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INTERARTERY DISCORDANCE IN FETUSES WITH GROWTH RESTRICTION

Authors:
John W. Ross, DO[1]; A. Dhanya Mackeen, MD, MPH[1]; Alexandria Betz, DO[1]; Wen Feng, MS[2]; Jay J. Bringman, MD, MBA[1]; Michael J. Paglia, MD, PhD[1]

Geisinger, Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine (1), and Biostatistics Core (2), 100 N. Academy Ave, Danville, Pennsylvania, 17821 USA

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Abstract

OBJECTIVES: Our objectives were two-fold: 1) to determine the frequency of discordant umbilical artery Doppler systolic to diastolic (S/D) ratios in the individual umbilical arteries of growth-restricted fetuses and 2) to examine the impact of the frequency of discordance on clinical outcomes.

METHODS: This was a prospective, observational study of growth-restricted fetuses. Doppler velocimetry was performed weekly and two S/D ratios were obtained for each fetal umbilical artery. Inter-artery discordance was defined as a difference in measurement categories (i.e., normal, elevated, absent, reversed) between the arteries. The number of abnormal measurements per visit was summed to 0-4 out of 4 values. A composite average number of abnormal Doppler measurements was calculated and fetuses were stratified based on degree of average number of abnormalities in increments of 25%: 0-<25%, 25-<50%, 50-<75%, and 75-100% abnormality.

RESULTS: Of a total 241 fetuses (1762 visits), 110 (45.6%) had abnormal UAD flow and 189 (66%) demonstrated discordance. Abnormal values were noted in only one artery in 53% (n=151) of visits. Fetuses with any abnormal Doppler testing had smaller birthweights compared to fetuses with consistently normal testing (2485g vs 2623g, p <0.01); birthweight decreased as composite average of abnormal measurements increased (p = 0.03).

CONCLUSION: The majority (66%) of fetuses with abnormal testing demonstrated UAD discordance. Up to 53% of fetuses could have been misdiagnosed if only one artery was tested. Fetuses with a higher frequency of Doppler abnormalities had lower birthweights. We propose obtaining two measurements from each umbilical artery in growth-restricted fetuses. .

Key words: *fetal growth restriction, umbilical artery systolic/diastolic ratios, estimated fetal weight, discordance*

INTRODUCTION

Fetal growth restriction (FGR) is associated with an increased risk of fetal demise and neonatal morbidity and mortality.[1] Umbilical artery Doppler (UAD) testing is the standard management tool that helps differentiate small for gestational age fetuses from those with pathologic growth restriction due to placental insufficiency.[2,3] Numerous studies have correlated abnormal UAD systolic to diastolic (S/D) ratio assessments with adverse perinatal outcomes; S/D ratio assessments have been established as an effective parameter for monitoring growth restricted fetuses.[4-6] Both the Society for Maternal-Fetal Medicine and the American College of Obstetricians and Gynecologists support the use of S/D ratio assessments to help establish delivery timing in growth restricted pregnancies.[1,2,7] In the setting of a growth restricted fetus with elevated S/D ratios, delivery is recommended earlier in gestation as compared to 38-39 weeks in the setting of normal S/D ratios.[7]

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Previous cross-sectional studies have demonstrated flow[8] and size discordance[9,10] between the two umbilical arteries. However, these studies were not limited to pregnancies complicated by fetal growth restriction; this limits their applicability in clinical practice as Doppler velocimetry of the fetal umbilical arteries is not typically assessed in normally grown fetuses. These prior studies do raise the concern that evaluation of a single artery in a growth restricted fetus may not delineate the full clinical picture.

As the primary purpose of serial Doppler examination of growth restricted fetuses is to help decrease fetal morbidity and optimize delivery timing (balancing the risks of prematurity versus in utero fetal demise), it is imperative to ensure that obstetric ultrasound providers are appropriately interrogating the fetal umbilical arteries and that the implications of abnormal testing are clear with regard to fetal and neonatal outcomes. In our clinical practice, we noticed that the UAD S/D ratios often differ between the

Corresponding author: John W. Ross, Do; 100 N. Academy Ave, Danville, PA 17822
Phone: 570-271-860 (work); Email: jwross@geisinger.edu

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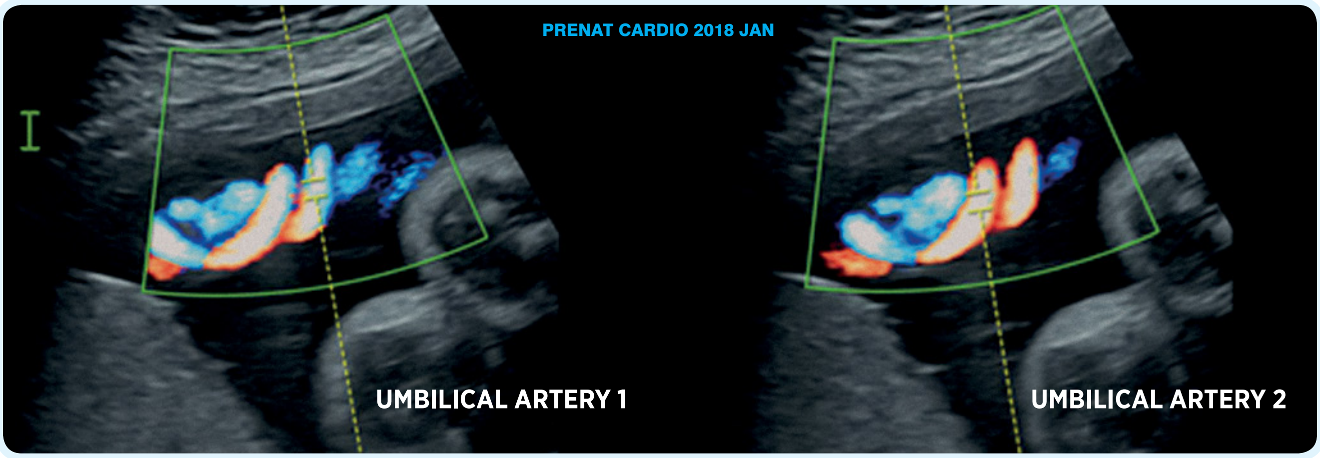

Fig 1.Interrogation of the individual umbilical arteries

individual umbilical arteries, yielding a mix of both normal and abnormal results. This creates a diagnostic dilemma that may lead to earlier intervention and more intensive fetal testing, which may or may not be warranted. To our knowledge, studies have not assessed whether one or both umbilical arteries should be interrogated in the fetus with FGR; therefore, the extent to which discordance affects this population is unclear. Our objectives were two-fold: to determine the extent to which UAD S/D ratios are discordant between the individual umbilical arteries in fetuses with growth restriction; and to evaluate the effect of increased frequency of Doppler abnormalities on clinical outcomes, such as neonatal birthweight.

MATERIALS AND METHODS

This is an Institutional Review Board (IRB) approved prospective, observational study of growth-restricted fetuses performed by the Division of Maternal-Fetal Medicine (MFM) at Geisinger from 2012 to 2015. FGR was defined as an estimated fetal weight less than the 10th percentile based on the Hadlock[11] growth curve incorporating the abdominal circumference, femur length, biparietal diameter, and head circumference.

Women age 18 years or older carrying a singleton fetus with a 3-vessel umbilical cord were included in the study. We excluded multifetal gestations, fetuses with a single umbilical artery, women aged less than 18 years and non-English speaking patients. We also excluded visits in which the MFM physician interpreting the ultrasound image could not confirm that the individual arteries were interrogated, whether this was secondary to poor maternal acoustics, fetal position or otherwise.

At our institution, once a fetus is identified as being growth-restricted, MFM evaluates fetal well-being by ultrasound weekly. MFM surveillance includes weekly UAD interrogation and biophysical profile, while growth is assessed every 3 weeks. Fetuses greater than 28 weeks gestation also have non-stress testing performed approximately 3 days after the biophysical profile to achieve twice-weekly fetal surveillance. UAD measurements were obtained by one of nine registered diagnostic medical sonographers in the MFM division and interpreted by one of five board certified MFM physicians. All sonographers were specifically trained in how to assess the individual umbilical arteries by the lead author to ensure consistency with measurements. Fetal echocardiograms were performed as indicated as per the American Institute of Ultrasound Medicine (AIUM) criteria,[12] particularly in the setting of maternal cardiac disease or first-degree relative (of fetus) with a congenital heart defect.

We assessed UAD velocimetry transabdominally in a free-floating loop of umbilical cord.[13,14] Both umbilical arteries were identified in a longitudinal fashion (Figure 1) and each artery was individually interrogated using pulsed wave Doppler velocimetry with a 1-5 or 4-8 MHz curvilinear probe during periods of fetal apnea. We obtained the mean systolic peaks and diastolic troughs over multiple beats using autotrace and the S/D ratio was calculated by the GE Voluson E8. This was performed twice on each umbilical artery. We only accepted values in which the individual arteries could be clearly differentiated as is depicted in Figure 1. If there was fetal or cord movement or we could not document that the values truly represented two values from each artery, all values were repeated and the previously obtained values were not used. If repeat attempts were unsuccessful, UAD data was not entered in the study for that visit.

Though obtaining UAD S/D ratios from both arteries was considered standard of care for the Geisinger MFM Division, we obtained consent from all women who were prospectively enrolled to collect their demographic data, medical and pregnancy history, delivery, and neonatal information. Separate medical release consents were signed by women who delivered outside of Geisinger so that delivery and neonatal data could be obtained. In an effort to include the majority of the women whose fetuses were followed based on the Geisinger MFM protocol, we also obtained IRB approval to retrospectively include all women whose pregnancies were managed by the Geisinger MFM protocol prior to IRB approval of the prospective study. Departmental guidelines for management of these fetuses did not change between the two time points.

The impedance in the individual umbilical arteries was assessed for abnormalities such as elevated S/D ratios per gestational age nomograms (at or above the 95th percentile),[15] and absent or reversed end diastolic flow.[1,2,7] Inter-artery discordance was defined as a discrepancy in the results between each artery with respect to the pattern of normal or abnormal testing. In situations in which differences were noted within a single artery, discordance was assigned if the other artery did not display the same pattern of findings. Discordant results were managed based on the most abnormal Doppler finding. As some institutions assess pulsatility index (PI) values, we abstracted PI data for all patients with abnormal S/D findings.

The number of abnormal Doppler measurements per visit was summed to 0-4 out of the 4 values obtained at each visit. The sum was divided by 4 to calculate a percentage of abnormal measurements, which was then averaged across all visits for each patient to calculate a composite UAD S/D abnormality measure. Fetuses with 0% abnormal measurements were considered to have normal Doppler flow; fetuses with >0% abnormal measurements were considered to have abnormal Doppler flow. Fetuses with abnormal Doppler flow were further categorized by percentages of abnormal measures, in increments of 25%: 0-<25%, 25-<50%, 50-<75%, and 75-100% abnormality. Growth restricted fetuses with abnormal Doppler measurements at any point in the pregnancy were compared to those with persistently normal testing. We performed a test of trend analysis based on the composite average of abnormal S/D Doppler measurements that were observed throughout pregnancy.

Our study had two primary aims. The first was to determine the percentage of pregnancies in which the UAD evaluation was discordant between the two arteries. For this, we obtained two sample measurements from each of the individual fetal umbilical arteries. The second aim was to assess the implications of having 4 Doppler values upon which to base pregnancy management. To assess this latter aim, we examined the primary outcome of infant birthweight, adjusted for gestational age at delivery (using a linear regression model) and potential demographic confounders. Secondary outcomes were neonatal Apgar scores, admission to the neonatal intensive care unit (NICU), and NICU length of stay (LOS). Outcomes were examined based on the presence of normal (0/4) Doppler findings as compared to the composite average of abnormal UAD findings. Additional outcome assessments included: a description of the distribution of abnormal visits (one visit abnormal or multiple visits abnormal) with respect to single or dual vessel UAD abnormalities, birthweight (adjusted for gestational age) with respect to single or dual vessel UAD abnormalities, and the number of visits until the next abnormal S/D ratio, stratified by number of discordant findings (1/4 to 4/4) in the first abnormal visit.

Data abstraction from the electronic medical and ultrasound records were performed by two physicians (JWR and AB) who directly entered the data into an MS Access 2013 database. We collected demographic information on patients including age, highest level of education attained, race, marital status, insurance type, height, pre-pregnancy weight, parity, presence of pregnancy comorbidities (e.g., history of growth-restricted fetus, maternal hypertension or endocrinologic disorders, opioid maintenance use and asthma requiring medication beyond an albuterol inhaler), smoking status (defined as ≥ 1 cigarette per day) and illicit drug use. We collected the following information on the fetus and neonate: UAD measurements, estimated fetal weight at time of ultrasound, gestational age at the time of ultrasound and delivery, betamethasone administration, mode of delivery, and infant gender.

Descriptive statistics for each variable were inspected to identify influential points and to assess distributional assumptions. Demographic variables and other patient characteristics were compared between fetuses with normal and abnormal UAD measurements using the two-sample t, Pearson's Chi-square, and Fisher's Exact tests. Linear regression models were used to estimate the birthweight outcomes, adjusting for gestational age. Demographic characteristics that were significantly different between the groups were adjusted in the analysis of our primary outcome. A linear model was used to evaluate the trend of decreasing birthweight as the abnormal S/D ratio increased. Poisson regression models were used to evaluate the number of

Table 1. Maternal Demographics

Demographic Variable	Normal Doppler flow N = 131	Abnormal Doppler flow N = 110	P value
Age, yrs, mean ± SD	27.4 ± 6.0	28.1 ± 5.8	0.33
Education, yrs, mean ± SD	13.2 ± 2.6	12.9 ± 2.1	0.33
Race, n (%): White	117 (89.3)	104 (94.5)	0.20
Marital Status, n (%): Married	49 (37.7)	43 (39.1)	0.97
Insurance, n (%): Private	56 (43.7)	49 (44.5)	0.94
Pre-pregnancy body mass index, kg/m2, mean ± SD	28.7 ± 8.6	27.9 ± 8.8	0.51
Multiparous, n (%)	84 (64.1)	62 (56.4)	0.22
Medical comorbidities, n (%)			
Prior pregnancy complicated by fetal growth restriction	12 (9.2)	14 (12.7)	0.37
Hypertension	5 (3.8)	8 (7.3)	0.24
Diabetes mellitus	6 (4.6)	7 (6.4)	0.54
Hypothyroidism	9 (6.9)	6 (5.5)	0.65
Opioid maintenance	7 (5.3)	19 (17.3)	<0.01
Asthma requiring more than albuterol	8 (6.1)	14 (12.7)	0.08
Tobacco use, n (%)	48 (36.6)	46 (41.8)	0.41
Illicit drug use, n (%)	4 (3.1)	9 (8.2)	0.05

Table 2. Treatment and delivery variables for all growth-restricted fetuses

Variable	Normal S/D Doppler	Composite Average Abnormal S/D Doppler					P value
	N = 131	Any N = 110	<25% N = 74	25-<50% N=20	50-<75% N=10	75-100% N=6	
Betamethasone, n (%)	15 (12)	71 (65)	44 (60)	15 (75)	7 (70)	5 (83)	<0.01
Gestational age at delivery, weeks*	38.1 ± 2.4	37.8 ± 2.4	38.6 ± 1.3	36.8 ± 3.3	36.2 ± 2.9	34.6 ± 2.9	0.34
Fetal gender: Male	51 (42)	31 (31)	23 (32)	2 (12)	3 (38)	3 (50)	0.26
Mode of delivery, n (%)							
Vaginal	75 (57)	66 (60)	50 (68)	11 (55)	5 (50)	0	0.46
Cesarean	56 (43)	44 (40)	24 (32)	9 (45)	5 (50)	6 (100)	
Infant birthweight, grams*	2637 ± 556	2422 ± 584	2636 ± 419	2103 ± 640	1867 ± 600	1702 ± 636	<0.01
Adjusted infant birthweight, grams†	2623	2485	2703	2299	1986	1607	<0.01
5-minute Apgar <7, n (%)	6 (5)	6 (6)	3 (4)	2 (11)	1 (13)	0	0.73
NICU admission, n (%)	27 (21)	19 (17)	6 (8)	4 (20)	5 (50)	4 (67)	0.07
NICU LOS, days‡	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	2 (0, 32)	15 (0, 23)	0.25

** Mean ± standard deviation*
† Adjusted for gestational age and maternal opioid maintenance
‡ Median (IQR); LOS, length of stay; NICU, neonatal intensive care unit

visits until the next abnormal visit. All tests were two-sided and p-values < 0.05 were considered significant. All the analyses were performed using SAS v9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

A total of 241 fetuses were evaluated over 1860 visits. Of these visits, the interpreting physician could not confirm that the individual arteries were interrogated in 98 visits, therefore, 1762 visits were analyzed. One-hundred and ten fetuses (45.6%) had abnormal UAD measurements at some point in pregnancy. Growth-restricted fetuses with abnormal UAD findings did not differ from those with normal UAD findings with respect to demographic and clinical characteristics, except for opioid maintenance in pregnancy (Table 1). Demographics also differed only with respect to opioid maintenance in pregnancy when we compared those with versus without PI data. Additionally, the Spearman correlation coefficient between PI and S/D abnormality levels (0-<25%, 25-<50%, etc.) is 0.747 (p<.0001); this indicates a strong correlation between PI and S/D abnormality. Therefore, we can expect that we would have similar findings if we were to use PI instead of S/D.

There were 12 fetuses within our study sample with aneuploidy or anomalies, diagnosed in utero or at birth. The following 7 had normal Doppler flow: three with unilateral renal agenesis, one with cleft lip, one with giant omphalocele, one with ventricular septal defect and pericardial effusion, and one with multiple fetal anomalies and 7q32.3-7q36.3 microdeletion. The following 5 had abnormal Doppler flow: two with Monosomy X, one with trisomy 21, two with multiple fetal anomalies.

Most visits revealed concordant normal UAD values (1477/1762, 84.0%). Abnormal findings occurred in 285 visits (16.0%). There were a total of 189 visits (66.3%) with discordant abnormal findings. One hundred fifty-one (53%) of these abnormal values were noted in only one artery, while the other artery revealed normal testing. There were a total of 96 visits (33.7%) with concordant abnormal findings (Figure 2). Over 60% of fetuses that demonstrated multiple abnormal values had a subsequent normal value at some point during follow-up evaluation.

Infant birthweight was significantly lower in those with abnormal UAD (p <0.01) and this persisted after adjusting for gestational age at delivery and maternal opioid maintenance (p <0.01) (Table 2). As the composite average of abnormal Doppler values increased, infant birthweight (adjusted and unadjusted) decreased (p = 0.04 and 0.03, respectively). Gestational age at delivery, delivery mode, fetal gender, neonatal Apgar score < 7 at 5 minutes and NICU admission did not differ between the groups (Table 2). Fetuses with abnormal Doppler impedance were significantly more likely to receive betamethasone, which is consistent with the MFM protocol for management of growth-restricted fetuses. There was no difference in the number of infants admitted to the NICU based on presence or absence of abnormal Doppler testing (17% vs 21%, Table 2). However, as the composite average of abnormal Doppler values increased, so did the percent of fetuses admitted to the NICU (test of trend, p = 0.01). NICU length of stay (LOS) was not longer in those with abnormal Doppler testing.

Seventeen percent of the growth-restricted fetuses with abnormal Doppler impedance had mothers managed with opioid maintenance as compared to only 5% of those with normal Doppler testing (p < 0.01). In a set of logistic regression models predicting abnormal Doppler flow (not shown), the association between birthweight and abnormality (increasing birthweight decreases odds of abnormality, p=0.0060) did not change noticeably when adjusted for opioid maintenance (same association, p=0.0055). The association between NICU LOS and abnormality was not significant unadjusted (p=0.5613) or when adjusted for opioid maintenance (p=0.6697). The association between opioid maintenance and abnormality was significant (increased odds of abnormality) in both adjustment models (p=0.0042 for birth weight model, p=0.0053 for NICU LOS model). Therefore, though pregnancies complicated by opioid maintenance were more likely to demonstrate abnormal Doppler flow, this difference does not account for the other findings presented here.

Abnormal UAD measurements were seen in 110 fetuses over 285 visits. Abnormalities occurred in both arteries as often (53%) as in a single artery (47%). Approximately 63% of fetuses with single artery abnormalities had only one abnormal visit. Conversely, approximately 64% of those with dual artery abnormalities had multiple visits with abnormal findings. There was a significant difference in birthweight, adjusted for gestational age at delivery, when comparisons were made between those with dual artery abnormalities at one or multiple visits (p = 0.03). This was not the case for those with single artery abnormalities.

Lastly, we assessed every visit in which there was abnormal Doppler testing to determine how long it would take until that fetus had a subsequent abnormal measurement. Fetuses with 3 or 4 out of 4 abnormal values had a significantly shorter interval (median 1 week, p = 0.02 and p <0.01, respectively) to the next abnormal UAD finding as compared to fetuses with only 1 out of 4 abnormal values (median 2.3 weeks). This indicates that an abnormal result was more likely to persist in subsequent examinations if there were 3 or 4 out of 4 abnormal as compared to only 1 out of 4 abnormal values. The presence of discordant or concordant abnormal UAD findings did not affect the amount of time between visits in which abnormal UAD testing was documented.

Fig 2. Interrogation of the individual umbilical arteries

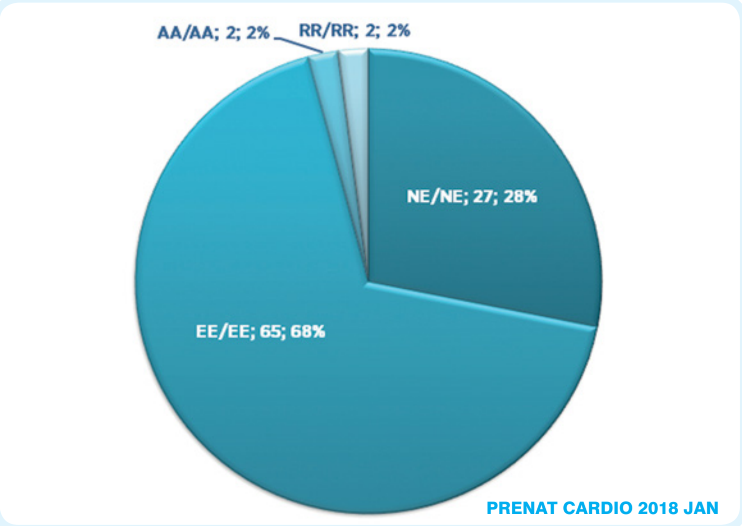

Fig 2a. Abnormal UAD Assessments: Concordant

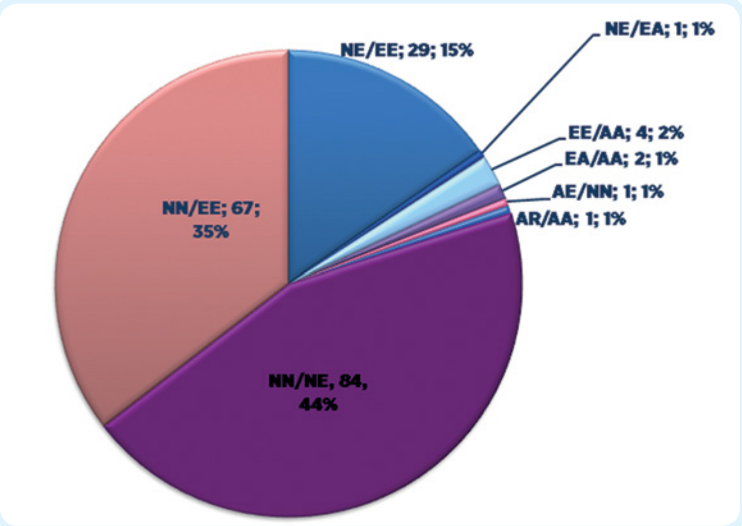

Fig 2b. Abnormal UAD Assessments: Discordant

Testing results: N (normal); E (elevated); R (reversed); A (absent).

DISCUSSION

Our study highlights several important points. First is that the majority (66.3%) of fetuses with abnormal UAD measurements display interartery discordance. Second, as the composite average of Doppler discordance increased, birthweight decreased. Third, dual artery abnormalities were more likely to persist and affect infant birthweight. Lastly, given the increased percentage of NICU admission with advancing composite Doppler abnormality, the number of abnormal Doppler measurements may have clinical implications for the infant after delivery.

We are unaware of any studies assessing inter-artery discordance in FGR fetuses. In a study of 80 normally grown fetuses, one-quarter had a disparity more than 20% (S/D maximum minus S/D minimum) between umbilical arteries.[8] This relationship decreased with advancing gestational age, so that 9% of the term pregnancies had this difference; this was attributed to biological variability in artery size and anastomoses. We noted a decrease in the percent discordance when comparing 23-26 weeks, 27-34 weeks, versus 35-39 weeks ($p < 0.05$). As in our study, Maggio et al. found that FGR fetuses with abnormal Doppler testing had lower birthweights than those with normal Doppler values, though the individual umbilical arteries were not specifically assessed.[16]

The strengths of our study include that it was prospective in a single institution, with management per a set algorithm for care during the study. All sonographers were trained to obtain UAD measurements in a similar manner. Board certified MFM physicians interpreted the UAD results at the time of the ultrasound and guided the management of care. Two physicians performed data abstraction and entry, thus limiting the potential for data entry errors. Due to the wide geographic coverage area, some patients delivered outside of our system, limiting our ability to obtain some neonatal information. Patients who delivered outside of Geisinger were asked to sign additional consent forms so that study personnel could review delivery records.. We were unable to obtain delivery records for twelve subjects; this was unlikely to affect study results as these patients were evenly distributed with normal and abnormal results. The umbilical arteries were assessed in a free loop[14], which precluded tracking abnormalities by specific artery (right or left); however, this was not the purpose of our study. Finally, while we planned to analyze the placenta and cord gases, these were inconsistently obtained (per the delivering physician's discretion), limiting the outcome analyses.

Identifying the physiologic cause for the variation in Doppler testing is an area for future research. For example, studies could evaluate for variations in placental size, cord insertion site, volume of flow per artery, umbilical artery dimensions, and Hyrtl's anastomosis and correlate this with Doppler discordance. The Hyrtl anastomosis is a vascular link between the two umbilical arteries near the placental cord insertion that provides a shunt from the artery with higher resistance to the artery with lower resistance and likely provides a mechanism for equalization of flow between the arteries.[17] Altered development of this anastomosis may result in discordant flow between the arteries.[9] The changes observed in S/D ratios over time in the FGR fetus may represent a physiologic response to improve overall blood flow or pressure regulation within the placenta.

Up to 53% of fetuses with abnormal UAD testing could have been *mis*diagnosed with normal flow if two UAD values had not been obtained from each artery. Measuring only one artery may result in a false positive or negative test, leading to inappropriate management. Though assessment of umbilical arteries is the standard of care when following a fetus with growth restriction, there is a lack of consistency as to how and which artery should be assessed. Therefore, we strongly advocate interrogation of the individual umbilical arteries with at least two measurements of each artery so that the way we interrogate the arteries becomes standardized. Fetuses with abnormal values in both arteries are more likely to have persistent abnormal results. Infant birthweight was significantly lower in those with abnormal Doppler testing; and the more abnormal measurements (out of 4) for more visits, the lower the infant birthweight.

References

1. American College of Obstetricians and Gynecologists. ACOG practice bulletin 134: Fetal growth restriction. Obstet Gynecol. 2013;121(5):1122-1133.

2. 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(4):300-308.

3. Baschat AA. Doppler application in the delivery timing of the preterm growth-restricted fetus: Another step in the right direction. Ultrasound Obstet Gynecol. 2004;23(2):111-118. doi: 10.1002/uog.989 [doi].

4. Baschat AA, Weiner CP. Umbilical artery doppler screening for detection of the small fetus in need of antepartum surveillance. Am J Obstet Gynecol. 2000;182(1 Pt 1):154-158. doi: S000293780068225X [pii].

5. Bruner JB, Levy DW, Arger PH. Doppler ultrasonography of the umbilical cord in complicated pregnancies. South Med J. 1993;86(4):418-422.

6. Boers KE, Vijgen SM, Bijlenga D, et al. Induction versus expectant monitoring for intrauterine growth restriction at term: Randomised equivalence trial (DIGITAT). BMJ. 2010;341:c7087. doi: 10.1136/bmj.c7087 [doi].

7. Spong CY, Mercer BM, D'alton M, Kilpatrick S, Blackwell S, Saade G. Timing of indicated late-preterm and early-term birth. Obstet Gynecol. 2011;118(2 Pt 1):323-333 [Review, Guideline].

8. Predanic M, Kolli J, Yousefzadeh P, Pennisi J. Disparate blood flow patterns in parallel umbilical arteries. Obstet Gynecol. 1998;91(5 Pt 1):757-760.

9. Predanic M, Perni SC. Antenatal assessment of discordant umbilical arteries in singleton pregnancies. Croat Med J. 2006;47(5):701-708.

10. Dolkart LA, Reimers FT, Kuonen CA. Discordant umbilical arteries: Ultrasonographic and doppler analysis. Obstet Gynecol. 1992;79(1):59-63.

11. Hadlock FP, Harrist RB, Sharman RS, Deter RL, Park SK. Estimation of fetal weight with the use of head, body, and femur measurements--a prospective study. Am J Obstet Gynecol. 1985;151(3):333-337. doi: 0002-9378(85)90298-4 [pii].

12. American Institute of Ultrasound in Medicine.
AIUM practice parameter for the performance of
Fetal echocardiography . 2013:2/14/2018.

13. Forouzan I, Cohen AW, Arger P. Measurement of systolic-diastolic ratio in the umbilical artery by continuous-wave and pulsed-wave doppler ultrasound: Comparison at different sites. Obstet Gynecol. 1991;77(2):209-212.

14. Mari G. Doppler ultrasonography in obstetrics: From the diagnosis of fetal anemia to the treatment of intrauterine growth-restricted fetuses. Am J Obstet Gynecol. 2009;200(6):613.e1-613.e9. doi: 10.1016/j.ajog.2008.10.054 [doi].

15. Acharya G, Wilsgaard T, Berntsen GK, Maltau JM, Kiserud T. Reference ranges for serial measurements of umbilical artery doppler indices in the second half of pregnancy. Am J Obstet Gynecol. 2005;192(3):937-944. doi: S0002937804010373 [pii].

16. Maggio L, Dahlke JD, Mendez-Figueroa H, Albright CM, Chauhan SP, Wenstrom KD. Perinatal outcomes with normal compared with elevated umbilical artery systolic-to-diastolic ratios in fetal growth restriction. Obstet Gyencol. 2015;125(4):863-69.

17. Raio L, Ghezzi F, di Naro E, et al. In-utero characterization of the blood flow in the hyrtl anastomosis. Placenta. 2001;22(6):597-601. doi: 10.1053/plac.2001.0685 [doi].

Division of work:

John Ross and Dhanya Mackeen have contributed equally to design of the study, acquisition and analysis of data, and drafting and revision of manuscript.

Alexandria Betz contributed to acquisition and analysis of data.

Michael Paglia made substantial contributions to design of the study, interpretation of data, and revising for intellectual content of manuscript.

Wen Feng contributed to statistical design, data analysis and interpretation, and writing statistical methods for the manuscript.

A. George Neubert made substantial contributions to design of the study, and revising for intellectual content of manuscript.

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