



Temporal changes in doppler indices and their role in determining optimal timing of delivery in fetal growth restriction

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Abstract

Background: Fetal growth restriction (FGR) is a major contributor to perinatal morbidity and mortality, primarily resulting from placental insufficiency. Doppler velocimetry provides insight into fetal hemodynamic adaptation; however, the temporal progression of these changes and their role in determining optimal timing of delivery remain incompletely defined.

Objective: To evaluate the temporal changes in fetal Doppler indices and their role in determining the optimal timing of delivery in pregnancies complicated by FGR.

Methods: A prospective longitudinal analytical study was conducted in a tertiary care center over 24 months, including 180 singleton pregnancies with FGR (≥ 24 weeks). Serial Doppler assessments of the umbilical artery (UA), middle cerebral artery (MCA), cerebroplacental ratio (CPR), and ductus venosus (DV) were performed. The progression of Doppler abnormalities and time intervals between stages were analyzed. Time-to-delivery analysis, Cox regression, and ROC curve analysis were used to assess associations with delivery timing and adverse perinatal outcomes.

Results: Doppler abnormalities followed a sequential pattern, beginning with increased UA resistance, followed by cerebral redistribution, abnormal CPR, and eventual DV changes. The median time intervals between stages progressively shortened, indicating accelerated fetal deterioration. Time-to-delivery analysis demonstrated that DV abnormalities were associated with the shortest interval to delivery (log-rank $p < 0.001$), followed by CPR and UA abnormalities. DV abnormalities showed the strongest association with adverse perinatal outcomes (HR 5.6), while CPR demonstrated good predictive performance (AUC 0.86). Adverse outcomes occurred in 35.6% of cases, with high rates of preterm delivery and NICU admission.

Conclusion: Temporal progression of Doppler abnormalities provides valuable insight into fetal compromise and can guide optimal timing of delivery in FGR. While CPR serves as an early indicator, DV abnormalities represent a critical threshold for intervention. Integrating longitudinal Doppler assessment into clinical practice may improve perinatal outcomes.

Keywords: Fetal growth restriction, doppler ultrasound, cerebroplacental ratio, Ductus Venosus, timing of delivery

Introduction

Fetal growth restriction (FGR) remains a major contributor to perinatal morbidity and mortality worldwide and is associated with significant short- and long-term adverse outcomes. The condition is primarily linked to placental insufficiency, resulting in impaired nutrient and oxygen transfer to the fetus and consequent failure to achieve its genetically determined growth potential [1, 6, 7]. The underlying pathophysiology involves abnormal placental development and function, leading to chronic fetal hypoxia and adaptive hemodynamic changes [6, 7].

Doppler ultrasound has become an essential tool in the evaluation and management of FGR, providing non-invasive assessment of fetal and placental circulation. Current guidelines emphasize its role in screening, diagnosis, and surveillance, particularly in high-risk pregnancies [1]. Changes in Doppler indices reflect the progression of placental disease, beginning with increased resistance in the umbilical artery and followed by redistribution of blood flow to vital organs, commonly referred to as the “brain-sparing” effect [7, 8].

Early-onset FGR, typically diagnosed before 32 weeks of gestation, is associated with higher rates of perinatal mortality and morbidity compared to late-onset disease [2]. The management of such cases remains challenging, as clinicians must balance the risks of prematurity against the

risk of intrauterine fetal compromise. Evidence from randomized trials, including the Trial of Randomized Umbilical and Fetal Flow in Europe (TRUFFLE), has highlighted the importance of Doppler surveillance—particularly ductus venosus assessment—in guiding the timing of delivery to improve outcomes [3, 4].

Despite advances in Doppler technology and clinical protocols, uncertainty remains regarding the optimal integration of temporal Doppler changes into decision-making for delivery. Previous studies have primarily focused on the predictive value of individual Doppler indices or static measurements, while the dynamic progression of these changes over time has been less clearly defined. Furthermore, long-term outcome studies have demonstrated that the timing of delivery in FGR has significant implications for neurodevelopment, emphasizing the need for precise clinical strategies [10].

Therefore, this study aimed to evaluate the temporal progression of Doppler abnormalities and to determine their role in guiding the optimal timing of delivery in pregnancies complicated by fetal growth restriction.

Literature Review

Doppler surveillance has been extensively studied as a tool for monitoring fetal hemodynamic adaptation in fetal growth restriction (FGR). Early longitudinal work

demonstrated that fetuses with growth restriction exhibit a progressive sequence of Doppler changes involving both arterial and venous circulations, reflecting worsening placental insufficiency and fetal compromise [11]. These findings established the basis for using Doppler velocimetry not only for diagnosis but also for ongoing surveillance. Standardization of FGR definition has further improved the consistency of research and clinical practice. The Delphi consensus by Gordijn *et al.* provided a uniform definition incorporating biometric and Doppler parameters, enabling better stratification of severity and facilitating comparison across studies [13]. International guidelines, including those from ISUOG, ACOG, and RCOG, emphasize the importance of integrating Doppler assessment—particularly of the umbilical artery, middle cerebral artery, and ductus venosus—into routine management protocols for FGR [15-17]. These guidelines highlight the role of Doppler in guiding surveillance frequency and determining timing of delivery. Arterial Doppler studies have shown that increased resistance in the umbilical artery is an early marker of placental dysfunction, while redistribution of blood flow to the fetal brain represents a compensatory mechanism in response to hypoxia [20]. The cerebroplacental ratio has emerged as a useful composite index reflecting both placental resistance and fetal adaptation. However, arterial Doppler parameters alone may be insufficient in predicting critical deterioration.

Venous Doppler assessment, particularly of the ductus venosus, has been shown to provide additional prognostic value in advanced stages of FGR. Baschat *et al.* demonstrated that qualitative analysis of venous waveforms improves prediction of adverse perinatal outcomes, underscoring its importance in identifying fetuses at imminent risk [18]. Similarly, studies evaluating Doppler pulsatility indices and velocity ranges across fetal vessels have contributed to understanding normal and pathological hemodynamic patterns [19].

The integration of Doppler findings with clinical management strategies remains a key challenge. Recent protocols, such as the OPTICORE study, aim to optimize interventions like antenatal corticosteroid administration based on disease progression, highlighting the importance of timing in improving neonatal outcomes [12]. Additionally, evidence suggests that intrapartum monitoring and fetal heart rate analysis play complementary roles in assessing fetal well-being during labor, particularly in compromised pregnancies [21, 22].

Despite these advances, most studies have focused on cross-sectional or predictive models rather than the dynamic progression of Doppler changes over time. While earlier research has described the sequence of hemodynamic alterations, the precise temporal relationships between these changes and their direct application in determining optimal timing of delivery remain incompletely defined. Therefore, a longitudinal approach examining the temporal evolution of Doppler indices is essential to bridge this gap and improve clinical decision-making in FGR.

Methodology

1. Study Design

A prospective longitudinal analytical study was conducted to evaluate the temporal progression of fetal Doppler indices and their role in determining optimal timing of delivery in

pregnancies complicated by fetal growth restriction (FGR). The study focused on dynamic changes in Doppler parameters rather than single time-point assessments.

2. Study Setting and Population

The study was carried out over 24 months in a tertiary-level fetal medicine unit with neonatal intensive care support. Singleton pregnancies of ≥ 24 weeks' gestation with confirmed FGR—defined as estimated fetal weight (EFW) < 10 th percentile with abnormal Doppler or < 3 rd percentile irrespective of Doppler—were included. Cases with multiple gestation, fetal anomalies, intrauterine infections, uncertain dating, or incomplete follow-up were excluded.

3. Sample Size and Baseline Assessment

A minimum sample size of 180 participants was calculated based on expected Doppler progression and adverse outcomes, with 80% power and 5% alpha error, accounting for attrition. At enrollment, maternal demographics, obstetric history, and baseline ultrasound parameters including fetal biometry and amniotic fluid were recorded.

4. Serial Doppler Surveillance

Participants underwent standardized serial Doppler examinations at two-week intervals in stable cases and more frequently when abnormalities were detected. Parameters assessed included umbilical artery (UA) pulsatility index with assessment of absent/reversed end-diastolic flow, middle cerebral artery (MCA) pulsatility index, cerebroplacental ratio (CPR), and ductus venosus (DV) indices including a-wave status. Measurements were obtained under uniform conditions using the mean of three consecutive waveforms.

5. Assessment of Temporal Changes

The progression of Doppler abnormalities was categorized into sequential stages: normal Doppler, elevated UA resistance, UA absent/reversed end-diastolic flow, reduced MCA pulsatility index, abnormal CPR, and abnormal DV waveform. The time interval between each stage was recorded in days to identify critical transition points associated with fetal deterioration.

6. Clinical Management and Outcomes

Clinical management followed institutional protocols independent of the study. Delivery decisions were based on Doppler findings and fetal condition, with immediate delivery in cases of abnormal DV or fetal compromise and earlier intervention in persistent severe UA or worsening CPR abnormalities. The primary outcome was optimal timing of delivery in relation to Doppler progression and composite adverse perinatal outcomes (stillbirth, neonatal death, severe morbidity). Secondary outcomes included gestational age at delivery, birth weight, Apgar score, NICU admission, and mode of delivery.

7. Statistical Analysis

Data were analyzed using SPSS/R software. Continuous variables were expressed as mean \pm SD or median (IQR), and categorical variables as frequencies and percentages. Longitudinal Doppler changes were assessed using mixed-effects models. Time-to-delivery was analyzed using Kaplan–Meier curves, and predictors of adverse outcomes

were evaluated using Cox regression. ROC curve analysis was performed to assess diagnostic performance. A p-value <0.05 was considered statistically significant.

Results and Discussion

1. Baseline Characteristics

A total of 180 pregnant women with fetal growth restriction (FGR) were enrolled and followed until delivery. The mean maternal age was 27.4 ± 4.8 years, with the majority being primigravida (58.3%). The mean gestational age at recruitment was 30.8 ± 3.1 weeks. Early-onset FGR (<32 weeks) constituted 46.1%, while late-onset FGR (≥ 32 weeks) accounted for 53.9% of cases.

Table 1: Baseline Maternal and Clinical Characteristics (n = 180)

Parameter	Value
Maternal age (years)	27.4 ± 4.8
Primigravida	105 (58.3%)
Multigravida	75 (41.7%)
BMI (kg/m ²)	23.2 ± 2.6
Gestational age at recruitment (weeks)	30.8 ± 3.1
Early-onset FGR (<32 weeks)	83 (46.1%)
Late-onset FGR (≥ 32 weeks)	97 (53.9%)
Hypertensive disorders	68 (37.8%)

This table 1 shows that the study population largely consisted of young primigravida women, with a significant proportion having early-onset FGR, which is typically associated with more severe disease and Doppler abnormalities.

2. Temporal Progression of Doppler Abnormalities

Serial Doppler surveillance demonstrated a predictable sequential pattern of deterioration. The earliest abnormality observed was increased umbilical artery (UA) resistance, followed by cerebral redistribution and venous compromise.

Table 2: Sequence and Frequency of Doppler Abnormalities

Doppler Stage	Number (%)
Elevated UA PI	128 (71.1%)
UA AEDF/REDF	74 (41.1%)
Reduced MCA PI	136 (75.6%)
Abnormal CPR	122 (67.8%)
Abnormal DV	38 (21.1%)

Table 2 demonstrates that arterial Doppler abnormalities occur earlier and more frequently, while ductus venosus changes are less common but represent advanced fetal compromise.

Table 6: Association of Doppler Indices with Adverse Outcomes

Parameter	Adverse Outcome (%)	No Adverse Outcome (%)	p-value
UA abnormal	78.1	34.2	<0.001
MCA abnormal	85.9	49.1	<0.001
CPR abnormal	88.3	42.7	<0.001
DV abnormal	92.1	12.8	<0.001

Ductus venosus abnormalities showed the strongest association with adverse outcomes, followed by CPR, confirming their importance in clinical decision-making.

7. Time-to-Delivery Analysis

Time-to-delivery analysis demonstrated a significantly shorter interval to delivery in pregnancies with abnormal ductus venosus

3. Time Interval Between Doppler Changes

The median time intervals between sequential Doppler abnormalities were analyzed.

Table 3: Temporal Intervals Between Doppler Stages

Transition	Median Time (days)	IQR
UA abnormal → MCA change	6	4–9
MCA → CPR abnormal	4	3–7
CPR → DV abnormal	3	2–5
DV abnormal → Delivery	2	1–3

Table 3 highlights that progression accelerates as fetal compromise worsens, with the shortest interval observed between DV abnormality and delivery, emphasizing its role as a late and critical marker.

4. Timing of Delivery in Relation to Doppler Changes

Delivery was closely associated with Doppler deterioration, particularly venous abnormalities.

Table 4: Doppler Findings at Time of Delivery

Doppler Parameter	Frequency (%)
UA AEDF/REDF	82 (45.6%)
CPR abnormal	124 (68.9%)
DV abnormal	40 (22.2%)
Normal Doppler	18 (10.0%)

Most deliveries occurred after significant arterial Doppler abnormalities, while DV abnormalities prompted urgent delivery, supporting its role in decision-making.

5. Perinatal Outcomes

Adverse perinatal outcomes were observed in 64 (35.6%) cases. The most common outcomes included NICU admission and preterm delivery.

Table 5: Perinatal Outcomes

Outcome	Value
Preterm delivery	118 (65.6%)
Cesarean section	126 (70.0%)
NICU admission	96 (53.3%)
Low Apgar (<7 at 5 min)	42 (23.3%)
Perinatal mortality	10 (5.6%)

This reflects the high-risk nature of FGR pregnancies, with a high rate of intervention and neonatal morbidity.

6. Association Between Doppler Changes and Adverse Outcomes

Abnormal Doppler indices were significantly associated with adverse perinatal outcomes.

(DV) Doppler compared to those with isolated arterial Doppler abnormalities (log-rank $p < 0.001$). As illustrated in Figure 1, cases with DV abnormalities showed the most rapid decline in the probability of ongoing pregnancy, followed by abnormal cerebroplacental ratio (CPR) and umbilical artery (UA) Doppler changes, while cases with normal Doppler findings had the longest duration before delivery.

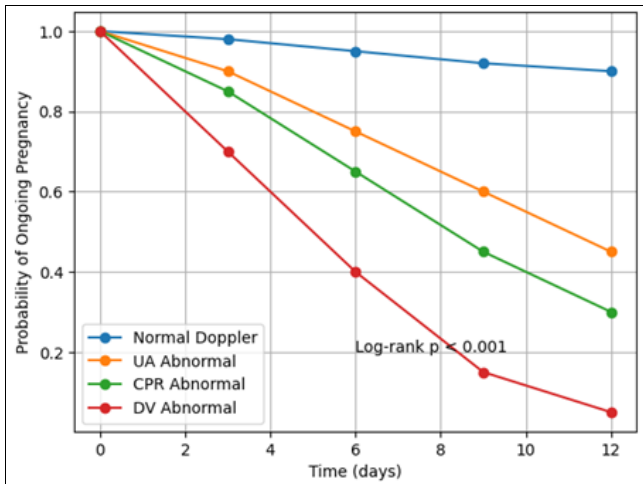


Fig 1: Time-to-Delivery Analysis Based on Doppler Abnormalities

The graph depicts the probability of ongoing pregnancy over time (days) across different Doppler categories. A steeper decline in the curve indicates a shorter interval to delivery. Pregnancies with DV abnormalities demonstrated the fastest progression to delivery, reflecting advanced fetal compromise, whereas normal Doppler findings were associated with more prolonged continuation of pregnancy.

8. Predictors of Early Delivery and Adverse Outcome

Cox regression analysis identified independent predictors.

Table 7: Cox Proportional Hazards Model

Variable	Hazard Ratio (HR)	95% CI	p-value
UA abnormal	2.4	1.5–3.9	0.001
CPR abnormal	3.1	1.9–5.2	<0.001
DV abnormal	5.6	3.2–9.4	<0.001

DV abnormality had the highest hazard ratio, indicating the strongest predictor of both early delivery and adverse outcomes.

9. Diagnostic Performance of Doppler Indices

Table 8: ROC Curve Analysis

Parameter	AUC	95% CI
UA PI	0.78	0.70–0.85
MCA PI	0.74	0.66–0.82
CPR	0.86	0.79–0.92
DV	0.91	0.85–0.96

DV demonstrated the highest predictive accuracy, followed by CPR, supporting their combined use in clinical practice.

Discussion

The present study demonstrated a predictable temporal progression of Doppler abnormalities in fetal growth restriction, beginning with increased umbilical artery resistance, followed by cerebral redistribution, abnormal cerebroplacental ratio, and culminating in ductus venosus (DV) abnormalities. This sequence reflects established pathophysiology of placental insufficiency, where progressive hypoxia leads to adaptive fetal hemodynamic changes. Unlike previous studies, this study quantified the time intervals between stages, showing that deterioration accelerates with advancing compromise.

DV abnormalities were strongly associated with imminent delivery and adverse perinatal outcomes. As illustrated in Figure 1, DV changes showed the most rapid decline in the probability of ongoing pregnancy, consistent with findings from the TRUFFLE trial. In contrast, the cerebroplacental ratio acted as an early and sensitive marker, useful for surveillance but associated with a longer interval to delivery.

Time-to-delivery analysis confirmed that delivery timing closely correlates with the severity of Doppler deterioration, supporting a staged management approach in which early changes warrant monitoring and venous abnormalities necessitate prompt intervention. The high rates of preterm delivery and NICU admission highlight the clinical challenges in balancing prematurity with intrauterine risk.

The strengths of this study include its prospective longitudinal design and time-based analysis of Doppler progression. Limitations include its single-center nature, operator dependency of Doppler measurements, and lack of long-term follow-up.

Conclusion

This study demonstrates that fetal Doppler abnormalities in growth-restricted pregnancies follow a predictable temporal sequence, with progressive acceleration of deterioration. Ductus venosus abnormalities represent a critical threshold associated with imminent delivery and adverse outcomes, while cerebroplacental ratio serves as an early indicator of fetal compromise.

Time-based analysis of Doppler progression provides a valuable framework for clinical decision-making and may improve the timing of delivery in FGR. Incorporating longitudinal Doppler surveillance into routine practice can enhance risk stratification and potentially improve perinatal outcomes.

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