International Journal of General Medicine Dovepress

Open Access Full Text Article ORIGINAL RESEARCH

Factors Predicting Fetal Growth Restriction and Fetal Cardiac Remodeling

XiaoLe Chen, Lili Xiao, Daozhu Wu, Saida Pan

Department of Ultrasonic Diagnosis, the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, People's Republic of China

Correspondence: Saida Pan, Department of Ultrasonic Diagnosis, the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, No. 109, Xue-Yuan West Road, Wenzhou, Zhejiang, People's Republic of China, Email psdbird511@163.com

Objective: This study aimed to investigate factors influencing fetal growth restriction (FGR) occurrence and assess the clinical significance of fetal cardiac parameters in FGR prediction.

Methods: Pregnant women with clinically suspected FGR (n=179) and uncomplicated pregnancies (n=53) were included. All had undergone routine obstetric ultrasonography and fetal echocardiography. Umbilical artery flow (UAF) and fetal cardiac parameters (left atrial transverse diameter (LAd), right atrial transverse diameter (RAd), left ventricular transverse diameter (LVd), right ventricular transverse diameter (RVd), foramen ovale width, atrial septum diameter, interventricular septal thickness, left ventricular posterior wall thickness, right ventricular free wall thickness, aortic diameter, pulmonary artery diameter, mitral E velocity, mitral A velocity, tricuspid E velocity, tricuspid A velocity, aortic valve peak flow velocity, and pulmonary valve peak flow velocity) were detected. Follow up was conducted until birth, various fetal clinical parameters were collected: maternal body mass index (BMI), hypertensive disorders complicating pregnancy (HDCP), abnormal umbilical artery flow, placental or umbilical cord anomalies, low amniotic fluid volume, preterm birth, emergency cesarean delivery, maternal height, maternal age, gestational diabetes mellitus (GDM), hypothyroidism, assisted reproductive technology (ART), parity, and neonatal gender. Participants were categorized into confirmed FGR (n=119) and control (n=113) groups based on neonatal birth weight.

Results: Significant differences were observed between groups in maternal BMI, HDCP, abnormal UAF, placental or umbilical cord anomalies, low amniotic fluid volume, preterm birth, and emergency cesarean delivery. FGR was positively related to abnormal UAF, placental or umbilical cord anomalies, preterm birth and emergency cesarean delivery and negatively to maternal BMI (r=−0.276). Compared to the control group, the FGR group exhibited significantly larger RAd, RVd, RA/LA, and RV/LV.

Conclusion: Fetal growth-restricted fetuses have enlarged right heart structures. Fetal cardiac examinations are valuable for early FGR diagnosis, potentially improving neonatal body weight and reducing adverse pregnancy outcomes.

Keywords: fetal growth restriction, fetal echocardiography, cardiac remodeling

Introduction

Fetal growth restriction (FGR) is a pathological condition wherein the fetus fails to achieve its intrauterine growth and developmental potential.[1] Affecting 5–10% of pregnancies, FGR ranks as the second most common cause of perinatal mortality,[2,3] with adverse outcomes spanning from fetal to adult life.

Numerous factors contribute to FGR, typically involving the mother, fetus, and placental umbilical cord. FGR is predominantly attributed to placental insufficiency.[4] A dysfunctional placenta prevents the fetus from getting enough oxygen and nutrients. Importantly, the heart, as the central organ in intrauterine adaption to placental insufficiency, has to adapt to the hostile intrauterine environment by changing its shape, structure and function in order to maintain the appropriate perfusion of vital organs. This is called cardiac remodeling.[5] In this process, heart first compensates by changing its shape from ellipsoid to spherical and then cardiac dysfunction follows.[6] FGR can induce fetal heart remodeling and dysfunction, serving as both an intermediary process precipitating various adverse outcomes.

Received: 13 August 2024
Accepted: 12 November 2024
Published: 20 November 2024

Epidemiological evidence suggests a strong relationship between FGR and cardiovascular disease in adulthood, supporting the existence of a maladaptive programming process in utero that affects the cardiovascular system in the long term.[7]

The prenatal diagnosis rate of FGR is still very low, despite the use of growth curves, cardiotocography, umbilical artery doppler, and middle cerebral artery doppler in the diagnosis of FGR. A large number of studies[6,8–18] have shown changes in the cardiac structure and function of the FGR fetuses. It is of great significance to assess the fetal cardiac morphology and functional changes in early FGR diagnosis. Cardiac remodeling can be assessed via morphometric and functional parameters. Lobmaier et al[11] found that left myocardial performance index in FGR fetuses was significantly increased while MAPSE, TAPSE and left cardiac output were significantly lower compared to controls after adjustment for gestational age. Recent researches[12–15] had put the spotlight on speckle tracking echocardiography and found a decreasing global longitudinal strain (GLS) in FGR fetuses. However, functional parameters are particularly susceptible to influences from heart rate and fetal movement, leading to inconsistent findings and poor reproducibility in previous studies. In addition, fetal cardiac dysfunction appears after cardiac morphological changes. Tao[16] observed that reduced stroke volume (SV) occurred at the initial stage of fetal deterioration before the discovery of abnormal EF in FGR fetuses. In recent years, numerous of studies[6,17,18] showed that FGR fetuses develop early stages of cardiovascular remodeling as shown by global sphericity index (GSI) changes. Therefore, we focused on cardiac morphological changes. Morphometric changes entail alterations in chamber cavity size and wall thickness. Measurement of chamber cavity size and thickness in the four-chamber view is simple, easy, and exhibits high repeatability with minimal inter-examiner variation. This study screened for significant changes in many fetal cardiac parameters to explore the value of these indicators for future clinical application.

This study investigates maternal-fetal and placental pathological factors related to FGR and discusses the clinical value of fetal cardiac parameters in predicting FGR, laying a theoretical groundwork for early screening, diagnosis, intrauterine monitoring, and treatment of fetal growth restriction.

Materials and Methods

Subjects

The pregnant women who visited our hospital between June 2018 and August 2023 and were diagnosed with FGR in the medical records were recruited in this study. Finally, 179 pregnant women with clinically suspected FGR (estimated fetal weight or fetal abdominal circumference below the 10th percentile for gestational age) were included.[1] In addition, 53 women with uncomplicated pregnancies were chosen randomly during the same period. Inclusion criteria were as follows: 1. Definite time of conception; 2. Singleton pregnancies; 3. Absence of fetal structural malformations on prenatal ultrasound screening. Exclusion criteria were: 1. Pregnant women with heart, liver, kidney, or other significant organ dysfunction; 2. Pregnant women with malignant tumors; 3. Pregnant women with substance abuse; 4. Fetal chromosomal abnormalities detected on prenatal examination. All pregnant women had undergone routine obstetric ultrasound and fetal echocardiography examinations conducted by experienced sonographers. Fetal echocardiography examinations were performed between 21–38 weeks of gestation. Prior to enrollment, all participating women were informed about the sensitivity, accuracy, and limitations of fetal echocardiography, and signed informed consent was obtained from each woman. The study protocol was approved by the ethics committee of the Second Affiliated Hospital of Wenzhou Medical University (approval number 2022-K-307-01) and conformed to the ethical standards for medical research involving human subjects in the Declaration of Helsinki and later amendments.

Ultrasonographic Examination

Ultrasonographic examination was performed using a high-resolution real-time scanner (PHILIPS EPIQ 7C, Germany) equipped with a 3.5 MHz convex transducer (C6-2). The ultrasound examination assessed fetal presentation and biometric indices, including biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), femur length (FL), amniotic fluid volume, placental characteristics, and umbilical cord status. Doppler examination of the umbilical artery (UA) was conducted, followed by detailed fetal echocardiography examination. In the fetal four-chamber view, measurements were taken for left atrial transverse diameter (LAd), right atrial transverse diameter (RAd),

left ventricular transverse diameter (LVd), right ventricular transverse diameter (RVd), foramen ovale width, diameter of the atrial septum, interventricular septal thickness, left ventricular posterior wall thickness, right ventricular free wall thickness, mitral E velocity, mitral A velocity, tricuspid E velocity, and tricuspid A velocity. Subsequently, ratios of RA/LA, RV/LV, mitral E/A, and tricuspid E/A were calculated. At the left ventricular outflow tract section, measurements were taken for the aortic diameter and the aortic valve peak flow velocity. At the right ventricular outflow tract section, measurements were taken for the pulmonary artery diameter and the pulmonary valve peak flow velocity.

Neonatal Assessment

All women were followed until delivery, and neonatal assessment was conducted. Confirmation of FGR was based on newborn body mass at birth. All infants were categorized based on whether their body mass fell below the 10th percentile according to Chinese newborn weight statistics for various gestational ages (2011–2014).[19] Out of 232 pregnant women, 119 cases were confirmed to have FGR, while 113 cases were classified as non-FGR.

Maternal and infant information, including maternal age, maternal height, maternal BMI, hypertensive disorders complicating pregnancy (HDCP), gestational diabetes mellitus (GDM), parity, mode of delivery, assisted reproductive technology (ART), and neonatal gender, were retrieved from electronic medical records. Flowchart of this study see Figure 1.

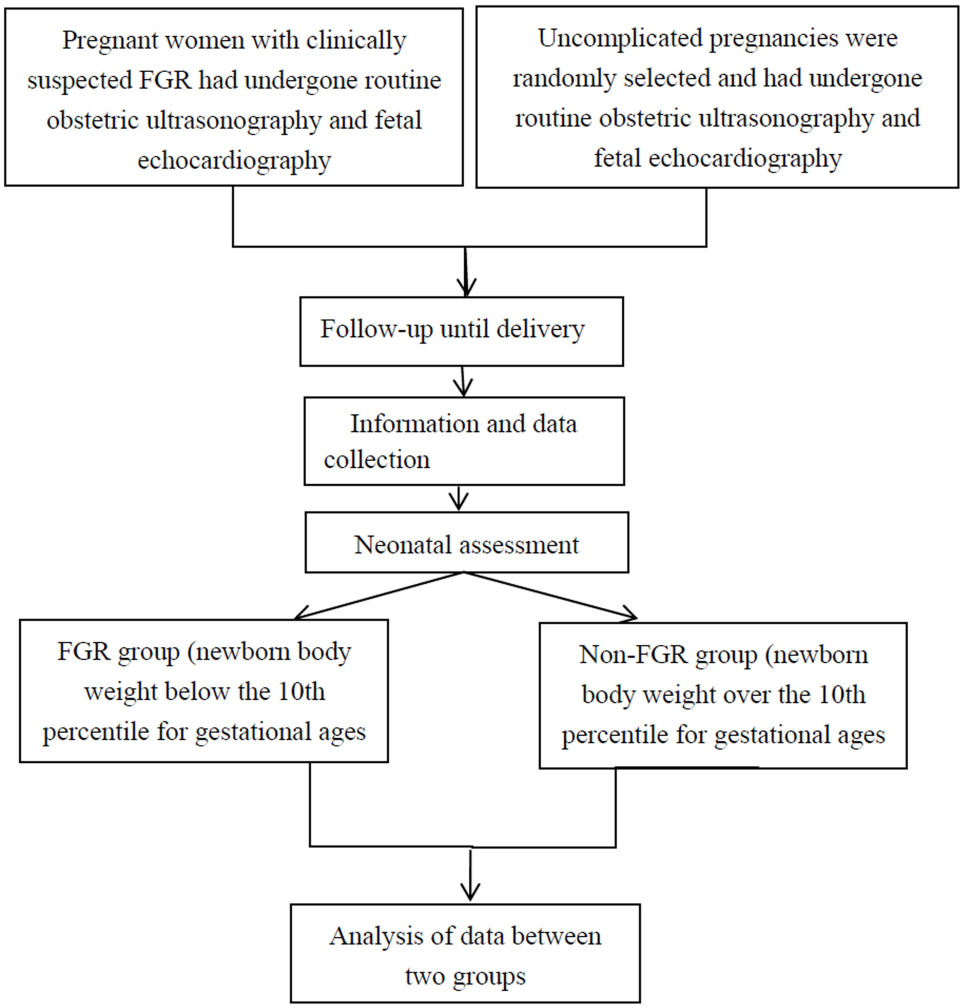

Figure 1 Flowchart of this study. FGR: Fetal growth restriction.

Statistical Analysis

Data were recorded and analyzed using SPSS version 29.0 (IBM, Chicago, IL, USA). Before statistical testing, a Shapiro–Wilk test was conducted to assess variables for normality. Quantitative variables were presented as mean ± SD, while qualitative variables were expressed as numbers with percentages. Student's *T* test was used for comparing quantitative variables, and the Chi-squared test was employed for qualitative variables. Univariate linear regression analysis was conducted using Pearson correlation coefficient. Pearson's correlation coefficient $|r|\geq 0.20$ was considered indicative of correlation. A P-value < 0.05 was deemed statistically significant. Receiver operating characteristic curves (ROC curves) for RA, LA, RV, LV, RA/LA, and RV/LV were constructed to evaluate their predictive ability for FGR.

Results

Basic Characteristics and Pregnancy Outcomes

In the FGR group, maternal age ranged from 18 to 44 years, with an average of 28.95±4.525 years, and birth weight ranged from 930 g to 2980 g, with an average of 2252.38±450.051 g. In the control group, maternal age ranged from 20 to 44 years, with an average of 30.15±4.98 years, and birth weight ranged from 1760 g to 4400 g, with an average of 3069.65±451.503 g. Among the FGR group, 39 cases were classified as severe FGR (defined as birth weight below the 3rd percentile), with birth weight ranging from 1400g to 2500g, and an average of 2102.05±336.65 g.

Maternal BMI was lower in the FGR group compared to the control group, with significant difference (25.09±3.184 vs 27.04±3.653 kg/m^2, P<0.05). However, there were no significant differences in maternal age and height between the two groups (P>0.05) (Table 1).

Analysis of Other Factors Affecting Fetal FGR

Statistically significant differences were observed in the following factors between groups: HDCP, abnormal umbilical artery flow, placental or umbilical cord anomalies, low amniotic fluid volume, preterm birth, and emergency cesarean delivery (P<0.05). However, no statistically significant differences were found between groups in the following factors: GDM, hypothyroidism, ART, parity, and neonatal gender (P>0.05) (Table 2)

The correlation of FGR with abnormal umbilical artery flow, preterm birth, emergency cesarean delivery, placental or umbilical cord anomalies and maternal BMI, were 0.290, 0.236,0.219, 0.241 and −0.276, respectively (Table 3).

Analysis of Fetal Cardiac Parameters

There was no statistical difference in the gestational age at inspection between two groups. However, compared with the control group, the FGR group exhibited significantly higher values of right atrial transverse diameter (RAd), right ventricular transverse diameter (RVd), RA/LA ratio, RV/LV ratio, and aortic valve peak flow velocity; these differences were statistically significant. There were no statistical differences observed in foramen ovale width, diameter of the atrial septum, interventricular septal thickness, left ventricular posterior wall thickness, right ventricular free wall thickness, aortic diameter, pulmonary artery diameter, mitral E/A ratio, tricuspid E/A ratio, left atrial transverse diameter (LAd) and left ventricular transverse diameter (LVd) between the two groups (Table 4). The area under the ROC curve for RA/LA ratio and RV/LV ratio were 0.77 and 0.75, respectively (Figure 2).

Table 1 Basic Characteristics and Pregnancy Outcomes

Characteristics	FGR Group (n=119)	Control Group (n=113)	t-value	P-value
Neonate body weight (g)	2252.38±450.051	3069.65±451.503	−13.803	<0.001[a]
Maternal age (years)	28.95±4.525	30.15±4.98	−1.919	0.056
Maternal height (cm)	157.92±5.006	158.58±4.450	−1.058	0.291
Maternal BMI (kg/m^2)	25.09±3.184	27.04±3.653	−4.095	<0.001[a]

Abbreviations: FGR, Fetal growth restriction; BMI, Body mass index; a, statistically significant.

Table 2 Univariate Analysis of Factors Affecting FGR [n (%)]

Factors	Number (n=232)	FGR group (n=119)	Control group (n=113)	χ^2 value	P-value
Umbilical artery flow				19.478	<0.001[a]
Abnormal	32	28 (23.52)	4 (3.54)		
Normal	200	91 (76.47)	109 (96.46)		
GDM				0.467	0.494
Present	63	30 (25.21)	33 (29.20)		
Absent	169	89 (74.79)	80 (70.80)		
HDCP				4.528	0.033[a]
Present	32	22 (18.49)	10 (8.85)		
Absent	200	97 (81.51)	103 (91.15)		
Parity				2.196	0.138
Primipara	132	73 (61.34)	59 (52.21)		
Multipara	99	45 (37.82)	54 (47.79)		
ART				0.391	0.532
Yes	16	7(5.88)	9 (7.96)		
No	216	112 (94.12)	104 (92.04)		
Placental or umbilical cord anomalies				13.396	<0.001[a]
Present	45	34 (28.57)	11 (9.73)		
Absent	186	84 (70.59)	102 (9.03)		
Neonate gender				2.034	0.154
Male	103	58 (48.74)	45 (39.82)		
Female	128	60 (50.42)	68 (60.17)		
Hypothyroidism				0.147	0.701
Present	22	12 (10.08)	10 (8.85)		
Absent	207	104 (87.39)	103 (91.15)		
Emergency cesarean delivery				10.870	<0.001[a]
Yes	53	37 (31.09)	16 (14.16)		
No	173	76 (63.87)	97 (85.84)		
Low amniotic fluid volume				7.862	0.005[a]
Yes	51	35 (29.41)	16 (14.16)		
No	181	84 (70.59)	97 (85.84)		
Preterm birth				12.926	<0.001[a]
Yes	37	29 (24.36)	8 (7.08)		
No	195	90 (75.63)	105 (92.92)		

Abbreviations: FGR, Fetal growth restriction; GDM, Gestational diabetes mellitus; HDCP, Hypertensive disorders complicating pregnancy; ART, Assisted reproductive technology; a, statistically significant.

Discussion

Fetal growth restriction (FGR), previously known as intrauterine growth restriction (IUGR), stands as one of the most common complications in the perinatal period, with an incidence ranging from 6% to 13%. However, early and accurate diagnosis of FGR remains challenging. Nawathe et al[20] suggested several reasons contributing to this challenge: 1) uncertain diagnostic criteria; 2) lack of a single reliable diagnostic test; and 3) variability in gestational age determination influenced by diverse factors. Consequently, FGR persists as a significant challenge in maternal-fetal and neonatal medicine.

Conventional two-dimensional ultrasound (2DUS) is commonly utilized for estimating fetal weight by measuring biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL).[21] Fetal biometry measurement serves as the cornerstone for investigating and diagnosing FGR. However, despite efforts to enhance accuracy, commonly used formulas for fetal weight estimation, which incorporate multiple biometric parameters, still lack precision. Consequently, early diagnosis of FGR remains challenging for clinicians and sonographers/

Table 3 Correlation of Factors with FGR

Factors	*r*	*p*
Maternal BMI	−0.276	<0.001[a]
HDCP	0.140	0.033[a]
Abnormal umbilical artery flow	0.290	<0.001[a]
Preterm birth	0.236	<0.001[a]
Emergency cesarean delivery	0.219	<0.001[a]
Placental or umbilical cord anomalies	0.241	<0.001[a]
Low amniotic fluid volume	0.184	0.005[a]
GDM	−0.045	0.496
Hypothyroidism	0.025	0.703
ART	−0.041	0.534
Parity	−0.097	0.140
Neonate gender	−0.094	0.155
Maternal height	−0.070	0.291
Maternal age	−0.126	0.056

Abbreviations: FGR, Fetal growth restriction; BMI, Body mass index; HDCP, Hypertensive disorders complicating pregnancy; GDM, Gestational diabetes mellitus; ART, Assisted reproductive technology; a, statistically significant.

Table 4 Comparison of Various Parameters of Fetal Heart [$\overline{x} \pm s$]

Parameters	FGR Group (n=119)	Control Group (n=113)	t-value	P-value	AUC	95% CI
Gestational age at inspection(W)	30.10±4.46	29.04±4.29	1.858	0.064	/	/
LAd (mm)	10.42±1.90	10.93±2.18	−1.870	0.063	0.56	0.49–0.64
RAd (mm)	12.42±2.30	11.53±2.34	2.920	0.004[a]	0.62	0.54–0.69
RA/LA ratio	1.20±0.18	1.06±0.11	7.311	<0.001[a]	0.77	0.71–0.83
LVd (mm)	10.57±1.89	10.60±2.09	−0.092	0.926	0.50	0.43–0.58
RVd(mm)	12.01±2.29	10.77±2.16	4.272	<0.001[a]	0.65	0.58–0.72
RV/LV ratio	1.15±0.16	1.02±0.09	7.134	<0.001[a]	0.75	0.69–0.81
Foramen ovale width (mm)	4.47±1.23	4.52±0.99	−0.288	0.774	/	/
Diameter of atrial septum (mm)	13.40±2.73	14.06±1571	−0.422	0.673	/	/
Interventricular septal thickness (mm)	2.38±0.44	2.44±0.40	−1.058	0.291	/	/
Left ventricular posterior wall thickness (mm)	2.39±0.49	2.45±0.41	−0.877	0.381	/	/
Right ventricular free wall thickness (mm)	2.401±0.55	2.46±0.40	−0.756	0.451	/	/
Aortic diameter(mm)	4.82±1.00	4.98±2.86	−0.594	0.553	/	/
Pulmonary artery diameter (mm)	6.19±1.25	5.95±1.04	1.583	0.057	/	/
Mitral E/A ratio	0.73±0.15	0.69±0.14	1.801	0.073	/	/
Tricuspid E/A ratio	0.73±0.18	0.70±0.14	1.141	0.255	/	/
Aortic valve peak flow velocity (m/s)	0.76±0.18	0.69±0.17	2.650	0.009[a]	/	/
Pulmonary valve peak flow velocity (m/s)	0.62±0.13	0.59±0.12	1.814	0.071	/	/

Abbreviations: LAd left atrial transverse diameter; RAd, right atrial transverse diameter; LVd, left ventricular transverse diameter; RVd, right ventricular transverse diameter.

sonologists. Moreover, the pathological mechanism of FGR is complex, and effective treatment is lacking. The prognosis of FGR hinges on its underlying etiology. Therefore, diagnosing FGR necessitates not only fetal weight estimation but also exploration of pathological factors contributing to FGR. This comprehensive approach can guide clinicians in implementing appropriate intervention measures against these adverse factors, ultimately reducing perinatal adverse outcomes.

Increased ventricular widths in FGR were initially observed using M-mode ultrasound by DeVore in 1988.[22] In FGR, it is believed that the RV is affected earlier and to a greater extent than the LV. This RV strain is characterized by earlier

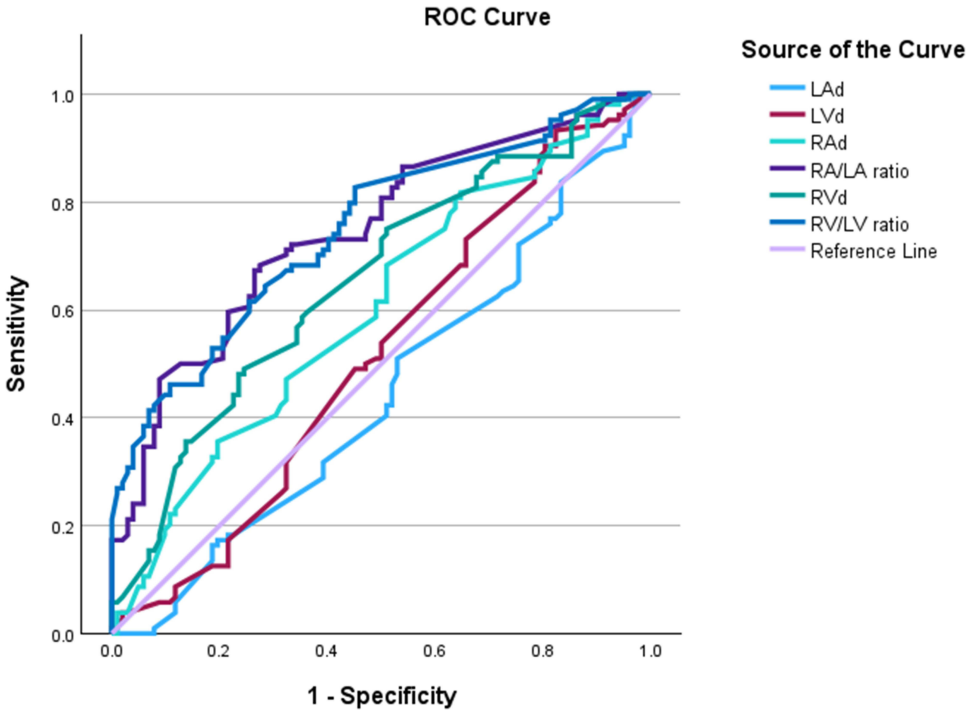

Figure 2 ROC curve analysis of fetal cardiac parameters to predict FGR.
Abbreviations: LAd, left atrial transverse diameter; RAd, right atrial transverse diameter; LVd, left ventricular transverse diameter; RVd, right ventricular transverse diameter.

dilation, hypertrophy, and dysfunction compared to changes in the LV.[23] These findings are attributed to the influence of fetal hypoxemia. In response to a low oxygen environment, the fetus adjusts cardiovascular output, redistributes blood flow to the brain and heart, and optimizes oxygen and nutrient supply to preserve normal function and growth in these vital organs. Fetal adaptation to hypoxemia results in increased right ventricular afterload due to pulmonary and systemic vasoconstriction, and decreased left ventricular afterload due to cerebrovascular vasodilation.[5,24,25] These changes in cardiac load correspond to alterations in cardiac morphology. Notably, the fetal heart exhibits greater adaptability compared to the postpartum period. Our study revealed larger RA and RV dimensions in the FGR group, with statistically significant differences noted. The RA/LA ratio and RV/LV ratio were increased in fetuses with FGR, and ROC curves demonstrated high diagnostic efficacy, with area under the curve values of 0.77 and 0.75, respectively. Assessment of fetal well-being and determination of the timing of delivery constitute the main management strategies for FGR, as effective clinical treatment options are currently limited. Therefore, we propose that an RA/LA ratio cutoff of 1.2 could be used, with a sensitivity of 48.7% and specificity of 87.6%, and similarly, an RV/LV ratio cutoff of 1.2 could be considered, with a sensitivity of 32.8% and specificity of 96.5%. These ratios exhibit high specificity and could aid in the diagnosis of FGR following ultrasound assessment of fetal biometric parameters. Additionally, our study observed increased fetal aortic valve peak flow velocity in the FGR group, which may also result from altered cardiac load.

The etiology of FGR is multifactorial and can be categorized into maternal, fetal, and uterine-placental vascular insufficiency causes. Overlapping etiological factors are not uncommon.[26,27] Maternal nutritional status during pre-pregnancy and gestational weight gain may directly affect fetal development. Both pre-pregnancy underweight and inadequate weight gain during pregnancy have been linked to an increased risk of FGR,[28] consistent with the findings of our study. We observed a higher incidence of FGR among pregnant women with low body weight.

While previous studies have generally identified maternal age >40 years as an independent risk factor for FGR,[29] our study did not find a significant association between maternal age and FGR incidence. This may be due to the small number of cases exceeding 40 years of age. Further research with larger sample sizes is warranted to thoroughly

investigate the relationship between maternal age and FGR. Additionally, no statistically significant differences were observed in maternal height, parity, and neonatal gender between the two groups.

HDCP have been confirmed to be associated with FGR occurrence, with the combined incidence of HDCP and FGR higher than that of FGR alone.[30,31] Although the precise mechanisms remain inconclusive, most scholars believe that HDCP leads to poor placental vascularization due to systemic arteriolar spasm, reducing uteroplacental perfusion. This impacts fetal oxygen and nutrient acquisition from the mother, ultimately affecting normal fetal development and, in severe cases, can lead to fetal hypoxia or stillbirth. All forms of hypertensive pregnancy disorders increase the incidence of FGR by two to threefold.[32] Consistently, our study also demonstrated an increased incidence of FGR among pregnant women with HDCP.

Multiple studies[33–35] have reported a higher incidence of FGR in pregnant women with GDM, hypothyroidism, or those who underwent ART procedures. However, the comparison between the FGR group and the control group in this study did not reveal statistically significant differences. This may be attributed to standardized maternity check-ups, increased attention to, and effective management of associated diseases, which mitigate their adverse effects on fetal growth. Moreover, the rates of preterm labor and emergency cesarean delivery were significantly higher in pregnant women in the FGR group compared to the control group, likely due to the predisposition of pregnant women in the FGR group to combined pregnancy complications or intrauterine distress, leading to an increased rate of emergency cesarean delivery and, indirectly, preterm labor.

The placenta and umbilical cord play crucial roles in the transfer of gases and nutrients from the mother to the fetus.[27] Placental anomalies (eg, bilobate or circumvallate placenta, small placenta, placental mesenchymal dysplasia) and umbilical cord anomalies (eg, single artery, velamentous or marginal cord insertion) are known causes of FGR.[36] Placental vascular insufficiency accounts for 75–80% of FGR cases,[37] primarily due to reduced blood flow secondary to decreased perfusion pressure. Consistently, this study also observed an increased incidence of FGR in pregnant women with placental and umbilical cord abnormalities. Notably, various placental problems (eg, rupture of placental marginal sinus, battledore placenta, bilobed placenta, complete placenta previa, placental adhesion, placental abruption) and umbilical cord issues (eg, velamentous insertion of the umbilical cord, long umbilical cord, umbilical cord torsion, single umbilical artery, umbilical artery embolism) were identified.

Umbilical artery flow Doppler testing serves as a crucial method for assessing fetal and placental conditions. As a vital link between maternal and fetal blood systems, the umbilical artery exhibits abnormalities in peripheral circulation before changes occur in fetal head circumference and abdominal circumference in cases of FGR. Utilizing color Doppler flow imaging enables the acquisition of fetal circulation information, facilitating earlier detection and improved diagnosis rates of FGR.[32] Umbilical artery flow effectively reflects placental function and fetal development, with its resistance level indicating the state of fetal-placental circulation. For Doppler blood flow monitoring in FGR, guidelines and literature unanimously acknowledge umbilical artery blood flow as the fundamental and widely used clinical monitoring index. Incorporating umbilical artery Doppler monitoring into standard prenatal testing for FGR led to a 29% reduction in perinatal mortality.[38] Consistently, this study also observed an increased incidence of FGR in pregnant women with abnormal umbilical artery flow. Pearson's correlation analysis revealed a high correlation coefficient between abnormal umbilical artery flow and FGR, with a coefficient of 0.290.

Amniotic fluid volume serves as a vital indicator for monitoring fetal condition. Adequate amniotic fluid volume is essential for normal fetal growth and development. One study reported an FGR incidence of 19.9% when the amniotic fluid index (AFI) ranged between 7 and 9 cm, significantly increasing to 40.3% when the AFI was <4 cm.[39] Amniotic fluid directly influences fetal circulation. Insufficient amniotic fluid volume not only restricts space for fetal growth but also impacts placental maternal blood perfusion, thereby leading to FGR. Consistently, this study observed a higher prevalence of FGR in pregnant women with low amniotic fluid, aligning with previous findings.

FGR significantly increases the risk of adverse pregnancy outcomes and long-term complications in offspring. Neonates affected by FGR often experience acute issues such as perinatal asphyxia, hypothermia, hypoglycemia, and polycythemia. Furthermore, they are susceptible to long-term complications including growth retardation, major and subtle neurodevelopmental handicaps, and developmental origins of health and disease.[27,40,41] Hence, conducting a comprehensive fetal echocardiography examination may aid in accurate diagnoses and reducing the incidence of

adverse pregnancy outcomes. Studies have indicated that FGR fetuses with the most impaired cardiac function tend to have the worst pregnancy outcomes.[8] Therefore, when FGR is clinically suspected, fetal cardiac examination should be conducted to monitor changes in cardiac morphology, facilitating better clinical diagnosis and evaluation of fetal prognosis.

However, the current study has several limitations. Firstly, it was conducted at a single center with a relatively small number of cases. Future research should involve larger sample sizes to enhance generalizability. Secondly, this study did not involve random sampling, and only one fetal echocardiography examination was performed for each case, thus failing to capture dynamic changes in cardiac parameters throughout gestation. Thirdly, the potential impact of image acquisition by different physicians was not assessed, which could introduce variability in the results.

Conclusion

FGR is correlated with various pathological factors, which is helpful for the etiological diagnosis of FGR. Cardiac remodeling occurs early in FGR fetuses, and can be evaluated by cardiac parameters such as RA/LA ratio and RV/LV ratio, suggesting that these fetal cardiac parameters have clinical value. In the future, we should explore the dynamic changes of cardiac parameters throughout gestation. And these cardiac parameters can be applied in the clinical diagnosis of FGR along with other parameters of fetal.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Morris RK, Johnstone E, Lees C, et al. Investigation and care of a small-for-gestational-age fetus and a growth restricted fetus (Green-top guideline No. 31). *BJOG*. 2024;131(9):e31–e80. doi:10.1111/1471-0528.17814
2. Albu AR, Anca AF, Horhoianu VV, Horhoianu IA. Predictive factors for intrauterine growth restriction. *J Med Life*. 2014;7(2):165–171.
3. Wieland U, Kreuter A. Prävention HPV-induzierter erkrankungen durch prophylaktische impfung [Prevention of HPV-induced diseases by prophylactic vaccination]. *Hautarzt*. 2021;72(2):106–113. doi:10.1007/s00105-020-04739-4
4. Tsikouras P, Antsaklis P, Nikolettos K, et al. Diagnosis, prevention, and management of fetal growth restriction (FGR). *J Pers Med*. 2024;14(7):698. doi:10.3390/jpm14070698
5. Papamichail M, Antsaklis P, Kurjak A, et al. Investigation of cardiac remodeling and cardiac function on fetuses with growth restriction: a review. *Donald Sch J Ultrasound Obstet*. 2022;16(2):124–137. doi:10.5005/jp-journals-10009-1928
6. Devi GG, Balakrishnan B, Batra M, et al. Role of global sphericity index in evaluation of fetal cardiac remodeling in late onset fetal growth restriction and small for gestational age fetuses. *J Clin Ultrasound*. 2023;51(5):796–802. doi:10.1002/jcu.23448
7. Nayak V, A JA, Lewis EL, et al. Subclinical myocardial dysfunction among fetal growth restriction neonates: a case-control study. *J Matern Fetal Neonatal Med*. 2024;37(1):2392783. doi:10.1080/14767058.2024.2392783
8. Patey O, Carvalho JS, Thilaganathan B. Perinatal changes in cardiac geometry and function in growth-restricted fetuses at term. *Ultrasound Obstetr Gynecol*. 2019;53(5):655–662. doi:10.1002/uog.19193
9. Semmler J, Abdel-Azim S, Anzoategui S, Zhang H, Nicolaides KH, Charakida M. Influence of birth weight on fetal cardiac indices at 35–37 weeks' gestation. *Ultrasound Obstetr Gynecol*. 2021;57(2):266–272. doi:10.1002/uog.23522
10. DeVore GR, Zaretsky M, Gumina DL, Hobbins JC. Right and left ventricular 24-segment sphericity index is abnormal in small-for-gestational-age fetuses. *Ultrasound Obstet Gynecol*. 2018;52(2):243–249. doi:10.1002/uog.18820
11. Lobmaier MS, Graupner O, Franke C, et al. Fetal cardiovascular function in a late-onset SGA and FGR cohort: CURIOSA study. *Ultraschall der Medizin*. 2024;2024.
12. Gallardo DC, García GN, Ullmo J, et al. Fetal left ventricle function evaluated by two-dimensional speckle-tracking echocardiography across clinical stages of severity in growth-restricted fetuses. *Diagnostics*. 2024;14(5):548. doi:10.3390/diagnostics14050548
13. Carla D, Nuria G, Johana U, et al. Longitudinal behavior of left-ventricular strain in fetal growth restriction. *Diagnostics*. 2023;13(7):1252
14. Graupner O, Ried C, Wildner NK. Myocardial deformation analysis in late-onset small-for-gestational-age and growth-restricted fetuses using two-dimensional speckle tracking echocardiography: a prospective cohort study. *J Perinat Med*. 2021;50(3):305–312. doi:10.1515/jpm-2021-0162
15. Wen W, JiFeng L, Hong Y, et al. Evaluation of fetal cardiac function in fetal growth restriction via fetal HQ analysis based on two-dimensional. *J Obstet Gynaecol Res*. 2023;49(6):1514–1524.
16. Tao Z. Assessment of left ventricular function by spatio-temporal image correlation in fetuses with fetal growth restriction. *Echocardiography*. 2022;39(9):1240–1244. doi:10.1111/echo.15438
17. Sedigheh B, Somayeh K, Sedigheh H, et al. Evaluation of cardiac sphericity index among intrauterine growth restriction and normal fetuses. *J Obstetrics Gynaecol*. 2021;42(4):1–6. doi:10.1080/01443615.2021.1887113
18. Giuseppe R, Cecilia M, Ilenia M, et al. Hemodynamic factors associated with fetal cardiac remodeling in late fetal growth restriction: a prospective study. *J Perinat Med*. 2019;47(7):683–688. doi:10.1515/jpm-2019-0217
19. Zhu L, Zhang R, Zhang S, et al. Chinese neonatal birth weight curve for different gestational age. *Chin J Pediatr*. 2015;53(2):97–103.
20. Nawathe A, Lees C. Early onset fetal growth restriction. *Best Pract Res Clin Obstet Gynaecol*. 2017;38:3824–3837.

21. Melamed N, Baschat A, Yinon Y. Figo (international federation of gynecology and obstetrics) initiative on fetal growth: best practice advice for screening, diagnosis, and management of fetal growth restriction. *Int J Gynaecol Obstet*. 2021;152(Suppl 1):3–57. doi:10.1002/ijgo.13522
22. DeVore GR. Examination of the fetal heart in the fetus with intrauterine growth retardation using M-mode echocardiography. *Semin Perinatol*. 1988;12(1):66–79.
23. Tynan D, Alphonse J, Henry A, Welsh AW. The aortic isthmus: a significant yet underexplored watershed of the fetal circulation. *Fetal Diagn Ther*. 2016;40(2):81–93. doi:10.1159/000446942
24. Sendra M, Dominguez JN, Torres M, et al. Dissecting the complexity of early heart progenitor cells. *J Cardiovasc Dev Dis*. 2021;9(1):5. doi:10.3390/jcdd9010005
25. Machado MLN, Rabachini CAC, Perez CAZ, et al. Fetal growth restriction: current knowledge. *Arch Gynecol Obstetrics*. 2017;295(5):1061–1077. doi:10.1007/s00404-017-4341-9
26. Lee IW, Chang CH, Cheng YC, et al. A review of three-dimensional ultrasound applications in fetal growth restriction. *J Med Ultrasound*. 2012;20 (3):142–149. doi:10.1016/j.jmu.2012.07.002
27. Chew LC, Verma RP. Fetal growth restriction. *J Magn Reson Imaging*. doi:10.1002/jmri.27792
28. Kac G, Arnold CD, Matias SL, et al. Gestational weight gain and newborn anthropometric outcomes in rural Bangladesh. *Matern Child Nutr*. 2019;15(14):e12816. doi:10.1111/mcn.12816
29. Odibo AO, Nelson D, Stamilio DM, et al. Advanced maternal age is an independent risk factor for intrauterine growth restriction. *Am J Perinat*. 2006;236(5):325–328. doi:10.1055/s-2006-947164
30. Sibai BM. Chronic hypertension in pregnancy. *Obstet Gynecol*. 2002;100(2):369–377. doi:10.1097/00006250-200212000-00037
31. Cnattingius S, Kramer MS, Norman M, et al. Investigating fetal growth restriction and perinatal risks in appropriate for gestational age infants: using cohort and within sibling analyses. *BJOG*. 2019;126(7):842–850. doi:10.1111/1471-0528.15563
32. Galan HL, Rigano SRadaelli T, Radaelli T, et al. Reduction of subcutaneous mass, but not lean mass, in normal fetuses in Denver, Colorado. *Am J Obstet Gynecol*. 2001;185(4):839–844. doi:10.1067/mob.2001.117350
33. Palieva P, Petrov P, Petrov PYA, et al. Carbohydrate metabolism an nd hemostatic system in women with gestational diabetes mellitus, preeclampsia, and fetal growth restriction. *Akush Ginekol*. 2021;2:69–76. doi:10.18565/aig.2021.2.69-76
34. Su PY, Huang K, Hao JH, et al. Maternal thyroid function in the first twenty weeks of pregnancy and subsequent fetal and infant development: a prospective population-based cohort study in China. *J Clin Endocrinol Metab*. 2011;96(10):3234–3241. doi:10.1210/jc.2011-0274
35. Schieve LA, Cohen BNannini A, Nannini A, et al. A population-based study of maternal and perinatal outcomes associated with assisted reproductive technology in Massachusetts. *Matern Child Health J*. 2007;11(6):517–525. doi:10.1007/s10995-007-0202-7
36. Burton GJ, Jauniaux E. Pathophysiology of placental-derived fetal growth restriction. *Am J Clin Exp Obstet Gynecol*. 2018;218(2):S745. doi:10.1016/j.ajog.2017.11.577
37. Zielinsky P, Beltrame PA, Manica JL, et al. Dynamics of the septum primum in fetuses with intrauterine growth restriction. *Clin Ultrasound*. 2009;37(6):342–346. doi:10.1002/jcu.20582
38. ACOG. Practice Bulletin No.204: Fetal growth restriction. *Obstet Gynecol*. 2019;133(2):97–109. doi:10.1097/AOG.0000000000003070
39. Spinillo A, Cesari S, Bariselli S, et al. Placental lesions associated with oligohydramnios in fetal growth restricted (FGR) pregnancies. *Placenta*. 2015;36(5):538–544. doi:10.1016/j.placenta.2015.02.007
40. Sharma D, Shastri S, Sharma P. Intrauterine growth restriction: antenatal and postnatal aspects. *Clin Med Insights Pediatr*. 2016;10:67–83. doi:10.4137/CMPed.S40070
41. Erich C, Tiziana F, Silvia V, et al. Consequences in infants that were intrauterine growth restricted. *J Pregnancy*. 2011;2011:364381. doi:10.1155/2011/364381