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Original Research

Machine Learning-Based Early Prediction of Selective Fetal Growth Restriction in Monochorionic Diamniotic Twins Using Crown–Rump Length Discordance and Abnormal Placental Cord Insertion

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Abstract

Background: To evaluate the prognostic value of crown–rump length (CRL) discordance and placental abnormal cord insertion (ACI) for predicting selective fetal growth restriction (sFGR) in monochorionic diamniotic (MCDA) twin pregnancies, and to assess their predictive performance using machine learning (ML) models. **Methods:** A total of 144 MCDA twin pregnancies (January 2015–December 2024) were retrospectively analyzed; 44 (30.56%) developed sFGR. According to the first-trimester ultrasound, 21 cases showed CRL discordance ≥0.60 mm, and 31 cases exhibited placental ACI. 8 supervised ML algorithms were developed and evaluated using a training set (70.14%, n = 101) and an independent validation set (29.86%, n = 43). **Results:** Placental ACI was significantly associated with sFGR ($p < 0.01$), whereas CRL discordance showed a nonsignificant positive trend. In the validation set, CRL discordance demonstrated modest discriminatory ability (area under the curve [AUC] = 0.687, 95% confidence interval [CI]: 0.4849–0.8881), whereas placental ACI showed limited discrimination based on AUC performance. For the categorical predictor (placental ACI), performance was primarily characterized using sensitivity and specificity derived from the validation set. **Conclusions:** CRL discordance and placental ACI provide complementary first-trimester information for early sFGR risk assessment in MCDA twins; however, overall discrimination was moderate, and external validation is warranted.

Keywords: monochorionic diamniotic twins; selective fetal growth restriction; crown–rump length discordance; abnormal cord insertion; machine learning

1. Introduction

The incidence of twin pregnancy has increased in recent years due to the expanded use of assisted reproductive technology and delayed childbearing [1]. Monochorionic diamniotic (MCDA) twins, which share a single placenta but develop in separate amniotic sacs, are particularly prone to complications such as twin-to-twin transfusion syndrome (TTTS) and selective fetal growth restriction (sFGR) [2,3]. sFGR occurs in approximately 12–25% of MCDA pregnancies and remains a major challenge in prenatal counseling and management [2]. Early prediction of sFGR is critical for improving outcomes. Previous studies have proposed several first-trimester ultrasound markers, including nuchal translucency thickness difference, ductus venosus Doppler indices, placental share inequality, and umbilical cord insertion abnormalities [4,5,6]. Among these, placental abnormal cord insertion (ACI) and crown–rump length (CRL) discordance have shown promising potential. Nevertheless, the predictive performance of these markers remains controversial, mainly due to limited sample sizes and measurement variability [7]. In recent years, machine learning (ML) has emerged as a powerful data-driven approach capable of capturing nonlinear relationships and improving predictive accuracy in obstetric research [8,9,10,11,12].

However, evidence regarding first-trimester CRL discordance and placental ACI for predicting sFGR in MCDA twins remains inconsistent. Reported effects vary due to heterogeneity in timing of assessment, cutoffs, definitions, and outcome criteria, as well as operator-dependent measurement variability, and many studies are limited by small cohorts and lack of independent validation. Therefore, we intentionally focused on two routinely available first-trimester ultrasound markers—CRL discordance and placental ACI—to evaluate their standalone and reproducible predictive value and to provide a practical baseline for future models integrating additional clinical and Doppler variables.

As such, this study combines conventional statistical analysis with ML modeling to evaluate the prognostic significance of CRL discordance and placental ACI for sFGR in MCDA twin pregnancies, using an updated cohort including cases up to December 2024.

2. Materials and Methods

The case selection and grouping flowchart is shown in Fig. 1.

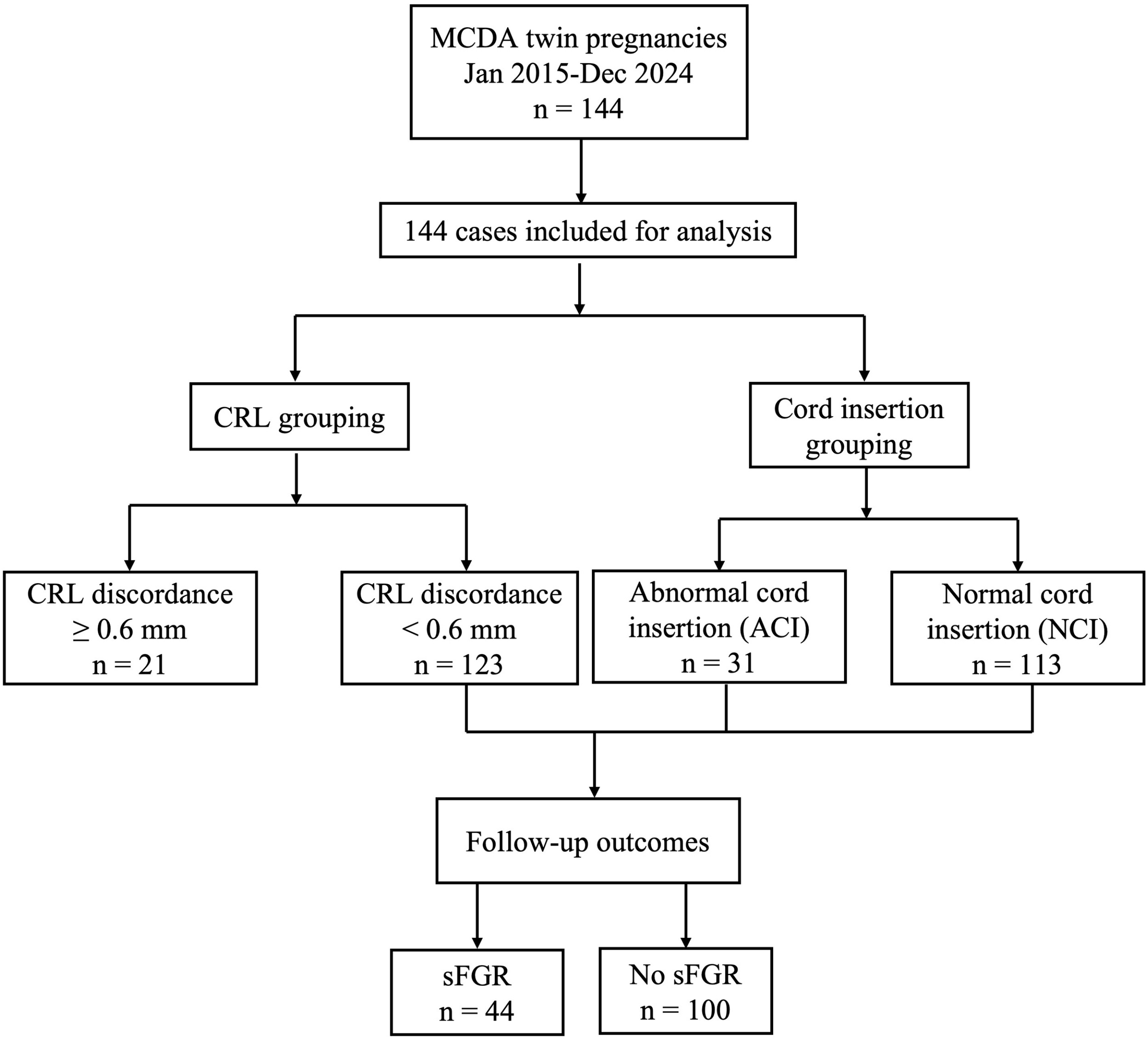

Fig. 1. Flowchart of case selection and grouping in the study cohort. MCDA, monochorionic diamniotic; CRL, crown–rump length; ACI, abnormal cord insertion; NCI, normal cord insertion; sFGR, selective fetal growth restriction.

2.1 Study Population

A total of 144 pregnant women with MCDA twin pregnancies at Jiaxing Maternity and Child Health Care Hospital, Affiliated Women and Children Hospital between January 2015 and December 2024 were retrospectively included. Among them, 44 cases (30.56%) developed sFGR during pregnancy. Based on early ultrasonography, 21 pregnancies showed CRL discordance ≥0.60 mm, and 31 pregnancies exhibited placental ACI. The diagnosis of sFGR typically relies on estimated fetal weight (EFW) and other sonographic parameters. According to the updated Delphi consensus criteria, sFGR is defined by either an EFW below the 3rd percentile in 1 twin or the presence of at least 2 of the following criteria: an EFW below the 10th percentile in 1 twin, an abdominal circumference below the 10th percentile, an intertwin EFW discordance ≥25%, or an umbilical artery pulsatility index in the smaller twin above the 95th percentile.

The inclusion criteria were as follows: (1) pregnant women diagnosed with MCDA twin pregnancy by first-trimester ultrasound examination at our hospital (conception through natural conception, artificial insemination, *in vitro* fertilization-embryo transfer, or other assisted reproductive technologies was acceptable); (2) gestational age determined by the last menstrual period or by CRL of the larger twin at the nuchal translucency scan; (3) completion of standard first-trimester ultrasound screening with clearly documented CRL measurements and umbilical cord insertion sites; and (4) availability of complete clinical mid- and late-trimester follow-up data, including pregnancy outcome records. Exclusion Criteria (cases meeting any of the fol-

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lowing conditions were excluded): (1) any fetus with major structural malformations (e.g., severe congenital heart disease or central nervous system malformations); (2) any fetus diagnosed prenatally or postnatally with aneuploidy or genetic disorders; (3) TTTS occurring prior to the diagnosis of sFGR; and (4) missing or incomplete clinical records or ultrasound imaging data insufficient for data extraction in this study.

Handling of missing data: Pregnancies lacking key first-trimester ultrasound data (CRL measurements or cord insertion assessment) and/or complete outcome follow-up were excluded. The final analytic cohort therefore comprised complete cases, and no data imputation was performed.

2.2 Ultrasonographic Measurements

Ultrasound examinations were performed using a GE E8 color Doppler system (3.5 MHz probe, General Electric Company, Boston, MA, USA) [13,14,15]. CRL was measured for each fetus in the midsagittal plane with the fetus in a neutral position during the nuchal translucency scan [16]. Three consecutive measurements were obtained and averaged. The umbilical cord insertion site of each fetus was assessed and classified as normal, marginal, or velamentous. Cases with marginal or velamentous insertion in one or both fetuses were categorized as placental ACI. A CRL discordance ≥0.60 mm was adopted based on previous reports suggesting that small first-trimester differences may reflect early developmental asynchrony in monochorionic twins [7,17].

2.3 ML Model Construction

Eight supervised ML algorithms were evaluated (logistic regression [LR] [18], decision tree [DT], random forest [RF] [19], k-nearest neighbors [KNN], support vector machine [SVM] [20], neural network [NN] [21], XGBoost [22], and LightGBM [23]) as a robustness-checking framework to assess whether conclusions based on routine first-trimester indicators were consistent across different modeling paradigms. Models were trained on 70.14% of the dataset (training set) and validated on the remaining 29.86% (validation set). The validation cohort comprised 43 pregnancies (30% of the total sample). Input variables included CRL discordance and cord insertion type.

2.4 Evaluation Metrics

Model performance was evaluated on a held-out validation set. For the categorical predictor (placental ACI), sensitivity, specificity, positive predictive value, and negative predictive value derived from the confusion matrix were considered the primary performance measures, whereas receiver operating characteristic (ROC) curves and area under the curve (AUC) were reported only as supplementary, standardized visualizations [24]. Accuracy, sensitivity, and specificity were computed from the confusion matrix. Primary performance was evaluated on the held-out validation set. To quantify uncertainty, 95% confidence intervals (CIs) for AUC and classification metrics were estimated using nonparametric bootstrapping (1000 resamples) of the validation dataset, with the 2.5th and 97.5th percentiles used as CI bounds. Confusion matrices were generated to derive accuracy, sensitivity, and specificity:

Accuracy = (TP + TN)/(TP + TN + FP + FN)

Sensitivity = TP/(TP + FN)

Specificity = TN/(TN + FP)

Decision curve analysis (DCA) was applied to evaluate clinical net benefit across a range of threshold probabilities [25,26].

2.5 Statistical Analysis

Statistical analyses were performed using SPSS version 29.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro-Wilk test and visual inspection of histograms and Q-Q plots. Normally distributed variables are presented as mean ± standard deviation (SD) and were compared using the independent-samples *t*-test (two groups); Welch's correction was applied when homogeneity of variance was violated (Levene's test). Non-normally distributed variables are presented as median (interquartile range [IQR]) and were compared using the Mann-Whitney U test. Categorical variables are presented as n (%) and were compared using the chi-square test when expected cell counts were adequate or Fisher's exact test when expected counts were small, as appropriate. All tests were two-sided, and $p <$ 0.05 was considered statistically significant. Given the exploratory nature of baseline comparisons in Table 1, no formal adjustment for multiple comparisons was applied.

3. Results

3.1 Clinical Characteristics

Table 1 summarizes baseline maternal and perinatal characteristics and pregnancy outcomes in 144 MCDA twin pregnancies, stratified by first-trimester CRL discordance and placental ACI. Maternal age was comparable across groups. Pregnancies with placental ACI had a significantly lower gestational age at delivery than those with normal cord insertion (NCI; 34.80 ± 2.00 vs. 35.90 ± 2.10 weeks, p = 0.01). Consistently, the birth weight of the smaller twin (F2) was significantly lower in the placental ACI group (1710 ± 420 g vs. 2130 ± 460 g, $p < 0.001$), whereas the birth weight of the larger twin (F1) did not differ significantly. The incidence of sFGR was significantly higher in the placental ACI group (58.06%) than in the NCI group (23.01%, $p < 0.001$), supporting an association between ACI and subsequent growth imbalance in MCDA pregnancies. In contrast, the incidence of sFGR was higher in pregnancies with CRL discordance ≥0.6 mm than in those with smaller discordance (38.10% vs. 29.27%, p = 0.42), although this difference was not statistically significant. To-

Table 1. Baseline characteristics and pregnancy outcomes according to CRL and placental ACI groups.

Variable	Total (n = 144)	CRL ≥0.60 mm (n = 21)	CRL <0.60 mm (n = 123)	Placental ACI (n = 31)	NCI (n = 113)	p-value (CRL)	p-value (Placental ACI)
Maternal age (years)	29.40 ± 5.10	30.20 ± 4.90	29.20 ± 5.00	29.90 ± 5.30	29.30 ± 5.00	0.40	0.57
Gestational age at delivery (weeks)	35.60 ± 2.10	34.90 ± 2.00	35.80 ± 2.10	34.80 ± 2.00	35.90 ± 2.10	0.07	0.01*
F1 birth weight (g)	2370 ± 450	2300 ± 440	2380 ± 460	2290 ± 470	2400 ± 410	0.45	0.24
F2 birth weight (g)	2030 ± 480	1860 ± 460	2050 ± 470	1710 ± 420	2130 ± 460	0.09	<0.001**
sFGR incidence n/N (%)	44/144 (30.56)	8/21 (38.10)	36/123 (29.27)	18/31 (58.06)	26/113 (23.01)	0.42	<0.001**

Values are presented as mean ± SD or n (%), as appropriate. p-values were calculated separately for the CRL grouping (CRL discordance ≥0.60 mm vs. <0.60 mm) and the cord insertion grouping (placental ACI vs. NCI). Continuous variables were assessed for normality (Shapiro–Wilk) and compared using the independent-samples t-test (Welch's correction when variances were unequal) or Mann–Whitney U test, as appropriate. Categorical variables were compared using the χ^2 test or Fisher's exact test. All tests were two-sided. *$p < 0.05$; **$p < 0.01$.

gether, these findings provide the clinical basis for subsequent ML analyses based on placental ACI and CRL parameters.

3.2 ML Results

To avoid redundancy, only three representative models (DT, RF, and XGBoost) are presented in the main text for both placental ACI-based and CRL-based classifiers. Confusion matrices for the remaining five supervised algorithms (LR, KNN, SVM, NN, and LightGBM) are provided in the **Supplementary Material** (**Supplementary Figs. 1,2**), as their classification patterns were highly consistent and did not alter the overall interpretation of model performance.

3.2.1 Predictive Performance of Placental ACI-Based Models

Placental ACI is a binary categorical variable. Accordingly, model performance was evaluated primarily using classification metrics derived from the confusion matrix, including sensitivity and specificity, rather than ROC-based metrics. ROC curves were generated to provide standardized visualization across algorithms (Fig. 2). Given the categorical nature of the predictor, discrimination as assessed by AUC should be interpreted cautiously. In the validation set, the AUC was 0.587 (95% CI: 0.3992–0.7754). ROC curves across different algorithms largely overlapped, consistent with all models being trained on the same single binary feature.

In the validation cohort (n = 43), ACI-based models demonstrated consistent classification behavior across representative algorithms. Confusion matrix analysis showed high specificity (88.9%), indicating a strong ability to correctly identify pregnancies without subsequent sFGR, whereas sensitivity was limited (28.6%), reflecting the restricted capacity of a single categorical marker to identify all sFGR cases. Overall classification accuracy was 79.0% (Fig. 3). Due to the effective feature space being extremely low-dimensional, different supervised learning algorithms converged to nearly identical decision rules, resulting in highly similar performance metrics across models. Therefore, LightGBM yielded an AUC of 0.50, corresponding to chance-level discrimination, reflecting the absence of additional informative splits under a single binary predictor rather than a model-specific limitation.

DCA further indicated that the ACI-based logistic regression model provided a limited net clinical benefit mainly within a low threshold probability range, approximately below 0.35. Beyond this range, the net benefit approached zero, supporting the interpretation of ACI as an adjunctive risk stratification marker rather than a standalone screening tool (Fig. 4).

3.2.2 Predictive Performance of CRL-Based Models

CRL discordance was treated as a continuous predictor. In contrast to placental ACI (a categorical variable), discrimination for a continuous predictor can be appropriately summarized using ROC curves and the AUC. In the validation cohort (n = 43), CRL-based models showed modest discrimination for predicting sFGR, with an AUC of 0.687 (95% CI: 0.4849–0.8881) (Fig. 5). ROC curves derived from different algorithms were largely overlapping, indicating similar discriminative performance across models.

Confusion matrices for the representative models are shown in Fig. 6, summarizing threshold-dependent classification performance in the validation set, including accuracy, sensitivity, and specificity. These results are provided to facilitate clinical interpretability of classification behavior at a given decision threshold rather than to emphasize differences between algorithms. Concordance across algorithms is expected because CRL discordance was the only input feature. Under this low-dimensional setting, different supervised learning methods tend to produce similar probability rankings and decision rules, resulting in comparable ROC curves and confusion-matrix–derived metrics. Accordingly, the ML analyses in this study are best inter-

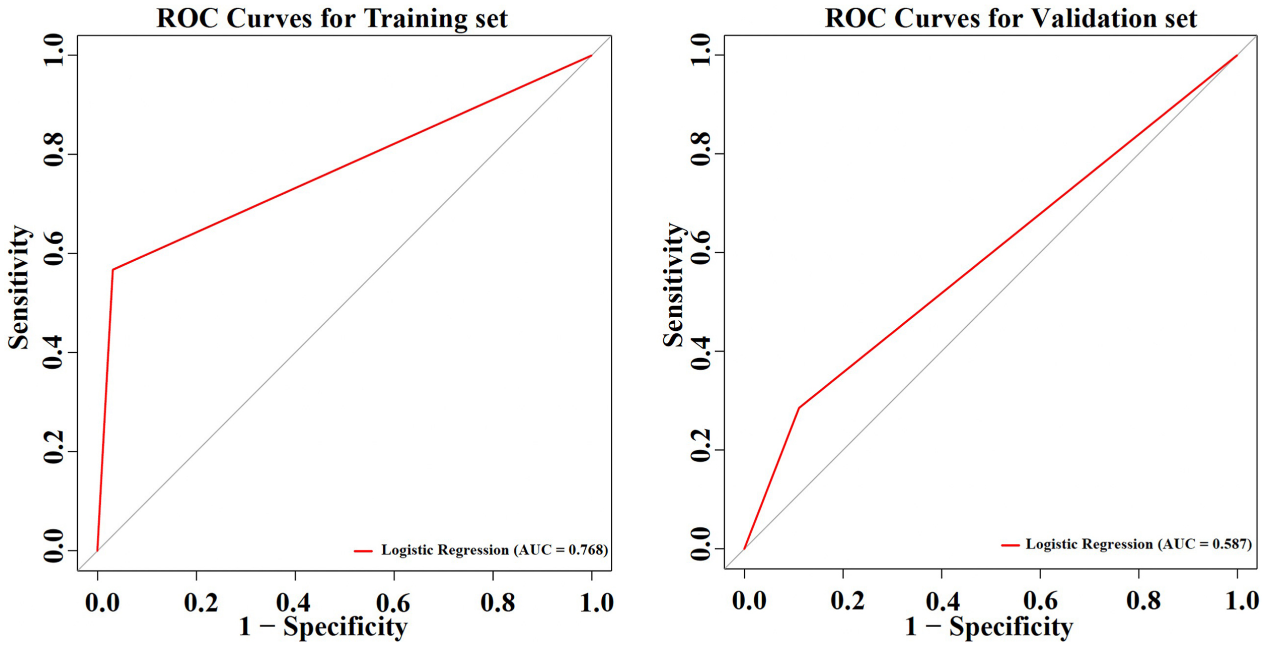

Fig. 2. ROC curves for predicting sFGR based on placental ACI in the training set (n = 101) and validation set (n = 43). Because ACI is a categorical predictor, interpretation should primarily focus on sensitivity and specificity derived from the confusion matrix. ROC curves are presented for completeness and standardized visualization only. Complete ROC curves for all algorithms are provided in the **Supplementary Material**. ROC, receiver operating characteristic.

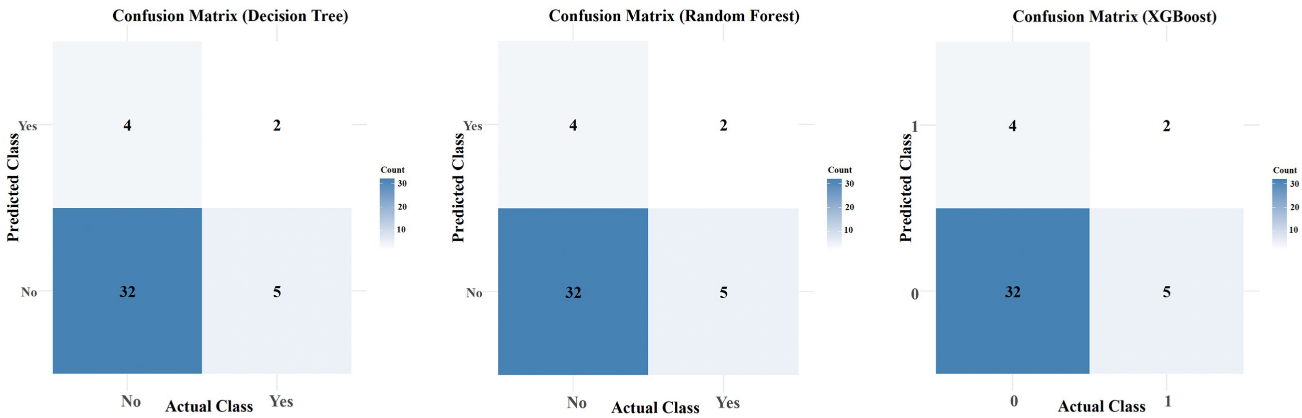

Fig. 3. Confusion matrices of representative placental ACI-based models (DT, RF, XGBoost). Confusion matrices were generated using the held-out validation set (n = 43). DT, decision tree; RF, random forest.

preted as a robustness check supporting the predictive utility of CRL discordance as a routine first-trimester indicator rather than evidence of superiority of any single algorithm.

DCA further evaluated potential clinical utility across a range of threshold probabilities (Fig. 7). CRL-based models showed modest net benefit over a limited range of threshold probabilities, supporting CRL discordance as an early risk indicator rather than a comprehensive standalone predictive tool.

4. Discussion

This study evaluated two first-trimester ultrasound parameters—CRL discordance and placental ACI—in relation to subsequent sFGR in MCDA twin pregnancies. Across both conventional analyses and multiple ML algorithms, placental ACI showed a clear association with subsequent sFGR, whereas CRL discordance was higher in sFGR pregnancies but did not reach statistical significance. Prior studies have similarly associated abnormal placental cord insertion (including marginal and velamentous types) with unequal placental sharing and adverse fetal growth outcomes in monochorionic twin pregnancies [4,6,7,17,27]. In contrast, the literature on first-trimester CRL discordance is inconsistent, with reported effects varying by assessment timing, cutoffs, and outcome criteria. Our findings align with studies suggesting limited standalone predictive value when CRL discordance is used in isolation [28].

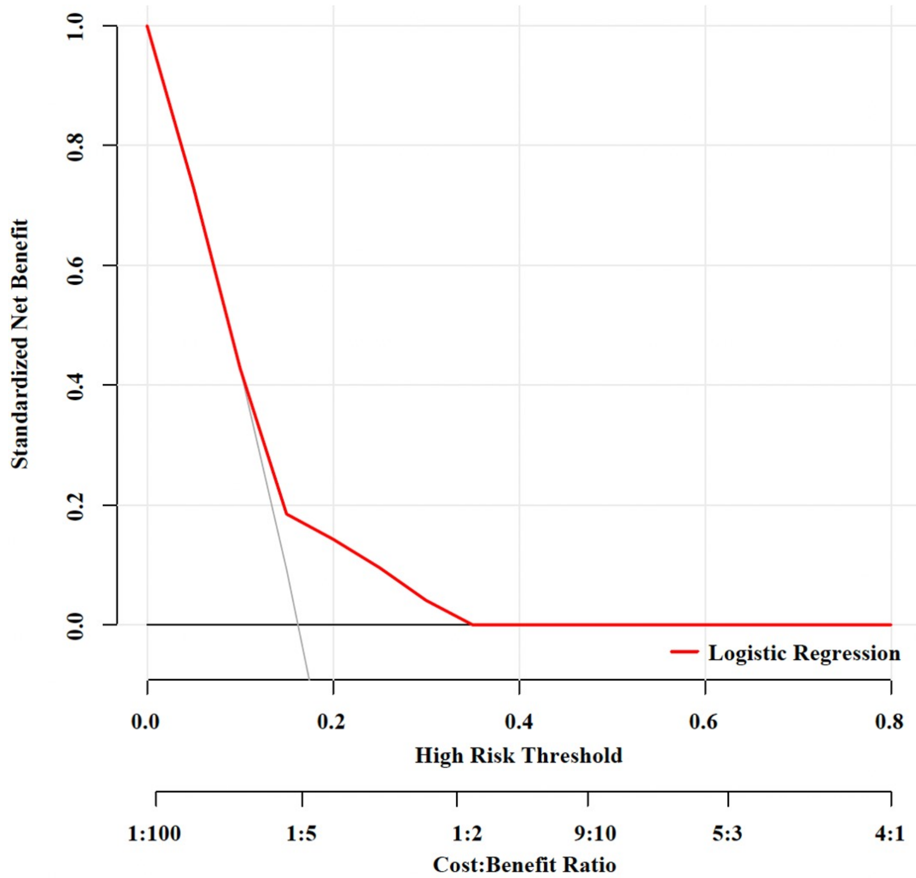

Fig. 4. DCA for predicting sFGR based on placental ACI in the validation set (n = 43). Net benefit was calculated using model-predicted probabilities across threshold probabilities, with "treat-all" and "treat-none" strategies shown as references. Due to the low-dimensional input, DCA curves from different algorithms largely overlapped; one representative curve is shown for clarity, with full results provided in the **Supplementary Material**. DCA, decision curve analysis.

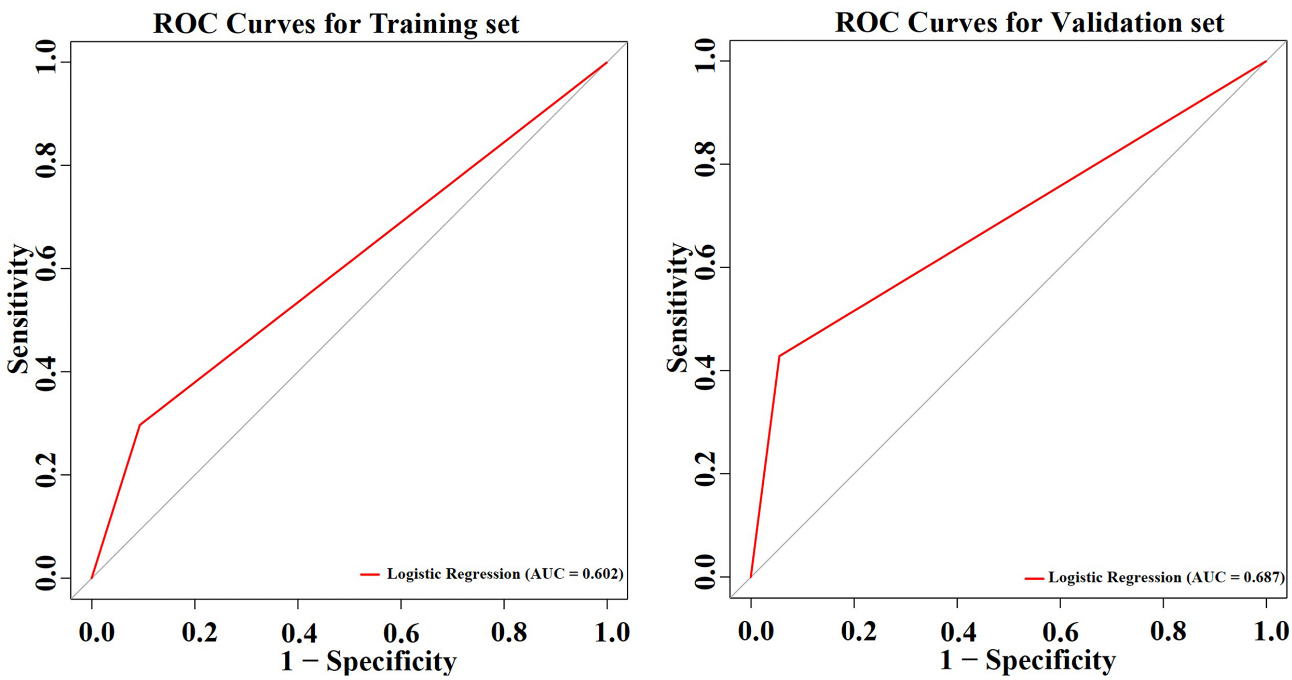

Fig. 5. ROC curves for predicting sFGR based on CRL discordance in the training set (n = 101) and validation set (n = 43). Complete ROC curves for all algorithms are provided in the **Supplementary Material**.

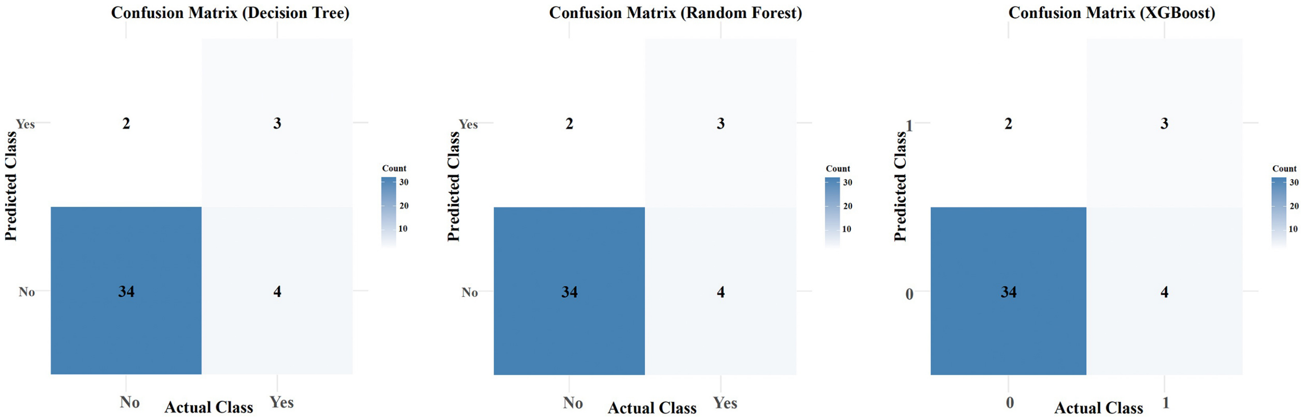

Fig. 6. Confusion matrices of representative CRL-based models (DT, RF, XGBoost). Confusion matrices are calculated using the held-out validation set (n = 43).

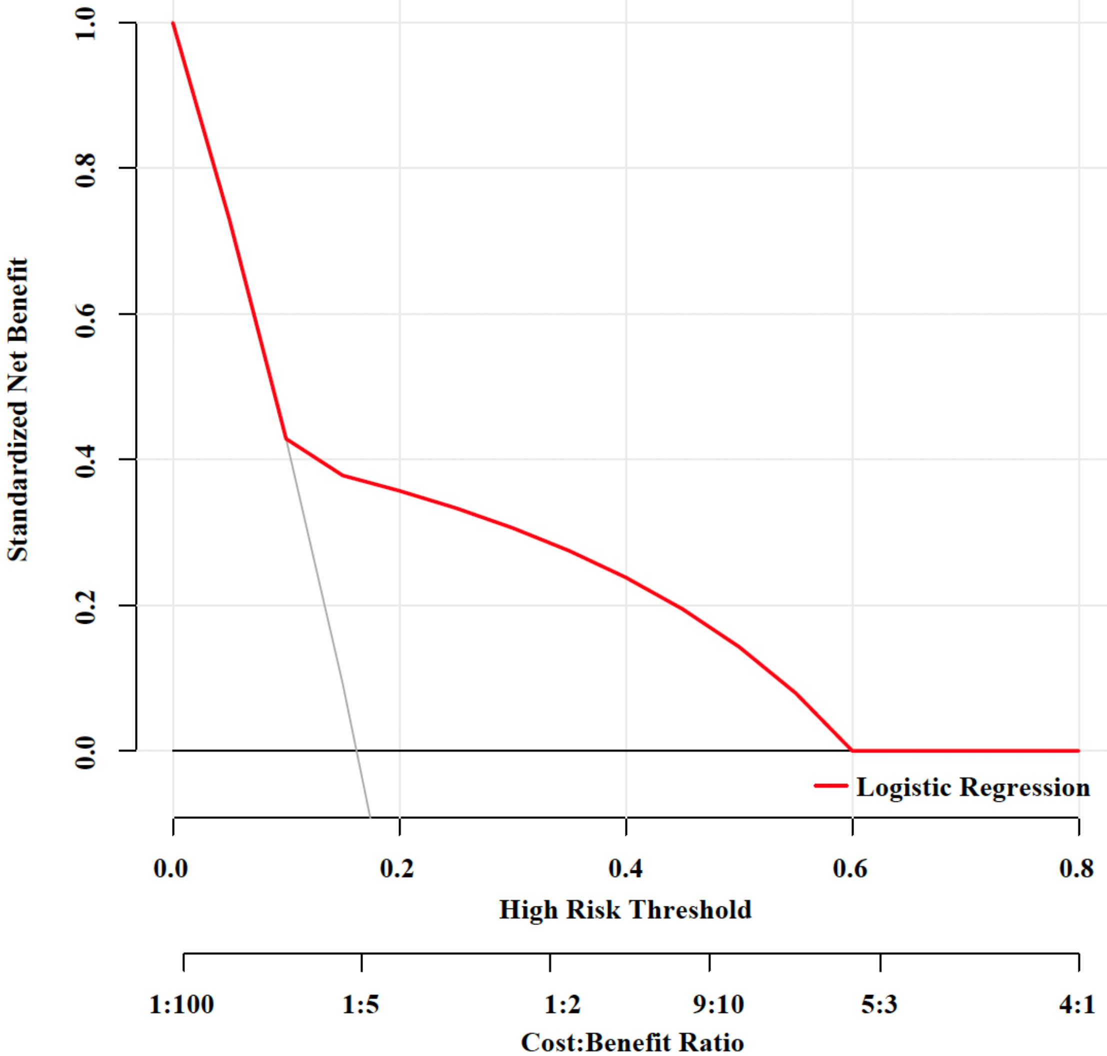

Fig. 7. DCA for predicting sFGR based on CRL on the validation set (n = 43). Net benefit was calculated using model-predicted probabilities across threshold probabilities, with "treat-all" and "treat-none" strategies shown as references. Due to the low-dimensional input, DCA curves from different algorithms largely overlapped; one representative curve is shown for clarity, with full results provided in the **Supplementary Material**.

The discriminatory performance of the ML models was modest (validation AUC <0.70). Given that only two predictors were included and both were encoded as binary variables, this level of performance is not unexpected and is comparable to other obstetric ML studies based on sparse feature sets [10,29,30,31]. Importantly, the models showed consistently high specificity, which may be of greater clinical relevance than a single summary metric. Rather than supporting a standalone screening tool, these results suggest a potential role for early ultrasound markers in identifying pregnancies at lower risk and in guiding the intensity of surveillance. The consistent direction of effects across different algorithms further suggests that the signal is not an artifact of a specific modeling approach but reflects clinically meaningful variation captured by routine first-trimester imaging. Accordingly, these models should be interpreted as exploratory benchmarks rather than screening tools, and small between-model differences should be viewed with caution.

From a biological perspective, placental ACI may reflect early placental territorial or vascular asymmetry, potentially predisposing to sustained imbalance in nutrient delivery and subsequent fetal growth restriction [32,33,34]. CRL discordance may capture early developmental asynchrony; however, small differences at this gestational age may also represent normal biological variation, which may explain the weaker association observed. Several methodological refinements could strengthen future models, including the incorporation of routinely available covariates (maternal characteristics, placental location, and Doppler indices), modeling CRL discordance as a continuous variable rather than dichotomizing it to avoid unnecessary loss of information, and validation in larger multicenter cohorts. External validation will be essential before any implementation in first-trimester counseling or risk-stratified follow-up pathways.

Limitations

Several limitations should be acknowledged. First, this was a single-center retrospective study with a relatively small sample size, particularly for sFGR cases, which may limit model stability and generalizability. Second, only two early sonographic features were included, which constrained model input space and resulted in modest discriminative performance of the ML models. Third, CRL and umbilical cord insertion assessments are operator-dependent, and inter-observer variability cannot be fully eliminated. Finally, external validation in independent cohorts was not performed. These limitations highlight the need for larger, multicenter studies integrating additional clinical and Doppler variables. In addition, ACI is a categorical predictor, and ROC curves for ACI were provided only as supplementary, standardized visualizations; interpretation should primarily rely on confusion matrix–derived measures. Finally, external validation in independent cohorts is warranted. Future multicenter studies incorporating additional clinical variables and Doppler features may support the development and validation of more comprehensive multivariable prediction models and further clarify clinical utility.

5. Conclusions

Early first-trimester sonographic features, including placental ACI and CRL discordance, provide complementary prognostic information for predicting sFGR in MCDA twin pregnancies. Although single-feature models show only moderate predictive performance, consistent patterns across multiple ML algorithms support the biological relevance of these markers. Integrating early ultrasound features into data-driven frameworks may enable individualized risk stratification and targeted surveillance in high-risk twin gestations.

Abbreviations

ACI, abnormal cord insertion; ROC, receiver operating characteristic; AUC, area under the curve; CRL, crown–rump length; DCA, decision curve analysis; DT, decision tree; KNN, k-nearest neighbors; LR, logistic regression; MCDA, monochorionic diamniotic; ML, machine learning; NCI, normal cord insertion; NN, neural network; RF, random forest; SD, standard deviation; sFGR, selective fetal growth restriction; SVM, support vector machine; TTTS, twin-to-twin transfusion syndrome; EFW, estimated fetal weight.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

YF and JL designed the study. YF and JL assisted with the data collection. JL and LA were responsible for data management. YF and JL drafted the manuscript. LA revised the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki. The research protocol was approved by the Ethics Committee of Jiaxing Maternity and Child Health Care Hospital (Ethic Approval Number: 2025YL-63), and all of the participants provided signed informed consent.

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Conflicts of Interest

The authors declare no conflicts of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT-3.5 in order to check spelling and grammar. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/CEOG48538.

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