration, with $P > 0.05$ indicating good calibration.

All tests were two-sided, and a P -value < 0.05 was considered statistically significant.

Results

Comparison of baseline characteristics between the two groups

A total of 154 pregnant women were included in this study, including 72 cases in the RSA group and 82 cases in the normal pregnancy group. Comparison of baseline data between the two groups showed that the age [(31.5 \pm 4.2) years vs. (28.9 \pm 3.8) years, $P = 0.012$], gravidity [3 (2, 4) times vs. 2 (1, 2) times, $P < 0.001$], the number of previous abortions [2 (2, 3) times vs. 0 (0, 0) times, $P < 0.001$] and the incidence of adverse pregnancy history (38.9% vs. 6.1%, $P < 0.001$) in the RSA group were significantly higher than those in the normal pregnancy group. No significant differences were observed between the two groups in BMI, gestational age, parity, education level, comorbidities, or history of smoking and alcohol consumption between the two groups (all $P > 0.05$) (**Table 1**).

Comparison of glucose metabolism and insulin resistance indexes between the two groups

At 6-10 weeks of gestation, FBG, FINS, and HOMA-IR in the RSA group were all significantly higher than those in the normal pregnancy group [FBG: (5.12 \pm 0.48) vs. (4.86 \pm 0.42) mmol/L, $P = 0.001$; FINS: 8.95 (6.82, 11.36) vs. 6.74 (5.21, 8.53) mIU/L, $P < 0.001$; HOMA-IR: 2.18 (1.56, 2.89) vs. 1.52 (1.18, 1.96), $P < 0.001$]. These findings suggest that women with RSA exhibit more pronounced disturbances in glucose metabolism and insulin resistance in early pregnancy (**Table 2**).

Comparison of uterine artery hemodynamics and TyG index between the two groups

During the 6-10 weeks of pregnancy, the RSA group showed significantly higher levels of TG

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Table 1. Comparison of baseline characteristics between the two groups

Item	Recurrent spontaneous abortion group (n = 72)	Normal pregnancy group (n = 82)	Statistical	P value
Age (years)	31.5 ± 4.2	28.9 ± 3.8	4.028	0.012
Body mass index (kg/m ²)	23.8 ± 3.1	22.9 ± 2.9	1.893	0.061
Gestational weeks (weeks)	9.2 ± 1.8	9.5 ± 1.6	-1.102	0.273
Gravidity [times, M (Q1, Q3)]	3 (2, 4)	2 (1, 2)	-4.512	< 0.001
Number of births [times, M (Q1, Q3)]	0 (0, 1)	0 (0, 1)	-1.234	0.218
Number of previous abortions [times, M (Q1, Q3)]	2 (2, 3)	0 (0, 0)	-9.856	< 0.001
Educational level [example (%)]			2.145	0.342
High school and below	20 (27.8)	18 (22.0)		
Junior college/undergraduate	38 (52.8)	42 (51.2)		
Master's degree or above	14 (19.4)	22 (26.8)		
Adverse pregnancy history [case (%)]	28 (38.9)	5 (6.1)	24.718	< 0.001
Complicated with medical diseases [case (%)]				
Thyroid dysfunction	12 (16.7)	6 (7.3)	3.296	0.069
Diabetes	5 (6.9)	3 (3.7)	0.274	0.601
Hypertension	4 (5.6)	2 (2.4)	0.355	0.551
Smoking history [case (%)]	3 (4.2)	2 (2.4)	0.018	0.893
Alcohol consumption history [case (%)]	5 (6.9)	4 (4.9)	0.022	0.882

Table 2. Comparison of fasting blood glucose and insulin resistance indices between the two groups

Index	Recurrent spontaneous abortion group (n = 72)	Normal pregnancy group (n = 82)	Statistical	P value
Fasting blood glucose (mmol/L)	5.12 ± 0.48	4.86 ± 0.42	3.562	0.001
Fasting insulin (mIU/L)	2.34 ± 0.92	1.61 ± 0.58	1.028	< 0.001
HOMA-IR [M (Q1, Q3)]	2.18 (1.56, 2.89)	1.52 (1.18, 1.96)	-4.562	< 0.001

Note: HOMA-IR, homeostatic model assessment of insulin resistance.

(1.52 ± 0.35 mmol/L), FBG (5.12 ± 0.48 mmol/L), TyG index (1.89 ± 0.44), as well as uterine artery blood flow parameters, including PI (1.18 ± 0.21), RI (0.82 ± 0.08), and S/D ratio (2.56 ± 0.38), compared with the normal pregnancy group (TG: 1.28 ± 0.30 mmol/L; FBG: 4.86 ± 0.42 mmol/L; TyG index: 1.52 ± 0.38; PI: 0.96 ± 0.18; RI: 0.74 ± 0.07; S/D: 2.18 ± 0.32) (all P < 0.01; **Table 3**).

Multivariate Logistic regression analysis of risk factors of RSA

RSA was set as the dependent variable, and variables with statistical significance in the univariate analysis, including age, adverse pregnancy history, HOMA-IR, PI and TyG index were included in the multivariate logistic regression model.

Considering the potential collinearity among FBG, FINS, and HOMA-IR, only HOMA-IR was included in the model as a representative indi-

cator of insulin resistance. Similarly, due to the strong correlations among the three hemodynamic parameters (PI, RI and S/D), the most commonly used PI index was selected for inclusion in the multivariate analysis.

Multivariate logistic regression analysis showed that age (OR = 1.185, 95% CI: 1.028-1.366, P = 0.019), adverse pregnancy history (OR = 6.892, 95% CI: 2.156-22.034, P = 0.001), HOMA-IR (OR = 2.856, 95% CI: 1.492-5.467, P = 0.002), PI (OR = 5.231, 95% CI: 1.892-14.467, P = 0.002) and TyG index (OR = 5.234, 95% CI: 1.678-16.327, P = 0.004) were independent risk factors for RSA (**Tables 4, 5**).

Development and validation of the prediction model for RSA

Based on the results of multivariate logistic regression analysis, a combined predictive model was constructed. The predicted probability (P) for each patient was calculated using

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Table 3. Comparison of uterine artery hemodynamic parameters and TyG index between the two groups

Index	Recurrent spontaneous abortion group (n = 72)	Normal pregnancy group (n = 82)	Statistical value	P value
Glucose-lipid metabolism indices				
TG (mmol/L)	1.52 ± 0.35	1.28 ± 0.30	4.562	< 0.001
FBG (mmol/L)	5.12 ± 0.48	4.86 ± 0.42	3.562	0.005
TyG index	1.89 ± 0.44	1.52 ± 0.38	5.612	0.001
Uterine artery hemodynamic parameters				
Pulsatility index (PI)	1.18 ± 0.21	0.96 ± 0.18	6.984	< 0.001
Resistance index (RI)	0.82 ± 0.08	0.74 ± 0.07	6.562	< 0.001
Systolic/diastolic velocity ratio (S/D)	2.56 ± 0.38	2.18 ± 0.32	6.723	< 0.001

Notes: TG, triglyceride; FBG, fasting blood glucose; TyG, triglyceride-glucose index.

Table 4. Variable assignment and description

Variable name	Meaning of variable	Assignment description
Baseline characteristics		
Age	Age	Continuous variable, actual age (years)
Pre-pregnancy BMI	Pre-pregnancy body mass index	Continuous variable, actual value (kg/m ²)
Adverse pregnancy history	History of adverse pregnancy	0 = no, 1 = yes
Glucose-lipid metabolism indices		
TG	Triglyceride	Continuous variable, actual value (mmol/L)
FBG	Fasting blood glucose	Continuous variable, actual value (mmol/L)
TyG index	Triglyceride-glucose index	Continuous variable, actual calculated value = $\ln [TG (mg/dL) \times FBG (mg/dL)/2]$
HOMA-IR	Homeostatic model assessment of insulin resistance	Continuous variable, actual calculated value = $FBG (mmol/L) \times FINS (mU/L)/22.5$
Uterine artery blood flow parameters		
PI	Pulsatility index of uterine artery	Continuous variable, actual detected value
RI	Resistance index of uterine artery	Continuous variable, actual detected value
S/D	Systolic/diastolic velocity ratio	Continuous variable, actual detected value
Interaction term		
Adverse pregnancy history × HOMA-IR	Interaction term	Product of adverse pregnancy history (0/1) and HOMA-IR (continuous variable)

Notes: TG, triglyceride; FBG, fasting blood glucose; TyG, triglyceride-glucose index; HOMA-IR, homeostatic model assessment of insulin resistance; PI, pulsatility index; RI, resistance index; S/D, systolic/diastolic velocity ratio.

the following logistic regression equation: $\text{Logit}(P) = -28.654 + 0.170 \times \text{Age} + 1.930 \times \text{Adverse pregnancy history} + 1.049 \times \text{HOMA-IR} + 3.751 \times \text{PI} + 1.655 \times \text{TyG index}$.

The discriminative ability of the model was evaluated using ROC curve analysis. The results showed that the AUC of the combined predictive model was 0.881, indicating good discrimination. The Hosmer-Lemeshow test yielded a χ^2 value of 8.414 ($P = 0.394$), suggesting good model calibration (**Figure 1**). Internal validation using the Bootstrap resampling method (1,000 resamples) yielded a bias-corrected AUC of 0.842 (95% CI: 0.782-0.902), which was close to the apparent AUC (0.858), indicating no significant overfitting. The calibration curve dem-

onstrated good agreement between predicted and observed probabilities (Hosmer-Lemeshow test, $P = 0.327$; **Figure 2**). Furthermore, Delong test showed that the predictive performance of HOMA-IR alone was comparable to that of the combined model ($P = 0.762$), both of which were significantly better than age and adverse pregnancy history ($P < 0.001$; **Tables 6, 7**).

Correlation between uterine artery hemodynamics and metabolic indices

Pearson correlation analysis showed that both TyG index and HOMA-IR were significantly positively correlated with uterine artery PI, RI and S/D in pregnant women with RSA (all $P < 0.05$) (**Table 8**).

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Table 5. Multivariate Logistic regression analysis of influencing factors of recurrent spontaneous abortion

Variable	B value	Standard error	Wald χ^2 value	P value	OR	95% CI
Age	0.170	0.072	5.523	0.019	1.185	1.028-1.366
Adverse pregnancy history	1.930	0.593	10.591	0.001	6.892	2.156-22.034
Insulin resistance index (HOMA-IR)	1.049	0.332	9.993	0.002	2.856	1.492-5.467
Pulsatility index (PI) of uterine artery	3.751	1.190	9.933	0.001	5.231	2.156-12.689
Triglyceride-glucose index (TyG index)	1.655	0.581	8.112	0.004	5.234	1.678-16.327
Interaction term (Adverse pregnancy history \times HOMA-IR)	0.898	0.312	8.287	0.004	2.456	1.325-4.552

Notes: The interaction term (history of adverse pregnancy and childbirth \times HOMA-IR) OR = 2.456 (95% CI: 1.325-4.552, P = 0.004), indicating that when the two factors are combined, they have a synergistic effect in increasing the risk of RSA.

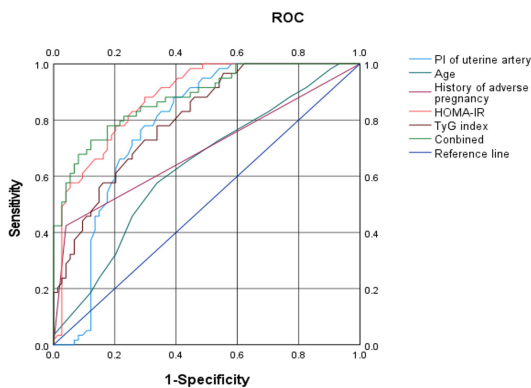


Figure 1. ROC curves for individual predictors and their combination for outcome prediction. ROC: receiver operating characteristic.

Discussion

The pathogenesis of RSA involves a variety of factors, including genetic, anatomic, endocrine, immunological and metabolic factors; however, there are few studies focusing on metabolic disorders in RSA [10]. In recent years, with changes in lifestyle and an increasing proportion of advanced maternal age, insulin resistance and insufficient uterine blood perfusion have been recognized as important contributors to the occurrence and development of RSA, both of which are closely related to metabolic disorders [11]. Therefore, it is of great significance to investigate the correlation between RSA and metabolic disorders.

Previous studies have demonstrated that HOMA-IR levels are higher in patients with RSA than those in normal controls, and abnormal glucose metabolism has been identified as an independent risk factor for early pregnancy loss [12]. Consistent with these findings, the

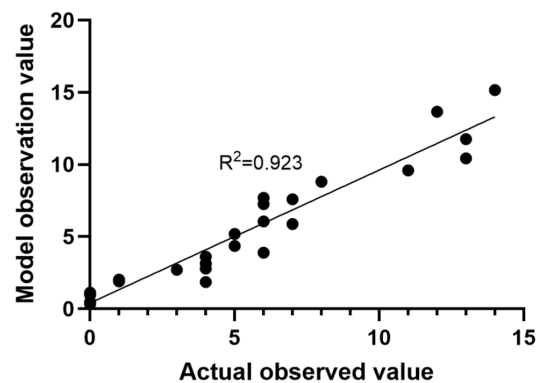


Figure 2. Predictive efficacy of the combined model for recurrent spontaneous abortion. The R^2 value represents the goodness-of-fit of the calibration curve, which is used to assess the consistency between the predicted probabilities of the model and the actual observed results. The closer the R^2 value is to 1, the better the calibration accuracy of the model.

present study also demonstrated that women in the RSA group exhibited higher levels of FBG, FINS, and HOMA-IR, indicating that insulin resistance may be involved in the pathogenesis of RSA. Furthermore, multivariate Logistic regression analysis further confirmed that HOMA-IR and TyG index were independent risk factors for RSA, which finding is consistent with previous reports [13].

The underlying mechanisms may involve several pathways. First, insulin resistance induces compensatory hyperinsulinemia, which may impair normal follicular development and reduce endometrial receptivity. In addition, hyperinsulinemia directly reduces the production of insulin-like growth factor binding protein-1 (IGFBP-1), thereby affecting endometrial decidualization and hindering embryo implantation.

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Table 6. Predictive performance of each predictor for recurrent spontaneous abortion

Test result variables	AUC (95% CI)	Standard error	P value	Cut-off value	Sensitivity (%)	Specificity (%)
TyG index	0.879 (0.822-0.936)	0.029	< 0.001	1.31	84.7	82.9
Joint prediction probability	0.881 (0.824-0.937)	0.029	< 0.001	0.52	86.1	84.1
HOMA-IR	0.805 (0.733-0.876)	0.037	< 0.001	1.85	79.2	75.6
Uterine artery PI	0.781 (0.701-0.862)	0.041	< 0.001	1.02	76.4	73.2
Adverse pregnancy history	0.692 (0.598-0.786)	0.048	< 0.001	0.5*	63.9	74.4
Age	0.634 (0.539-0.729)	0.048	0.008	31.5	61.1	62.2

Note: *: For the dichotomous variable “adverse pregnancy history” (coded as 0 = no, 1 = yes), the cut-off value of 0.5 represents the theoretical threshold for positivity. The cut-off value is determined based on the maximum Youden index (Youden index = Sensitivity + Specificity - 1), that is, the predicted probability value corresponding to the maximum Youden index is selected as the optimal cut-off value. After calculation, when the predicted probability is 0.52, the Youden index reaches its maximum of 0.767. At this point, the model has the best predictive efficacy for RSA. TyG, triglyceride-glucose index; HOMA-IR, homeostatic model assessment of insulin resistance; PI, pulsatility index.

Table 7. Pairwise comparison of AUC of each predictor (DeLong test)

Comparison	Difference in AUC	Standard error	Z value	P value	Comparison	Difference in AUC
Combined model vs. TyG index	0.124	0.048	2.583	0.010	Combined model vs. TyG index	0.124
Combined model vs. PI	0.156	0.052	3.000	0.003	Combined model vs. PI	0.156
Combined model vs. HOMA-IR	0.089	0.041	2.171	0.030	Combined model vs. HOMA-IR	0.089
TyG index vs. PI	0.032	0.038	0.842	0.400	TyG index vs. PI	0.032
TyG index vs. HOMA-IR	0.035	0.035	1.000	0.317	TyG index vs. HOMA-IR	0.035
PI vs. HOMA-IR	0.067	0.040	1.675	0.094	PI vs. HOMA-IR	0.067

Notes: TyG, triglyceride-glucose index; HOMA-IR, homeostatic model assessment of insulin resistance; PI, pulsatility index.

Table 8. Correlation between uterine artery hemodynamic parameters and TyG index, HOMA-IR

Group	Index	TYG index		HOMA-IR	
		r value	P value	r value	P value
RSA group (n = 72)	PI	0.312	0.005	0.345	0.002
	RI	0.287	0.012	0.301	0.008
	S/D	0.241	0.021	0.273	0.014
Normal pregnancy group (n = 82)	PI	0.068	0.412	0.075	0.368
	RI	0.052	0.521	0.061	0.487
	S/D	0.041	0.603	0.055	0.512

Note: RSA: recurrent spontaneous abortion.

Second, insulin resistance is closely associated with a state of chronic low-grade inflammation [14]. Specifically, elevated insulin levels can activate inflammatory signaling pathways, such as nuclear factor- κ B (NF- κ B), promoting the release of pro-inflammatory cytokines, including TNF- α and IL-6. These inflammatory factors may disrupt maternal immune tolerance and induce a pro-inflammatory microenvironment at the maternal-fetal interface, thereby increasing the risk of pregnancy loss [14]. Third, insulin resistance impairs fibrinolytic function and promotes a hypercoagulable state,

leading to placental microthrombosis and compromised uteroplacental perfusion, which in turn restrict embryonic growth and increase the risk of miscarriage, as supported by the prior research [15].

Regarding the TyG index, previous studies have demonstrated its utility in predicting RSA, with reported diagnostic performance (AUC = 0.86) superior to that of HOMA-IR [16]. The present study also confirmed the favorable predictive performance of the TyG index, which can be attributed to the fact that the TYG index, as a

simple and reliable indicator reflecting insulin resistance, integrates information from both triglyceride and fasting blood glucose, thereby providing a more comprehensive evaluation of systemic metabolic disorders compared with a single indicator. Similar conclusions have been reported in previous studies [17, 18], which further validate the reliability of our findings on the TyG index.

As the main blood vessel supplying the uterine-placental circulation, the hemodynamic status of the uterine artery directly influences the blood perfusion level required for embryonic development [19, 20]. Previous studies have shown that increased uterine artery PI is significantly positively correlated with an elevated risk of miscarriage, and that combining PI with maternal age improves the predictive performance for RSA. In line with these findings, the results of the present study showed that uterine artery PI, RI, and S/D ratio in the RSA group were significantly higher than those in the normal pregnancy group. Moreover, multivariate logistic analysis confirmed that PI is an independent risk factor for RSA, further verifying the presence of impaired uterine perfusion in affected patients.

The underlying mechanism may primarily involve insufficient trophoblast infiltration and/or abnormal immune responses at the maternal-fetal interface in RSA patients, which leads to impaired spiral artery remodeling and sustained high vascular resistance. These findings further emphasize the key role of uteroplacental perfusion in the maintenance of pregnancy, supporting the conclusions of previous studies [21, 22]. Meanwhile, ROC curve analysis showed that the combined application of TyG index, HOMA-IR, and PI achieved an AUC of 0.881 in predicting RSA, with sensitivity of 86.1% and specificity of 84.1%, significantly higher than each marker alone. These findings support the notion that both insulin resistance and uterine artery hemodynamic parameters are involved in the pathogenesis of RSA [23].

Notably, this study further explored the intrinsic correlation between insulin resistance indexes and uterine artery parameters, demonstrating that TyG index and HOMA-IR were significantly positively correlated with uterine artery PI, RI, and S/D, a finding that supple-

ments the existing research on the interaction between metabolic disorders and uterine hemodynamics [24]. The potential mechanisms underlying this correlation may include the following: First, hyperglycemia can impair vascular endothelial function, indirectly promote the synthesis and release of endothelin-1 (ET-1) by activating the mitogen-activated protein kinase (MAPK) pathway, inhibit the activity of endothelial nitric oxide synthase (eNOS), and reduce nitric oxide (NO) production, resulting in impaired vasodilation and increased vascular resistance. Second, insulin resistance can cause lipid metabolism disorders (e.g., elevated triglycerides), promote the formation of oxidized low-density lipoprotein (ox-LDL), and further aggravate endothelial dysfunction and microcirculation disorders, ultimately compromising placental perfusion. Third, insulin resistance can also lead to endothelium-dependent vasodilation dysfunction, exacerbating uterine artery blood flow disorders. These mechanisms are consistent with the conclusions of previous scholars [25, 26], further supporting the rationality of our findings.

This study still has several limitations. First, as a retrospective study, it is subject to potential selection bias and information bias, and the relatively small sample size may limit the generalizability of the findings. In addition, the absence of external verification may affect the robustness of the predictive model, and further validation is warranted. Second, the insulin resistance indices and uterine artery hemodynamic parameters were measured at single time point, which may not fully reflect dynamic changes during pregnancy. Finally, this study did not measure biomarkers related to uterine or placental function, which should be incorporated in future investigations.

Conclusion

RSA is associated with insulin resistance, uterine artery hemodynamic alterations, and maternal baseline characteristics. The combined prediction model incorporating insulin resistance-related indices, uterine hemodynamic parameters, age, and adverse pregnancy history demonstrated good predictive performance. These findings may provide a theoretical basis for early identification of high-risk patients and facilitate the implementation of targeted interventions.

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Disclosure of conflict of interest

None.

Address correspondence to: Shan Zheng, Department of Obstetrics and Gynecology, The First Affiliated Hospital of Fujian Medical University, No. 20 Chazhong Road, Taijiang District, Fuzhou 350005, Fujian, China. Tel: +86-13509356501; E-mail: zhen-shan_01@sina.com

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