THE MEDICAL BULLETIN OF
SISLI ETFAL HOSPITAL

DOI: 10.14744/SEMB.2025.73368
Med Bull Sisli Etfal Hosp 2025;59(1):119–126

Original Research

Relationship Between Adverse Neonatal Outcomes and Diastolic Deceleration Area on Fetal MCA Doppler in Patients with Late Fetal Growth Restriction

Gulsan Karabay,[1] Zeynep Seyhanli,[1] Betul Tokgoz Cakir,[1] Gizem Aktemur,[1] Serap Topkara Sucu,[2] Nazan Vanli Tonyali,[1] Mevlut Bucak,[1] Recep Taha Agaoglu,[1] Ahmet Arif Filiz,[1] Huseyin Levent Keskin,[2] Umut Karabay,[3] Seda Aydogan,[4] Gulsah Dagdeviren[1]

[1]Division of Perinatology, Department of Obstetrics and Gynecology, Ankara Etlik City Hospital, Ankara, Türkiye
[2]Department of Obstetrics and Gynecology, Ankara Etlik City Hospital, Ankara, Türkiye
[3]Department of Internal Medicine, Gulhane Training and Research Hospital, Ankara, Türkiye
[4]Department of Neonatology, Ankara Etlik City Hospital, Ankara, Türkiye

Abstract

Objectives: This study aimed to assess the predictive value of the Diastolic Deceleration Area (DDA), a novel Doppler ultrasound parameter, in detecting adverse neonatal outcomes in fetuses with late-onset fetal growth restriction (FGR). While Doppler parameters such as cerebroplacental ratio (CPR), umbilicocerebral ratio (UCR), and cerebralplacentaluterine ratio (CPUR) are commonly used for fetal monitoring, their predictive power varies. Given the importance of cerebral blood flow redistribution in fetal adaptation to hypoxia, we investigated whether DDA could serve as a reliable indicator of fetal distress and adverse perinatal outcomes.

Methods: This prospective case-control study was conducted between January 2024 and July 2024, including 90 pregnant women: 45 diagnosed with late-onset FGR and 45 gestational age-matched healthy controls. Doppler ultrasound measurements, including umbilical artery, uterine artery, middle cerebral artery Doppler indices, CPR, UCR, CPUR, and DDA, were performed. The primary outcome was the prediction of adverse neonatal events, such as neonatal intensive care unit (NICU) admission, neonatal sepsis, respiratory distress, low APGAR scores, and low cord blood pH. Receiver Operating Characteristic (ROC) curve analysis was used to determine the predictive ability of the Doppler indices.

Results: DDA values were significantly higher in the FGR group compared to controls ($p<0.001$). At a cut-off value of >7.23, DDA demonstrated 50% sensitivity and 88% specificity, making it the most specific Doppler parameter for predicting adverse neonatal outcomes. In comparison, CPR (cut-off ≤2.11), UCR (cut-off >0.46) and CPUR (cut-off ≤1.36) had higher sensitivity (96%, 96%, 54%) but lower specificity (32%, 31% and 85% respectively).

Conclusion: DDA is a promising Doppler parameter for identifying fetuses at risk in late-onset FGR. Its high specificity suggests it could be a valuable supplementary tool alongside traditional Doppler indices for better risk assessment and clinical decision-making. Further studies are needed to validate its role in perinatal care.

Keywords: Diastolic deceleration area, fetal growth restriction, neonatal outcome, prenatal ultrasonography

Please cite this article as "Karabay G, Seyhanli Z, Tokgoz Cakir B, Aktemur G, Topkara Sucu S, Vanli Tonyali N, et al. Relationship between Adverse Neonatal Outcomes and Diastolic Deceleration Area on Fetal MCA Doppler in Patients with Late Fetal Growth Restriction. Med Bull Sisli Etfal Hosp 2025;59(1):119–126".

Address for correspondence: Gulsan Karabay, MD. Division of Perinatology, Department of Obstetrics and Gynecology, Ankara Etlik City Hospital, Ankara, Türkiye
Phone: +90 553 533 79 31 **E-mail:** drgulsankarabay@gmail.com

Submitted Date: January 06, 2025 **Revised Date:** February 27, 2025 **Accepted Date:** March 07, 2025 **Available Online Date:** March 18, 2025

©Copyright 2025 by The Medical Bulletin of Sisli Etfal Hospital - Available online at www.sislietfaltip.org
OPEN ACCESS This is an open access article under the CC BY-NC license (http://creativecommons.org/licenses/by-nc/4.0/).

The failure of a fetus to fulfill its full genetically determined development potential is known as fetal growth restriction (FGR).[1] About 3–7% of pregnancies are affected by late-onset FGR, which usually appears after the 32nd week of pregnancy.[2] FGR that develops as a result of pathologies of the fetal-placental-maternal unit can lead to significant short- and long-term complications.[3]

Clinics use ultrasound examinations, a non-invasive technique, to diagnose and monitor FGR patients. The three primary Doppler parameters used are the uterine artery (UtA), middle cerebral artery (MCA), and umbilical artery (UA).[4,5] However, in high-risk pregnancies like those affected by FGR, it is believed that Doppler parameters alone cannot reliably indicate fetal hypoxia and adaptation changes, which has increased interest in combined ultrasonographic evaluations. In particular, Doppler evaluation, which integrates uterine, placental, and fetal vascular data, serves as a crucial modality for the early detection of uteroplacental insufficiency and the prediction of adverse neonatal outcomes.[6] The importance of the cerebroplacental ratio (CPR), umbilicocerebral ratio (UCR), and cerebroplacentouterine ratio (CPUR) values—which integrate information from the uterine, middle cerebral, and umbilical arteries—has been highlighted by a recent medical study. In cases of FGR, these parameters have been used to diagnose, monitor, and predict adverse neonatal outcomes.[4,5,7,8]

It has been shown that vascular resistance decreases and cerebral perfusion increases in response to long-term hypoxia in FGR patients (brain protective effect).[4,9] A helpful notch in the interpretation of cerebral vasodilation has also been described in the literature.[10] Dicrotic Notch (DN) arises from a transient rise in arterial blood pressure concurrent with the closure of the aortic valve. The DN aligns with the end-systolic pressure of the left ventricle, which concurrently signifies the initiation of diastole.[11] A unique metric known as the "diastolic deceleration area, or DDA," was created in a 2023 study to measure the degree of cerebral vasodilation in light of DN research. According to this study, DDA can be used independently to detect hypoxia in the latter phases of pregnancy.[10]

Because of their high metabolic rate, fetuses with late FGR have a decreased tolerance to hypoxemia, which makes postnatal care even more important.[7] Our study's objectives were to show the connection between FGR and DDA area, a novel Doppler parameter, and to clarify the distinct roles that several Doppler parameters play in forecasting unfavorable neonatal outcomes in fetuses with FGR.

Methods

This prospective case-control study was conducted at the Ankara Etlik City Hospital Perinatology Clinic between January 2024 and July 2024. The study population was divided into two groups: Group 1 consisted of 45 patients diagnosed with late-onset FGR, and Group 2 consisted of 45 control patients. The Ethics Committee approved the study protocol (approval number: AESH-EK1-20/12/2023-770). The guidelines of the World Medical Association's Declaration of Helsinki were followed in this study. Written informed consents was obtained from all patients who participated in the trial after they were fully informed.

FGR was defined in accordance with the Delphi consensus criteria, taking into account an estimated fetal weight (EFW) or abdominal circumference (AC) below the 3rd percentile or an EFW or AC below the 10th percentile, in conjunction with an abnormal umbilical Doppler (pulsatility index >95th percentile) or an abnormal cerebro-placental ratio (CPR) (<5th percentile). Late FGR is the term used to describe a diagnosis made after the 32nd week of pregnancy.[2] Fetuses initially classified within the 3rd–10th percentile range but showing normal Doppler parameters on follow-up assessments were excluded before data analysis, ensuring that only cases meeting the full FGR criteria were analyzed. The first day of the most recent menstrual cycle and/or the fetal crown-rump length, measured during the first trimester and confirmed by ultrasound examinations, were used to determine the gestational age. A control group was selected for each FGR patient to ensure comparability in gestational and maternal age. Participants in the study were between 32 and 37 weeks of gestation; patients identified beyond 37 weeks were excluded because the DDA range is reported in the literature as up to 37 weeks.[10] Exclusion criteria included patients with chronic maternal diseases (such as diabetes mellitus or thyroid dysfunction), smoking, alcohol consumption, presence of congenital anomalies and existing obstetric complications other than FGR (such as pre-eclampsia, oligohydramnios or gestational diabetes mellitus). The control group consisted of pregnancies with normal biometric parameters and Doppler findings, without any maternal comorbidities or obstetric complications. Doppler measurements for both groups were performed at the time of diagnosis for FGR cases and at the corresponding gestational week for the control group. All study participants provided demographic information, such as maternal age, weight attained during pregnancy, body mass index (BMI), and history of pregnancy (gravidity, parity, and abortion).

Patients underwent transabdominal sonography performed by an experienced perinatologist using a Voluson S10 Expert sonography machine (GE Healthcare, Milwaukee, WI), during the diagnosis. UA pulsatility index (PI), systolic/diastolic UA ratio (S/D), MCA Doppler peak systolic velocity (PSV), S/D and PI, UtA Doppler S/D and PI, CPR, UCR, CPUR, and DDA data were recorded. Formulated with CPR: MCA PI/ UA PI, UCR: UA PI/ MCA PI and CPUR: CPR/ UtA PI.[4,12,13] When there was no fetal movement and no respiration, the UA Doppler was recorded at the free portion of the umbilical cord, away from the umbilical cord insertion point. The probe was positioned vertically on both sides of the lower uterine segment in order to measure the maternal UtA, and the waveform was measured within 1 cm of the location where the UtA crossed the external iliac artery. An insonation angle of less than 30° in the section of the proximal MCA 2 mm from its origin in the internal carotid artery was used to calculate the MCA Doppler.[14] In the obtained MCA Doppler curve, the dicrotic notch, the end-diastolic velocity and the time between both points were determined. The DDA was calculated using the following formula: 1/2 (DN + D) Δt (Fig. 1).[10] The single deepest pocket (SDP) method was used to estimate amniotic fluid volume.[15]

The follow-up and treatment protocol for FGR in our clinic complies with the guidelines of the Society for Maternal-Fetal Medicine (SMFM).[16] FGR patients were delivered in our clinic at 37 weeks if no other fetal or maternal pathologies were present. Date of birth, birth weight, APGAR 1/APGAR 5 scores and all neonatal morbidities were recorded. Composite adverse neonatal outcomes included neonatal sepsis, the need for mechanical ventilation, the need for continuous positive airway pressure (CPAP), a 5th-minute APGAR score below 7, birth weight below 2000 g, and low neonatal cord blood pH.

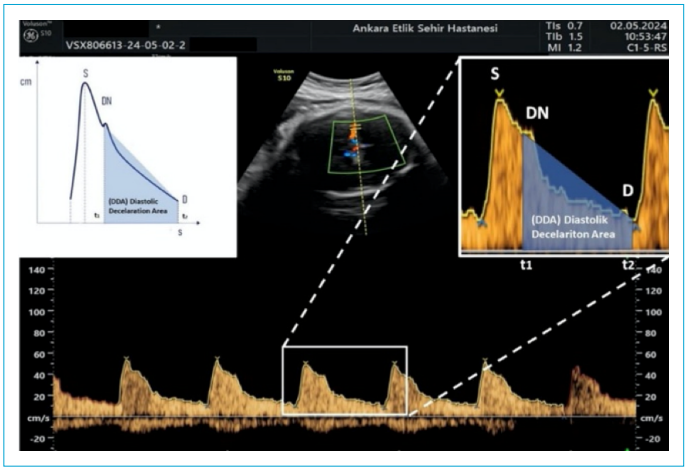

Figure 1. DDA is defined by DN: Dicrotic notch; D: End diastolic velocity and Δt: (t2–t1). DDA=½ (DN + D) Δt.

Statistical Analysis

The number of persons to be included in the study was determined using the G-Power 3.1.9.7 program. When calculating the estimated sample size, the DDA was used as the primary variable. The sample size was calculated using Student's Paired Test with a power of 80%, a probability of error of α=0.05 and a Cohen effect size of 'medium'. Accordingly, the study was planned to be conducted with a total of eighty patients, forty of whom were to be in both groups.

For all statistical analyses, RStudio was used to examine the data. To determine whether the variables had a normal distribution, they were analyzed using both visual and analytical methods, particularly the Kolmogorov-Smirnov/ Shapiro-Wilk's test. For data that was regularly distributed, descriptive analysis was used, which included means and standard deviations. Independent sample t-tests were used to compare group parameters. Medians and quartiles (Q1-Q3) were used in descriptive analysis for numerical data that was not normally distributed, and Mann-Whitney U tests were used for intergroup comparisons. Descriptive analysis was performed on categorical variables using percentage and frequency measures. When the chi-square test's assumptions were not fulfilled because of low anticipated cell counts, the connection between categorical variables was evaluated using either the chi-square test or Fisher's exact test. A ROC (Receiver Operating Characteristics) curve analysis was used to assess the prediction ability of several predictors for adverse neonatal outcomes. A p-value below 0.05 was considered statistically significant.

Results

Table 1 displays the traits and perinatal results of the pregnant research participants. The two groups were identical in terms of maternal age, gravidity, parity, weight gained during pregnancy, and the gestational week of ultrasound examination (p=0.917, p=0.360, p=0.237, p=0.209, p=0.062, respectively). However, there was a substantial difference in the BMI, with the control group having a higher BMI (p=0.001). The median gestational week for FGR patients in this study was 34 (33–35) weeks. The FGR group had higher values of UA PI, UA S/D, UtA PI, and UtA S/D in the ultrasonographic evaluation, while the control group had greater SDP (p=0.001, p=0.008, p=0.012, p=0.008, p=0.020). In all groups, the MCA Doppler values for PI, S/D, and PSV were similar (p=0.050, p=0.109, p=0.821, respectively). However, the FGR group had much lower composite Doppler measures like CPUR and CPR. On the other hand, UCR and DDA values were considerably greater in the FGR group (p<0.001, p<0.001, p<0.001, p<0.001). While gestational age and birth weight were significantly lower in the

Table 1. Maternal characteristics and perinatal outcomes of the pregnant woman included in the study

	Control n=45	FGR n=45	p
Maternal age (year)	27±4.8	27±5.3	0.917□
BMI at during test (kg/m2)	30.1 (26.7-32.9)	26 (24.9-28.1)	**0.001¥**
Weight gained during pregnancy (kg)	11.9±4.12	10.8±3.88	0.209□
Gravida	2 (1-3)	1 (1-2)	0.360¥
Parity	0 (0-1)	0 (0-1)	0.237¥
Week in which USG was performed	34 (33-36)	35 (34-36)	0.062¥
SDP (mm)	50±11	44±14	**0.020Φ**
UA S/D	2.51 (2.21-2.76)	2.62 (2.34-3.36)	**0.008¥**
UA PI	0.86 (0.78-0.98)	0.98 (0.85-1.16)	**0.001¥**
UtA S/D	1.85 (1.69-2.21)	2.20 (1.79-3.04)	**0.008¥**
UtA PI	0.70 (0.58-0.94)	0.97 (0.62-1.26)	**0.012¥**
MCA PSV (cm/s)	48 (39-55)	46 (38-55)	0.821¥
MCA S/D	5.45 (4.36 (6.79)	4.87 (3.69-6.35)	0.109¥
MCA PI	1.70±0.314	1.56±0.368	0.050□
CPR	1.99±0.470	1.60±0.491	**<0.001Φ**
CPUR	2.67 (1.87-3.59)	1.74 (1.03-2.72)	**<0.001¥**
UCR	0.49 (0.44-0.61)	0.61 (0.52-0.83)	**<0.001¥**
DDA	5.80 (5.22-6.45)	7.10 (5.73-8.76)	**<0.001¥**
Gestational age at delivery (week)	39 (38-40)	37 (36-37)	**<0.001¥**
Birth weight (gram)	3200 (2830-3455)	2240 (2018-2380)	**<0.001¥**
Preterm birth (<37 week)	4 (8.9)	18 (40)	**0.001£**
Birth method			0.072£
Normal spontaneous vaginal birth	20(44.4)	15 (33.3)	
Primary cesarean section	17 (37.8)	27 (60)	
Previous cesarean section history	8 (17.8)	3(6.7)	
Female gender	25 (55.6)	25 (55.6)	N/A£
Fetal distress	6 (13.3)	12 (26.7)	0.188£
APGAR Score at 1st minute	9 (9-9)	8 (7-9)	**<0.001¥**
APGAR Score at 5th minute	10 (10-10)	9 (8-10)	**<0.001¥**
NICU admission	5 (11.1)	19 (42.2)	**0.002£**
TTN	3 (6.7)	10 (22.2)	0.072£
Respiratory distress syndrome	0 (0)	4 (8.9)	0.117£
Need for CPAP	4 (8.9)	13 (28.9)	**0.031£**
Need for mechanical ventilator	0 (0)	5 (11.1)	0.056£
Need for phototherapy	1 (2.2)	3 (6.7)	0.616£
Neonatal sepsis	0 (0)	3 (6.7)	0.242£
Neonatal hematocrit (%)	54±4.2	56±5.6	0.124□
Neonatal cord blood pH	7.42 (7.37-7.44)	7.32 (7.23-7.38)	**0.009¥**
Composite adverse neonatal outcomes	5 (11.1)	19 (42.2)	**0.002£**

Data are expressed as mean±SD or median and quartiles (Q1-Q3 where appropriate. A p value of <0.05 indicates a significant difference. Statistically significant p-values are in bold. □Student t test, ¥ Mann-Whitney U test, £ Chi-squared test. FGR: Fetal growth restriction; BMI: Body mass index; SDP: Single deepest pocket; UA S/D: Umblical arterial systolic/diastolic ratio; UA PI: Umblical arterial pulsatility index; UtA S/D: Uterine artery systolic/diastolic ratio; UtA PI: Uterine artery pulsatility index; MCA PSV: Middle cerebral artery peak systolic velocity; MCA S/D: Middle cerebral artery systolic/diastolic ratio; MCA PI: Middle cerebral artery pulsatility index; CPR: Cerebroplacental ratio; CPUR: Cerebralplacentaluterine ratio; UCR: Umbilicalcerebral ratio; DDA: Diastolic deceleration area; NICU: Neonatal intensive care unit; TTN: Transient tachypnea of the newborn; CPAP: Continuous positive airway pressure. Composite adverse neonatal outcomes: Neonatal sepsis, need for mechanical ventilator, need for CPAP, 5th minute APGAR below 7, birth weight below 2000 g, neonatal low cord blood pH.

FGR group than in the control group, the rate of preterm births was higher (p<0.001, p<0.001, p=0.001). Both groups had similar delivery methods and fetal distress (p=0.072, p=0.188, respectively). Transient tachypnea of the newborn (TTN), respiratory distress syndrome (RDS), phototherapy requirement, neonatal sepsis rate, need for

mechanical ventilator and neonatal hematocrit levels were comparable in both groups when comparing perinatal outcomes (p=0.072, p=0.117, p=0.616, p=0.242, p=0.056, p=0.124, respectively). In addition, the APGAR values of the first and fifth minute and the pH value of the umbilical cord blood were significantly lower in the FGR group than in the control group. (p<0.001, p<0.001, and p=0.009, respectively). Composite adverse neonatal outcomes, neonatal intensive care unit admissions, and CPAP were more common in the FGR group than in the control group (p=0.002, p=0.002, and p=0.031).

Table 2 displays the results of the receiver operating characteristic (ROC) study done for composite Doppler indices. CPR, CPUR, UCR, and DDA were statistically substantially linked to adverse neonatal outcomes among these Doppler measures. With a sensitivity of 96% and a specificity of 32% (p=0.008), the cut-off value for CPR was ≤2.11. With a sensitivity of 54% and a specificity of 85% (p=0.018), the cut-off value for CPUR was ≤1.36. With a sensitivity of 96% and a specificity of 31% (p=0.008), the cut-off value for UCR was more than 0.46. With a sensitivity of 50% and a specificity of 88% (p=0.035), the cut-off value for DDA was more than 7.23 (Fig. 2).

Table 3 displays the results of the ROC analysis that was conducted for individual Doppler parameters. MCA PI and MCA S/D were statistically substantially linked to adverse neonatal outcomes among these Doppler measures. With a sensitivity of 71% and a specificity of 71% (p=0.003), the cut-off value for MCA PI was ≤1.52. The MCA S/D cut-off value was ≤4.09, with a 54% sensitivity and an 82% specificity

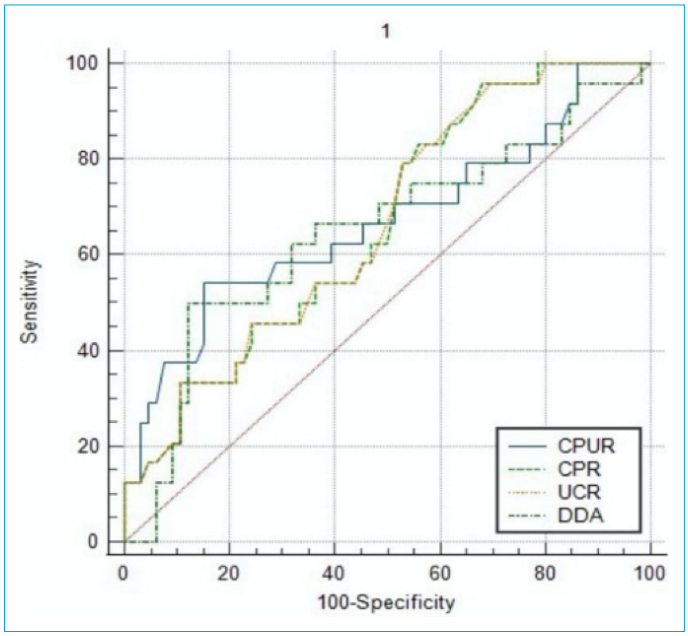

Figure 2. Receiver operating characteristic (ROC) curves to assess the usefulness of cerebroplacental ratio (CPR), umbilicalcerebral ratio (UCR), cerebralplacentaluterine ratio (CPUR) and diastolic deceleration area (DDA).

Table 2. Predictive roc analysis results of composite doppler indices for composite adverse neonatal outcomes

	AUC	CI (95%)	Cut-off	p	Sensitivity (%)	Specificity (%)
CPR	0.664	0.556-0.760	≤2.11	**0.008**	96	32
CPUR	0.669	0.562-0.765	≤1.36	**0.018**	54	85
UCR	0.664	0.557-0.760	>0.46	**0.008**	96	31
DDA	0.649	0.541-0.747	>7.23	**0.035**	50	88

CPR: Cerebroplacental ratio; CPUR: Cerebralplacentaluterine ratio; UCR: Umbilicalcerebral ratio; DDA: Diastolic deceleration area. Composite adverse neonatal outcomes: Neonatal sepsis, need for mechanical ventilator, need for CPAP, 5th minute APGAR below 7, birth weight below 2000 g, neonatal low cord blood pH.

Table 3. Predictive ROC analysis results of individual doppler parameters for composite adverse neonatal outcomes

	AUC	CI (95%)	Cut-off	p	Sensitivity (%)	Specificity (%)
MCA PI	0.693	0.586-0.786	≤1.52	**0.003**	71	71
MCA S/D	0.693	0.587-0.786	≤4.09	**0.002**	54	82
UA PI	0.534	0.426-0.640	>1.13	0.669	33	89
UA S/D	0.552	0.444-0.657	>2.91	0.506	46	82
UtA PI	0.633	0.525-0.732	>1.06	0.073	54	80
UtA S/D	0.633	0.525-0.732	>2.59	0.063	50	82

MCA PI: Middle cerebral artery pulsatility index; MCA S/D: Middle cerebral artery systolic/diastolic ratio; UA S/D: Umblical arterial systolic/diastolic ratio; UA PI: Umblical arterial pulsatility index; UtA PI: Uterine artery pulsatility index; UtA S/D: Uterine artery systolic/diastolic ratio. Composite adverse neonatal outcomes: Neonatal sepsis, need for mechanical ventilator, need for CPAP, 5th minute APGAR below 7, birth weight below 2000 g, neonatal low cord blood pH.

(p=0.002). Adverse neonatal outcomes were not linked to uterine artery S/D and PI levels or umbilical artery S/D and PI values.

Discussion

We showed in this study that adverse neonatal outcomes were statistically significant with a novel Doppler parameter, DDA area, and that various Doppler parameters contributed to the prediction of adverse neonatal outcomes in individuals with FGR. For CPR, the cut-off value was ≤2.11, and the sensitivity and specificity were 96% and 32%, respectively. CPUR's cut-off value was ≤1.36, and its sensitivity and specificity were 54% and 85%, respectively. The UCR cut-off value was more than 0.46, and the sensitivity and specificity were 96% and 31%, respectively. DDA's cut-off value was more than 7.23, and its sensitivity and specificity were 50% and 88%, respectively.

Detecting intrauterine fetal risks in FGR is extremely important to improve pregnancy outcomes in affected fetuses.[17] Doppler parameters used for this purpose in clinical practice serve as valuable guides. It is assumed that the Doppler changes in the fetus develop in a certain order.[18] Placental insufficiency and the resulting fetal hypoxia lead to an increase in PI, S/D and RI values during umbilical artery Doppler evaluation.[19,20] A brain-protective effect occurs when cerebral blood flow increases in response to these alterations in the umbilical artery Doppler. The brain-protective effect is accompanied by cerebral vasodilation, which can be monitored in the fetus via MCA Doppler imaging.[4] MCA PI values decrease with this change.[21] The FGR group in our study had higher umbilical artery Doppler values (S/D and PI). In contrast to previous investigations, the FGR and control groups' MCA PSV, S/D, and PI values were comparable. MCA Doppler S/D and PI indices were associated with adverse neonatal outcomes, while there was no correlation between umbilical artery Doppler scores and adverse neonatal outcomes. Placental dysfunction and impaired trophoblast invasion in patients with FGR lead to increased resistance in the maternal spiral arteries. Consequently, uterine artery Doppler parameter values increase.[22,23] Ghosh and Gudmundsson's[24] work highlighted the significance of uterine artery Doppler in FGR patients by finding a link between UtA Doppler and a poor perinatal outcome in patients with normal UA Doppler. The FGR group in our study had considerably higher uterine artery Doppler S/D and PI values, which were not linked to adverse neonatal outcomes.

Although placental insufficiency is the primary cause of FGR pathology, it is known that FGR does not occur in every case of placental insufficiency.[25] This scenario increases interest in combined Doppler assessments, raising the question of whether fetal and maternal Doppler measurements can identify hidden placental insufficiency. In their study, Gramellini et al.[25] compared the CPR values in patients with FGR. They discovered that fetal hypoxemia and an increased risk of long-term neurodevelopmental impairment are associated with CPR, which integrates MCA Doppler and umbilical artery Doppler. Later studies reached similar conclusions, demonstrating a link between CPR and adverse perinatal outcomes, leading to its widespread use in patients with FGR.[4,21,26] CPUR, a combined Doppler parameter that incorporates uterine artery Doppler into the CPR ratio, was studied in patients with FGR by MacDonald et al.[12] CPUR was found to be more significant in predicting adverse perinatal outcomes than CPR and UCR values. In our study, FGR patients had significantly lower UCR values and significantly higher CPR and CPUR values. Adverse neonatal outcomes were also associated with combined Doppler parameters. Among these parameters, CPUR was the strongest combined Doppler parameter associated with adverse neonatal outcomes.

Although these studies on FGR focus on Doppler parameters to predict the outcome of affected pregnancies, adverse perinatal outcomes can also be observed in pregnant women with normal Doppler values. This shows that the actual role of ultrasound in patients with FGR is not yet clear and leads to new research. Building upon the concept that cerebral vasodilation plays a crucial role in fetal adaptation to hypoxia, Ignatov et al.[10] introduced the Diastolic Deceleration Area as a novel Doppler parameter to better quantify changes in fetal cerebral blood flow. Their study demonstrated that DDA, which is calculated based on the area between the dicrotic notch and the end-diastolic velocity in the middle cerebral artery waveform, correlates with fetal oxygen deficiency. By analyzing third-trimester nomograms, they established reference ranges for DDA and suggested that this parameter could serve as an independent tool for identifying fetal hypoxia, either alone or in combination with other Doppler indices. Their preliminary findings indicated that DDA has the potential to improve fetal monitoring in late pregnancy. We attempted to demonstrate this new Doppler parameter in patients with FGR, and as a result, we found that the DDA interval is a significant parameter in the diagnosis of FGR and is associated with adverse neonatal outcomes. The area under the curve (AUC) value of DDA is 0.649, which is slightly lower than other Doppler indices such as CPR and UCR, but DDA appears to have a high specificity with a sensitivity of 50% and a specificity of 88%. In particular, in terms of specificity, DDA has the highest specificity among the parameters (32% for CPR, 31% for UCR, 85% for CPUR, 71% for MCA PI,

82% for MCA S/D). High specificity is particularly valuable in clinical decision-making, as it minimizes the likelihood of false-positive results, thereby reducing unnecessary interventions and hospitalizations. This shows that DDA can accurately exclude adverse neonatal outcomes. The cut-off point of DDA >7.23 indicates a severe change in fetal blood flow and may be an important indicator of fetal hypoxia or hemodynamic stress. Although it reflects the adaptive response of the fetal circulation, like other Doppler parameters, the high specificity of DDA indicates that this parameter can more accurately identify high-risk fetuses and play an important role in clinical decision-making. Due to its high specificity, DDA can be considered a valuable supplementary parameter for predicting poor neonatal outcomes in pregnancies affected by fetal growth restriction, despite its limited sensitivity for predicting adverse neonatal outcomes. This highlights the potential of DDA in clinical practice for enabling closer monitoring and early intervention, especially in high-risk cases.

The primary limitation of this study is its generalizability to broader populations, as it was conducted in a single-center setting with a relatively homogeneous patient cohort. While the sample size was determined based on power analysis and is statistically sufficient, the findings may not be directly applicable to diverse populations with varying demographic, clinical, and regional characteristics. Additionally, potential variations in Doppler indices over time were not accounted for, which could influence the predictive value of the parameters studied. Future multicenter studies with larger and more diverse populations are warranted to validate our results and enhance their applicability to clinical practice. Our study's strength is that it assessed several Doppler measures in patients with late-onset FGR in addition to being a prospective study. Additionally, this study is the first to look into the DDA range in patients with FGR.

Conclusion

In this study, we demonstrated the significance of the Diastolic Deceleration Area as a novel Doppler ultrasound parameter in predicting adverse neonatal outcomes in fetuses with late-onset fetal growth restriction. Among the Doppler indices analyzed, the cerebroplacental ratio exhibited the highest sensitivity (96%), while the Diastolic Deceleration Area demonstrated the highest specificity (88%) at a cut-off value of >7.23, making it a particularly valuable tool for identifying fetuses at high risk. Despite its relatively lower sensitivity (50%), the high specificity of DDA suggests its potential as a supplementary parameter to existing Doppler indices for clinical decision-making.

The findings underscore the importance of using combined Doppler parameters, such as CPR, CPUR, and UCR, alongside DDA for a comprehensive assessment of fetal well-being. This integrated approach could enhance the early detection of at-risk fetuses, enabling timely interventions to improve perinatal outcomes. Further multicenter studies are warranted to validate these findings and expand their clinical applicability.

Disclosures

Ethics Committee Approval: The study was approved by the Ankara Etlik City Hospital Clinical Research Ethics Committee No:1 (date: 20.12.2023, no: AESH-EK1-20/12/2023-770).

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declared that they have no conflict of interest.

Authorship Contributions: Concept – G.K., Z.S.; Design – G.K.; Supervision– H.L.K., G.D.; Materials – G.A., M.B., S.A.; Data Collection and/or Processing – B.T.C., N.V.T.; Analysis and/or Interpretation – S.T.S., A.A.F., U.K.; Literature Review – G.K., R.T.A.; Writing – G.K.; Critical Review – G.K.

Funding Statement: The authors declared that they received no financial support for this article's research, authorship, and publication.

Use of AI for Writing Assistance: The authors declared that no technologies that support artificial intelligence (AI) (e.g. large language models, chatbots or image generators) were used in the creation of the submitted work.

Informed Consent: Written informed consent was obtained from the patients who took part in the trial.

References

1. Lubchenco LO, Hansman C, Dressler M, Boyd E. Intrauterine growth as estimated from liveborn birth-weight data at 24 to 42 weeks of gestation. Pediatrics 1963;32:793–800. [CrossRef]
2. Gordijn SJ, Beune IM, Thilaganathan B, Papageorghiou A, Baschat AA, Baker PN, et al. Consensus definition of fetal growth restriction: a Delphi procedure. Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol 2016;48:333–9. [CrossRef]
3. Chew LC, Verma RP. Fetal Growth Restriction. StatPearls, Treasure Island (FL): StatPearls Publishing; 2023.
4. Coenen H, Braun J, Köster H, Möllers M, Schmitz R, Steinhard J, et al. Role of umbilicocerebral and cerebroplacental ratios in prediction of perinatal outcome in FGR pregnancies. Arch Gynecol Obstet 2022;305:1383–92. [CrossRef]
5. Kale RM, Tirupathi RG, Sheela SR. Role of ultrasonography and color doppler in the assessment of high-risk pregnancies and their accuracy in predicting fetal outcome. Cureus 2023;15:e39017. [CrossRef]
6. Srirambhatla A, Mittal S, Vedantham H. Efficacy of pulsatility index of fetal vessels in predicting adverse perinatal outcomes in

fetuses with growth restriction – differences in early- and late-onset fetal growth restriction. Mædica 2022;17:107–15. [CrossRef]
7. Yılmaz C, Melekoğlu R, Özdemir H, Yaşar Ş. The role of different Doppler parameters in predicting adverse neonatal outcomes in fetuses with late-onset fetal growth restriction. Turk J Obstet Gynecol 2023;20:86–96. [CrossRef]
8. Stampalija T, Arabin B, Wolf H, Bilardo CM, Lees C; TRUFFLE investigators. Is middle cerebral artery Doppler related to neonatal and 2-year infant outcome in early fetal growth restriction? Am J Obstet Gynecol 2017;216:521.
9. Gölbaşı C, Gölbaşı H, Kocahakimoğlu Gültekin C, Gülseren V, Zeytinli Akşit M, Bayraktar B, et al. Ischemia modified albumin levels in intrauterine growth restriction: levels are increased in fetal cord blood but not in maternal blood. Ginekol Pol 2022;93:993–8. [CrossRef]
10. Ignatov PN, Neykova KK, Yordanova-Ignatova T. Diastolic deceleration area in the fetal MCA: a new Doppler parameter. J Matern Fetal Neonatal Med 2023;36:2206939. [CrossRef]
11. Politi MT, Ghigo A, Fernández JM, Khelifa I, Gaudric J, Fullana JM, et al. The dicrotic notch analyzed by a numerical model. Comput Biol Med 2016;72:54–64. [CrossRef]
12. MacDonald TM, Hui L, Robinson AJ, Dane KM, Middleton AL, Tong S, et al. Cerebral–placental–uterine ratio as novel predictor of late fetal growth restriction: prospective cohort study. Ultrasound Obstet Gynecol 2019;54:367–75. [CrossRef]
13. Doğan O, Pulatoğlu Ç, Başbuğ A, Ellibeş Kaya A, Yassa M. Discriminating performance of early uterine and cervical artery pulsatility and resistivity in pre-invasive cervical lesions. Sisli Etfal Hastan Tip Bul 2018;52:206–11. [CrossRef]
14. Bhide A, Acharya G, Baschat A, Bilardo CM, Brezinka C, Cafici D, et al. ISUOG Practice Guidelines (updated): use of Doppler velocimetry in obstetrics. Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol 2021;58:331–9. [CrossRef]
15. Hughes DS, Magann EF. Antenatal fetal surveillance "Assessment of the AFV." Best Pract Res Clin Obstet Gynaecol 2017;38:12–23. [CrossRef]
16. Society for Maternal-Fetal Medicine Publications Committee; Berkley E, Chauhan SP, Abuhamad A. Doppler assessment of the fetus with intrauterine growth restriction. Am J Obstet Gynecol 2012;206:300–8. Erratum in: Am J Obstet Gynecol 2012;206:508. Erratum in: Am J Obstet Gynecol 2015;212:246. [CrossRef]
17. Adiyaman D, Atakul BK, Kuyucu M, Toklu G, Golbasi H, Koc A, et al. Can fetal fractions in the cell-free DNA test predict the onset of fetal growth restriction? J Perinat Med 2020;48:395–401. [CrossRef]
18. Oros D, Figueras F, Cruz-Martinez R, Padilla N, Meler E, Hernandez-Andrade E, et al. Middle versus anterior cerebral artery Doppler for the prediction of perinatal outcome and neonatal neurobehavior in term small-for-gestational-age fetuses with normal umbilical artery Doppler. Ultrasound Obstet Gynecol 2010;35:456–61. [CrossRef]
19. Maulik D, Mundy D, Heitmann E, Maulik D. Umbilical artery Doppler in the assessment of fetal growth restriction. Clin Perinatol 2011;38:65–82. [CrossRef]
20. Adedo AA, Arogundade RA, Okunowo AA, Idowu BM, Oduola-Owoo LT. Comparative study of the umbilical artery doppler indices of healthy and growth-restricted foetuses in Lagos. J West Afr Coll Surg 2022;12:63–9. [CrossRef]
21. Rizzo G, Mappa I, Bitsadze V, Słodki M, Khizroeva J, Makatsariya A, et al. Role of Doppler ultrasound at time of diagnosis of late-onset fetal growth restriction in predicting adverse perinatal outcome: prospective cohort study. Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol 2020;55:793–8. [CrossRef]
22. Triunfo S, Parra-Saavedra M, Rodriguez-Sureda V, Crovetto F, Dominguez C, Gratacós E, et al. Angiogenic factors and Doppler evaluation in normally growing fetuses at routine third-trimester scan: prediction of subsequent low birth weight. Fetal Diagn Ther 2016;40:13–20. [CrossRef]
23. Cruz-Martinez R, Savchev S, Cruz-Lemini M, Mendez A, Gratacos E, Figueras F. Clinical utility of third-trimester uterine artery Doppler in the prediction of brain hemodynamic deterioration and adverse perinatal outcome in small-for-gestational-age fetuses. Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol 2015;45:273–8. [CrossRef]
24. Ghosh GS, Gudmundsson S. Uterine and umbilical artery Doppler are comparable in predicting perinatal outcome of growth-restricted fetuses. BJOG Int J Obstet Gynaecol 2009;116:424–30. [CrossRef]
25. Gramellini D, Folli MC, Raboni S, Vadora E, Merialdi A. Cerebral-umbilical Doppler ratio as a predictor of adverse perinatal outcome. Obstet Gynecol 1992;79:416. [CrossRef]
26. Odibo AO, Riddick C, Pare E, Stamilio DM, Macones GA. Cerebroplacental Doppler ratio and adverse perinatal outcomes in intrauterine growth restriction. J Ultrasound Med 2005;24:1223–8. [CrossRef]