

Antenatal Assessment of Discordant Umbilical Arteries in Singleton Pregnancies

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Aim To assess the relationship between discordant umbilical arterial size and resultant blood flow parameters and determine the impact of discordance on fetal outcome.

Methods This is a descriptive, cross-sectional study of 200 patients with a singleton gestation, who underwent a fetal anatomy survey between 18 to 23 weeks of gestation, with documented umbilical cord morphological patterns and blood flow characteristics. Umbilical vessel diameters and Doppler parameters (umbilical vein blood flow volume, mean resistance index, and peak-systolic velocity) were analyzed for discordance. Discordances encountered were examined for their possible association with perinatal outcome.

Results We had adequate ultrasound umbilical cord images, Doppler flow parameters, and all necessary demographic data for 154 patients. Umbilical artery discordance averaged 13.1% and was significantly correlated with both the expected and the true percent of difference in resistance index values (RI, $P < 0.001$). In 12 patients (7.8%), a significant discordance of more than 29.5%, or 95th percentile, was observed between the two umbilical artery diameters. However, in these cases no associated adverse perinatal outcome or significant placental pathology was noted. There was no significant difference between patients discordant or concordant umbilical artery in terms of maternal, labor, and neonatal data.

Conclusion The magnitude of umbilical arteries' luminal discordance directly influences the corresponding blood flow parameters. In our sample of patients, the presence of discordant-in-size umbilical arteries was not associated with umbilical cord or placental abnormalities.

The umbilical cord normally contains one umbilical vein and two arteries. Although the arteries generally have similar luminal diameters, discordances have been reported. One umbilical artery is considerably smaller (hypoplastic) than the other in 0.7%-1.4% of the cases, while a complete congenital absence of one umbilical artery (single umbilical artery) occurs in 0.8%-1.9% of the cases (1-3). Discordance between umbilical artery diameters of more than 1-3 mm are also described (1,2,4) and are associated with significant differences in blood flow parameters, mainly higher resistance to blood flow in the smaller umbilical artery (2,4-7). A controversy exists as to whether discordance between the two umbilical arteries in size or blood flow characteristics has any clinical relevance. While several reports noted an absence of umbilical cord or placenta abnormalities in patients with significant umbilical artery discordance (4,7), others suggested a higher prevalence of cord hematomas (8), placental infarcts (6), and abnormal cord insertion (2). Although an increased resistance to blood flow could be related to umbilical cord and/or placental abnormalities, there is a significant relationship between resistance to blood flow and umbilical cord vessels' diameters. The resistance to blood flow is directly proportional to the vessel length and blood viscosity, and inversely proportional to the vessel diameter, expressed as the radius to the fourth power (9). Therefore, in theory, the magnitude of the difference in blood flow resistance between the two umbilical arteries should be directly related to the extent of discordance in their diameters. In contrast, detection of large difference in blood flow resistance between two parallel umbilical arteries that have similar diameters cannot be explained by the discordance in the vessels' diameters but rather by the existence of the umbilical cord or placental pathology that modulates blood flow resistance in the affected umbilical artery.

We undertook this study to assess the relationship between discordant umbilical artery di-

ameters and resultant blood flow parameters, as well as to review possible differences in maternal and neonatal demographic data and perinatal outcomes between groups of patients with concordant- and discordant umbilical arteries.

Material and methods

This descriptive, cross-sectional study was carried out between August 1 and September 21, 2003. Fetal anatomy ultrasound surveys were performed in 200 women between 18 and 23 weeks of gestational age. Patients who underwent ultrasound screening for fetal anomalies were included in the study. Ultrasound examinations were performed using 6-MHz transabdominal transducer, with multihertz and harmonic capability (Sequoia System 512; Acuson, Siemens Company, Mountain View, CA, USA). Gestational age was determined in relation to the estimated date of confinement (defined by 280 days from the last menstrual period, if it was discordant either by less than 7 days from a first-trimester ultrasound examination or by 14 days from a second-trimester ultrasound examination). Otherwise, an estimated date of confinement from the earliest ultrasound examination was used. Each patient was included only once. The inclusion criteria were a singleton pregnancy, absence of gross fetal anomalies, and scheduled delivery at our institution. Exclusion criteria encompassed multifetal pregnancy, inadequate demographic, antenatal, or labor data, and inadequate longitudinal or transverse images of the umbilical cord to allow for accurate vessels' diameter measurements and umbilical vessels' Doppler studies.

The longitudinal and transverse ultrasonographic images of the umbilical cord that were obtained at maximum magnification and images of the analyzed umbilical cord blood flow parameters that were recorded at the time of the ultrasound exam, were stored in digital imaging media KinetDx v.2.8.3. (Siemens, Malvern, PA, USA).

The umbilical blood flow parameters were: venous mean blood flow velocity (cm/s) and resistance index (RI) with peak systolic velocity (PSv, cm/s) of both umbilical arteries. The assessment of the umbilical vessel diameters was performed by one of the authors (MP) from the recorded digitalized umbilical cord images. The discordance in size, or percent difference, between two umbilical arteries (%AA) was calculated according to the formula: $\%AA = (A_1 - A_2) / A_1$, where A_1 and A_2 represent the larger and smaller umbilical artery luminal diameters, respectively. The results obtained from the first 50 studies of the umbilical vessels' diameters showed intra-observer variability of 4.9%, with an average measured intraclass correlation of 0.995 (95% confidence intervals, 0.975-0.991, and α reliability coefficient 0.995). The umbilical cord Doppler study was performed only once for the each vessel by the same ultrasound technician who performed fetal anatomy survey, which excluded the possibility of intra- and inter-observer error for the umbilical cord Doppler studies. The evaluation of the umbilical cord, which included recording of longitudinal cord images and Doppler studies of the umbilical vein and arteries, prolonged the fetal anatomy survey for 8 to 9 minutes. In all cases, we ensured that the angle of insonation between the umbilical cord vessels and Doppler beam is no more than 30° in order to obtain as accurate blood flow velocity recording as possible. The pulse Doppler gain between -10 and 10 dB, pulse gate between 2-4 mm, and the minimal wall filter were used in all patients. In addition to recorded umbilical vessel Doppler waveforms with assessed venous mean velocity and arterial RI and PSv values, we calculated the following blood flow parameters: 1) mean blood flow through the umbilical vein (mL/min/kg); 2) discordance in blood flow parameters [percent difference in RI (%RI) and percent of difference in PSv between two umbilical arteries (%PSv)]; and 3) expected difference in blood flow resistance (%RI_e) between two umbilical arteries based on

the observed percent difference in umbilical artery size discordance (%AA).

Mean blood flow through the umbilical vein was calculated using the formula: blood flow (mL/min/kg) = $[V\pi(D/2)^2]/EFW$, where V is mean umbilical vein velocity (cm/s); D the vein diameter (mm); EFW estimated fetal weight calculated from the composite score incorporating biparietal diameter, abdominal circumference, and femur length measurements; and π is the constant 3.14 (10). Discordance in blood flow parameters (%RI and %PSv) was calculated in a similar manner as discordance in the size of umbilical arteries, where RI₁ and PSv₁ corresponded to the larger umbilical artery (A_1), and RI₂ and PSv₂ to the smaller umbilical artery (A_2). In addition, we calculated the expected difference in blood flow resistance (%RI_e) between the two umbilical arteries, based on the observed percent difference in umbilical artery size discordance (%AA). To obtain %RI_e, we calculated the expected RI for the larger (RI_{e1}), and the smaller (RI_{e2}) umbilical artery according to the modified Poiseuille's formula for vessel resistance (9), in which vessel length and blood viscosity for both umbilical arteries were assumed to be the same. Each expected cord blood %RI_e value was correlated with the actual %RI that was obtained earlier.

After the analysis of umbilical cord vessels' diameter and blood flow parameters, we stratified our data into two groups of patients based on the magnitude of two umbilical arteries diameter discordance: a) discordant umbilical artery group where the umbilical arteries' diameter discordance was above 95th percentile of the percent of difference or %AA distribution, and b) concordant umbilical artery group with umbilical arteries' diameter discordance below 95th percentile. Maternal age, parity, gestational age, estimated fetal weight, mode of delivery, gestational age at delivery, neonatal birth weight, as well as umbilical vessels' diameters and blood flow parameters were compared between concordant

and discordant umbilical artery group. To obtain necessary information, patients' medical records were reviewed for maternal demographic characteristics, antepartum complications, and neonatal birth data.

Statistical analyses were performed using Prism software version 3.02. (GraphPad Software Inc. San Diego, CA, USA). Polynomial least square regression analysis and Mann-Whitney test were used to assess the relationship between umbilical vessel diameters, Doppler parameters, and calculated percent of differences for each Doppler variable. Maternal demographic and neonate birth data were described with arithmetic mean, standard deviation (SD), median, and range of values as appropriate. The trend analysis between regression curves (comparison of best-fit values between two sets of umbilical artery data) was performed by Wilcoxon matched pairs test (paired non-parametric *t* test analysis). The Institutional Review Board of the Weill Medical College of Cornell University evaluated and approved the study.

Results

During the study period, 200 consecutive women underwent fetal anatomy scans between 18 and 23 weeks of gestation. A total of 15 patients were excluded from the study on the basis multifetal gestation (9 patients), presence of gross fetal anomalies (4 patients), and presence of two-vessel umbilical cord (2 patients). Additional 31 patients who were initially included in the study had inadequate sonographic umbilical cord images, or incomplete Doppler studies, and/or maternal demographic, antenatal, and labor data (eg, they delivered in other institutions).

Mean maternal age was 32.4 ± 5.2 years (range 17-47), with the median parity of 0 (range 0-5). Mean gestational age at the time of the fetal anatomy ultrasound survey was 20.3 ± 0.9 weeks with mean EFW of 360 ± 64 g. Most delivered at term (94.5%) by spontaneous vaginal deliv-

ery (64.3%). Mean gestational age at delivery was 39.5 ± 1.8 weeks (range 30-41) and mean neonatal birth weight was 3376 ± 501 g (range 1195-4650 g).

Mean umbilical vein diameter was 3.26 ± 0.54 mm (range 1.80-4.90), while mean diameter of the larger and the smaller umbilical artery was 1.66 mm (range 0.90-2.80 mm) and 1.43 mm (range 0.80-2.30), respectively. Mean percent difference in diameters between two umbilical arteries (%AA) was $13.1 \pm 9.9\%$ (range 0.0%-53.0%) with the discordance of 29.5% at the 95th percentile of distribution.

Mean blood flow volume through the umbilical vein was 264.6 mL/min/kg (range 103.9-695.1), while mean RI value of the larger (RI₁) and the smaller (RI₂) umbilical artery was 0.70 (range 0.43-1.00) and 0.74 (range 0.54-1.00), respectively ($P < 0.001$). Mean percent difference (%RI) was 6.8% (range 0.0%-27.1%). Mean PSv value for the larger umbilical artery (PSv₁) was 26.0 cm/s (range 7.5-41.1) and for the smaller (PSv₂) 25.9 cm/s (range 2.6-41.4) (please provide the exact *P*). Figure 1 demonstrates direct correlation between %AA and %RI ($P < 0.001$). A polynomial regression curve of second order that predicts percentage difference of RI difference can be expressed as follows:

$$y = 4.401 + (0.1101 \times x) + (0.00364 \times x^2),$$

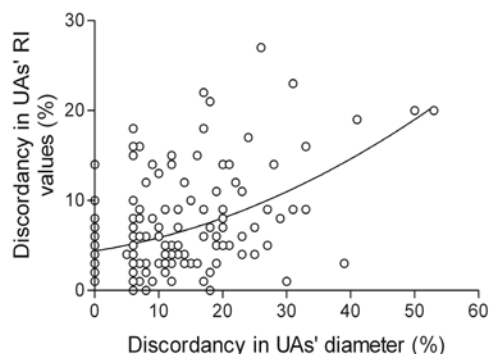


Figure 1. Scattergram of percent difference in umbilical arteries (UAs) diameters (%AA) stratified by percent difference in corresponding resistance index values (%RI). The correlation was statistically significant ($P < 0.001$, the polynomial regression of second order, $R_2 = 0.211$).

where y is %RI and x is %AA. Mean percent of difference in PSv between two umbilical arteries was 21.0 cm/s (range 0.0%-88.0%), and this did not correlate with %AA or %RI.

Finally, mean expected resistance to blood flow for the larger umbilical artery (RI_{e1}) was 3.0% (range 0.0 to 24.5%) and for the smaller (RI_{e2}) 5.9% (range 0.6 to 39.1%), while mean percent of expected RI difference (%RI_e) was 115% (range 0.0 to 1939.1%). Mean percent of expected RI difference was 17 times higher than the actual percent of RI difference between umbilical arteries. However, when expected percent of RI difference (%RI^c) was correlated with the actual %RI, a significant direct relationship was observed (*P*<0.001).

Table 1. Maternal demographic, neonatal birth, and ultrasound data for 12 patients with umbilical artery size discordance above 95th percentile (discordance difference of 29.5% and above) in comparison with subjects who had concordant in size umbilical arteries*

Characteristic	Umbilical arteries		P†
	discordant	concordant	
Number	12	142	–
Maternal age (y)	33.6 ± 4.1	32.3 ± 5.3	0.432
Maternal gravidity	2 (1.0-2.5)	2 (0.0-3.0)	0.402
Maternal parity	0 (0.0-1.0)	0 (0.0-1.0)	0.621
Gestational age at the time of US (weeks)	20.4 ± 0.8	20.3 ± 0.9	0.742
EFW at the time of US (g)	348 ± 52	361 ± 65	0.905
Vessels' diameters (mm):			
umbilical vein	3.4 ± 0.5	3.3 ± 0.5	0.548
larger umbilical artery (A ₁)	1.8 ± 0.3	1.6 ± 0.3	0.112
smaller umbilical artery (A ₂)	1.1 ± 0.3	1.5 ± 0.2	0.002
mean umbilical artery discordance (%)	36.2 ± 8.0	11.1 ± 7.3	<0.001
Blood flow parameters:			
venous blood flow (mL/min/kg)	274.9 ± 88.1	263.0 ± 10.7	0.549
resistance index (A ₁)	0.66 ± 0.09	0.71 ± 0.08	0.018
resistance index (A ₂)	0.75 ± 0.08	0.74 ± 0.07	0.166
mean umbilical artery RI's discordance (%)	12.6 ± 7.2	6.8 ± 5.6	0.004
A ₁ peak-systolic velocity (cm/s)	25.5 ± 5.6	26.1 ± 7.9	0.074
A ₂ peak-systolic velocity (cm/s)	25.8 ± 7.2	25.9 ± 6.3	0.803
Mode of delivery:			
vaginal uncomplicated delivery	7 (58.3%)	89 (62.7%)	0.029
assisted forceps/vacuum delivery	1 (8.3%)	7 (4.9%)	1.0
cesarean delivery:	4 (33.4)	46 (32.4)	0.058
non-reassuring status	2	15	0.493
breech presentation	1	8	0.671
failure to progress	0	9	0.187
elective or repeat cesarean	1	14	0.270
Gestational age at delivery (weeks)	39.4 ± 1.5	39.4 ± 2.0	0.773
Birth weight (g)	3545 ± 425	3359 ± 526	0.402
Apgar score 1 min	9 (9-9)	9 (9-9)	1.0
Apgar score 5 min	9 (9-9)	9 (9-9)	1.0
Significant placental pathology	none (n=5)	none (n=31)	

*Abbreviations: US – ultrasound; EFW – estimated fetal weight; NS – not significant, RI – resistance index. Data are represented as mean and standard deviation, or median and interquartile ranges.
†Mann-Whitney test.

In our study, we considered umbilical arteries to be discordant in size if a discordance of 29.5% and above was observed, based on the 95th percentile of the distribution. A total of 12 (7.8%) cases in our series had umbilical artery discordance of this magnitude (Table 1). There were no placental abnormalities (eg, cord hematomas, placental infarcts, or abnormal cord attachments) were found in any of the cases when a pathologist evaluated the placenta (5 in the discordant and 31 placentas in the concordant umbilical arteries group). A significant difference between the compared groups was noted for the discordance in the size of the smaller umbilical artery, and lower resistance to blood flow for the larger umbilical artery. Mean umbilical artery diameter discordance and corresponding mean RI (resistance to blood flow) discordance were also statistically significant. However, no other maternal, labor, or neonatal variables that were compared demonstrated any significant difference.

Discussion

Antenatal ultrasonic evaluation of the umbilical cord and blood flow parameters revealed significant discordance between the umbilical artery diameters and/or resistance to blood flow values in patients with significant cord or placental abnormalities. Sepulveda et al (8) demonstrated large discordance in umbilical artery flow velocity waveforms in a patient with an umbilical cord hematoma, as well as in two case reports where a considerable discordance in vessel diameter was noted (7). Others have demonstrated blood flow discordance ranging from 0.46 to 2.67 for pulsatility index (PI) which was related to the altered blood in the placental areas, with significant infarction (5,6). From these earlier reports, a plausible theory emerged that a significant discordance in blood flow parameters between two parallel umbilical arteries may signify potential umbilical cord pathology (8), placental infarcts (5,6), and/or aberrant Hyrtl anasto-

mosis (5). None of these reports, however, correlated umbilical artery diameters with blood flow indices. Studies using blood flow indices, such as resistance index (RI) or pulsatile index (PI), showed that resistance to blood flow was directly proportional to blood viscosity and the length of the vessel and inversely proportional to the vessel diameter (vessel radius to the fourth power) (9). If blood viscosity and umbilical artery length are assumed to be constant, then vessel diameter should solely modify the resistance to blood flow, ie, a smaller vessel diameter would produce a higher resistance to blood flow (higher RI or PI values). Therefore, umbilical arteries discordant-in-size would have discordant blood flow indices, and need not be associated with umbilical cord or placental pathology. In a series of 6 patients with umbilical artery diameter discordance ranging from 1 to 3 mm, which was associated with a significant difference between small and large artery systolic-diastolic ratios, no placental or cord abnormalities were found (4). In contrast, Raio et al (2) reported a series of 14 patients with umbilical artery discordance ≥ 1 mm and described an associated abnormal cord insertion (marginal, velamentous, or eccentric) in half of the patients and additional placental abnormalities in 8 patients (3 infarcts, 2 bipartite placentas, 1 succenturiate placenta, and 1 chorangioma and absence of Hyrtl anastomosis). In addition, in 3 patients they noted a considerably different RI value that roughly correlated with the percent difference in size between the hypoplastic and the normal umbilical artery. The authors proposed that discrepancies in either size or Doppler flow velocities between the two umbilical arteries represent the expression of placental macroscopic or microscopic abnormalities in the areas supplied by the smaller umbilical artery, while the absence or aberrant Hyrtl anastomosis could have an important role in the modification of the associated blood flow patterns (2).

The aim of our study was to establish the prevalence of umbilical artery discordance with

respect to size and blood flow parameters, and correlate these findings with perinatal outcome. We observed some degree of discordance in umbilical arteries diameters in almost every patient, with the mean percent discordance of 13.1%. The umbilical cord vessels' diameters in our study concur with the data published by Weissman et al (11), who found the umbilical vein diameter to range from 3.6 to 4.7 mm at 18 to 23 weeks of gestational age, while the corresponding mean artery diameter was 1.9 to 2.4 mm, or at average one half of the vein diameter. In contrast to the difference for umbilical artery diameters, we observed a lesser discordance in the associated resistance to blood flow. Although a statistically significant correlation between the difference for umbilical arteries' diameters and RI values was noted, the RI difference was 6.8%, which was less than twice the mean discordance in umbilical arteries' diameters. This meant that resistance to blood flow is a function of both the vessel size and the discordance between the two vessel diameters. In addition, the expected difference in RI was significantly higher than the observed RI difference. Using the modified Poiseuille's formula for vessel resistance, we calculated that mean expected difference for measured umbilical artery discordance was 115%, which was almost 20 times higher than the true RI difference. Although the percent difference for true and expected resistance to blood flow was significantly correlated, it appeared that the discordance in blood flow resistance between the two discordant umbilical arteries was blunted and significantly decreased by some other mechanism. In our previous work, we noted that the resistance to blood flow in one umbilical artery often differed considerably from the other, although this difference diminished with advancing gestation, likely due to progressive anatomic development and functional maturation of the Hyrtl anastomosis between the two arteries (12). In a study of 67 placentas with normal cord umbilical flow-velocity waveforms, Ullberg et al (13) demonstrat-

ed the existence of the Hyrtl anastomosis, which was visualized by angiography in 91.5% of the cases. When the diameter of Hyrtl's anastomosis was at least that of the connected vessels, the umbilical arteries supplied a significantly disproportionate area of the placenta. The opposite was true when the diameter of the anastomosis was smaller than any of the connected vessels, or even absent; the placental blood distribution by the corresponding umbilical artery was similar, even symmetrical, though with no difference when a cohort of small-for-age neonates was compared with normal size neonates (14). It appears that the presence of the Hyrtl anastomosis could act as a pressure-equalizing system between the umbilical arteries (12) and could be accurately demonstrated by conventional, color and pulsed Doppler ultrasound (15).

The prevalence of discordant umbilical arteries in our sample of patients was 7.8%. This is 4 to 10 times higher than previously published ranges of 0.7 to 1.4% (1,2), likely due to different definitions of discordance. If we would apply the previously published definitions of umbilical arteries in size discordance, eg, 1 mm difference between both umbilical arteries, than we would recruit 3 patients only, with a prevalence of 1.9%. We did not observe any perinatal adverse outcome or cord and placental abnormality in patients with significant umbilical artery discordance where placental pathologic evaluation was available. However, since all placentas had not been examined by a pathologist, there is a possibility of false negative findings. When the discordant and concordant umbilical arteries groups were compared, no maternal, neonatal or laboring data were significantly different. However, the percent of discordance in umbilical arteries' diameters that was 5 times higher in discordant umbilical arteries group was mainly contributed to the significantly smaller discordant umbilical artery when compared with the smaller concordant artery (1.1 mm vs 1.5 mm, $P < 0.001$). In contrast, the mean percent of RI difference was

two times higher in the discordant group mainly due to significantly lower resistance to blood flow in the larger discordant vs larger concordant umbilical artery (RI 0.66 vs 0.71, $P = 0.018$). This interesting discordance in results, which indicates that the larger umbilical artery will produce lower resistance to blood flow, but the smaller artery will not equally produce higher resistance to blood flow could be explained by the existence of Hyrtl's anastomosis as a pressure equalizer. It is possible that whenever a large discordance in umbilical arteries diameters exists, this anastomosis functions by lowering resistance to blood flow in the smaller umbilical artery at the expense of the larger umbilical artery. The opposite could be true, ie, that Hyrtl's anastomosis would be non-functional if no discordance in umbilical arteries' diameters was found.

We did not observe any adverse perinatal outcomes in our patients with discordant umbilical arteries. It is possible that the absence of adverse perinatal outcomes, while described in others (2,6-8), was due to the small number of patients, or because the magnitude of discordance between two umbilical arteries was too subtle to produce clinically recognizable effects. Nevertheless, we showed that the discordance in resistance to blood flow between two umbilical arteries was directly related to the equivalent discordance in vessel diameter. In addition, we also demonstrated that true percent difference in blood flow resistance was significantly smaller than expected, likely due to the presence of Hyrtl's anastomosis, which serves as discordant blood flow pressure-equalizing regulator.

In conclusion, the presence of a significant discordance in the resistance to blood flow between two umbilical arteries is unlikely to have clinical significance, provided that a similar discordance in vessel diameter is present. Future more detailed prospective studies that would evaluate umbilical arteries' diameters, associated blood flow parameters, morphologic and blood flow characteristics of Hyrtl anastomosis, as well

as evaluation of placental lobe blood flow distribution in relation to the diameter of the supplying umbilical artery, are required to elucidate the mechanisms of adverse perinatal outcomes in patients with discordant umbilical arteries.

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