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ORIGINAL ARTICLE

Longitudinal umbilical vein blood flow changes in normal and growth-retarded fetuses

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Objective. To explore whether the umbilical vein blood flow of growth-retarded fetuses with normal Doppler parameters changes over time differently to that of normally grown fetuses.
Methods. Fifteen consecutive women whose fetus was diagnosed to be growth restricted were compared with 30 women whose fetus was normally grown. Two ultrasonographic evaluations were conducted at 2-weekly intervals (±2 days) in all cases. At each sonographic evaluation, umbilical vein blood flow parameters were obtained by digital color Doppler velocity profile integration. To allow comparisons among fetuses, the umbilical vein blood flow per minute was normalized for abdominal circumference.
Results. The absolute vein blood flow was lower in growth-retarded than in normally grown fetuses (209 ml/min ± 73 vs. 313 ml/min ± 72, $p < 0.01$). The median (range) umbilical vein blood flow normalized for abdominal circumference was significantly lower in growth-retarded than in normally grown fetuses at the first [0.70 (0.32; 1.15) vs. 1.11 (0.65; 2.07), $p < 0.05$] and at the second [0.71(0.30; 1.09) vs. 1.14 (0.69; 2.05), $p < 0.05$] sonographic evaluation. The difference in umbilical vein blood flow normalized for abdominal circumference between the second and the first examination was significantly lower in growth-retarded than in appropriate for gestational age fetuses [−0.005 (−0.08; 0.06) vs. 0.02 (−0.08; 0.1), $p < 0.05$].
Conclusion. This study demonstrates that umbilical vein blood flow normalized for biometric parameters is lower in growth-retarded fetuses than in healthy fetuses even in the absence of umbilical artery Doppler abnormalities.

Key words: Doppler ultrasound, fetal growth restriction, umbilical cord, umbilical vein blood flow

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Uteroplacental insufficiency is a major cause of perinatal mortality and morbidity in growth-restricted fetuses (1). The use of artery Doppler velocimetry of different feto-placental vascular areas has been used to assess fetal well being with the aim of preventing neonatal sequelae (2). Severely impaired feto-placental blood flow characterized by absent or reversed diastolic flow in the umbilical artery has been associated to an increased fetal risk of perinatal morbidity and mortality (3,4). However, it has been demonstrated that Doppler waveform analysis of the umbilical artery blood flow is a nonsensitive method to detect mild to moderate reduction in placental flow (5–8). An alternative approach to evaluate placental function is to measure the umbilical vein blood flow. Laurin *et al* (9) demonstrated that the diagnostic accuracy of umbilical venous flow assessment was better than umbilical artery Doppler evaluation to identify fetuses at increased risk of adverse neonatal outcome. Recent studies have shown that umbilical vein blood flow quantification is feasible and reproducible starting in the second trimester of gestation (10–12). Moreover, the introduction of new technologies such as the digital color Doppler velocity profile integration allows a fast and simple method for blood flow quantification (13).

Absolute umbilical vein blood flow increases as a function of gestational age and it is strongly correlated with umbilical vein diameter (10). Ferrazzi *et al* (11) recently reported that umbilical vein blood flow is significantly reduced in intrauterine growth restricted (IUGR) fetuses, as they noted a relationship between umbilical vein blood flow and the degree of fetal compromise. Moreover, Gill *et al* (14) reported that a reduction in the umbilical vein blood flow might be present up to 3 weeks before the fetal growth failure is detectable by conventional biometric measurements.

Intrauterine growth restriction fetuses occurring late in gestation with normal Doppler parameters in the absence of fetal or maternal diseases represent a distinct group of fetuses with a low but not negligible risk of perinatal complications (15). Therefore, we sought to explore whether umbilical vein blood flow in these fetuses changes over time differently to that of normally grown fetuses.

Materials and methods

Fifteen consecutive women whose fetus was diagnosed to be IUGR and referred to our department for fetal Doppler evaluation in the third trimester of gestation were compared to 30 women whose fetus was appropriate for gestational age (AGA). Matching criteria were gestational age at examination (±2 days) and parity. Inclusion criteria were (1) singleton gestation (2), intact membranes (3), absence of congenital or chromosomal abnormalities (4), absence of pregnancy complications (i.e. hypertensive disorders, diabetes) (5), normal amniotic fluid, and (6) umbilical artery pulsatility index within the normal range for gestational age. For each case of IUGR fetus included in the study, the subsequent two women undergoing routine sonographic examination whose fetus was AGA and who met both the matching and inclusion criteria were enrolled in the study.

In all patients, gestational age was determined by a reliable recollection of the last menstrual period and by an ultrasonographic examination before 20 weeks of gestation. Two ultrasonographic evaluations were conducted at 2-weekly intervals (±2 days) in all cases. As the second sonographic evaluation was performed after 34 weeks of gestation in all patients and no umbilical artery Doppler abnormalities were detected, patients were further managed by the referring obstetrician.

The ultrasonographic evaluation included the measurement of fetal anthropometric parameters (biparietal diameter, abdominal circumference, femur length), the computation of umbilical cord and umbilical vessels' cross-sectional areas, Doppler interrogation of the umbilical arteries and the estimation of the blood flow through the umbilical vein. The umbilical cord measurements were obtained as previously described (16,17). Intra- and interobserver variabilities were 4.3 and 5.1%, respectively (18). Umbilical artery Doppler flow velocity waveforms were recorded when at least three consecutive waveforms showing a consistent pattern were obtained. The umbilical vein blood flow was measured by digital color Doppler velocity profile integration. This function specifies an arbitrary line on a playback color Doppler image, displays the waveform of the accuracy data concerning each pixel on the specified line as a profile, indicates changes in brightness as waveform data, and integrates data corresponding to several frames and displays it as a blood flow. Doppler parameters were obtained at three different parts of the umbilical cord. The mean of the parameters obtained was used for the purpose of statistical analysis. Mean flow velocity and flow volume per minute were computed. To allow comparisons among fetuses, the umbilical vein blood flow per minute was normalized for abdominal circumference and for head circumference. The pulsatility index as well as the umbilical vein blood flow parameters were measured during fetal apnea and in the absence of uterine contractions. The ultrasound examinations were performed with an Aloka Prosound 5500 unit (Aloka, Tokyo, Japan) equipped with a 3.5-MHz transducer. No clinical decisions were taken upon umbilical vein blood flow parameters. Intra- and interobserver variability for the computation of the umbilical vein blood flow were 7.1% and 8.7%, respectively.

A fetus was defined as IUGR when the abdominal circumference was below the 5th centile for gestational age in the presence of normal previously measured biometric parameters. An umbilical cord was defined lean when its cross-sectional area was below the 10th centile for gestational age (15). The Human Research Review Committee approved this study.

Statistical analysis

Statistical analysis was performed using SPSS 7.0 (SPSS Inc., Chicago, IL) and EpiStast 4.0 (EpiStat Services, Richardson, TX). Mann–Whitney *U*-test, Student *t*-test and analysis of variance for repeated measurements were used for comparison of continuous variables, while proportions were analyzed using Fisher's exact test. Statistical significance was considered achieved when p was less than 0.05.

Results

The clinical characteristics of the study population are shown in Table I. All IUGR fetuses had a birthweight below the 10th centile for gestational age. The indications for the performance of a cesarean section in the IUGR group were breech presentation ($n = 1$), fetal heart rate disturbance in labor ($n = 3$), previous cesarean delivery ($n = 1$) and failed induction of labor ($n = 1$), while in the AGA group indications were breech presentation ($n = 2$), fetal heart rate disturbance in labor ($n = 3$), previous cesarean delivery ($n = 2$) and arrest of labor ($n = 1$).

Table II displays the umbilical cord morphometric characteristics at the two sonographic evaluations. No difference was found in the umbilical cord morphometric characteristics between the first and the second examination in both the IUGR and AGA fetuses. The proportion of fetuses with a lean umbilical cord was higher among the IUGR fetuses than among the AGA fetuses (6/15 vs. 1/30, $P < 0.01$). The absolute vein blood flow was lower in the IUGR than in the AGA fetuses either at the first (209 ± 73 ml/min vs. 313 ± 72 ml/min, $p < 0.01$) and at the second examination (213 ± 75 ml/min vs. 338 ± 65 ml/min, $p < 0.01$). No difference was found in the mean absolute umbilical vein blood flow between the first and second examination in both the IUGR and the AGA fetuses. The proportion of fetuses with an absolute vein blood flow below the 5th centile for gestational age at the first examination was higher among the IUGR fetuses than among the AGA fetuses (6/15 vs. 1/30, $p < 0.01$)(Figs 1 and 2). This figure did not change after the second examination (7/15 vs. 2/30, $p < 0.01$). The proportion of fetuses with a lean umbilical cord was higher among the IUGR fetuses with an absolute vein blood flow below the 5th centile at the second examination than among those with normal umbilical vein blood flow (5/7 vs. 1/8, $p = 0.04$).

Similarly, the proportion of fetuses with an absolute vein blood flow below the 25th centile for gestational age at the first examination was higher among the IUGR fetuses than among the AGA fetuses [8/15 (53.3%) vs. 5/30 (16.7%), $p < 0.01$]. This figure also did not change after the second examination [12/15 (80%) vs. 8/30 (26.7%), $p < 0.01$].

Figures 3 and 4 show the umbilical vein blood

Table I. Patient characteristics

Characteristics	IUGR fetuses ($n = 15$)	AGA fetuses ($n = 30$)	Significance
Maternal age (year)	30.3 ± 6.05	30.9 ± 5.91	NS
Nulliparous women	8 (53.3%)	16 (53.3%)	NS
Gestational age at first examination (week)	33.7 ± 1.87	33.7 ± 1.84	NS
Gestational at delivery (week)	37.6 ± 1.53	39.1 ± 1.45	$p < 0.01$
Cesarean delivery	6 (40%)	8 (26.7%)	NS
5-min Apgar score ≤7	3 (20%)	0	$p = 0.03$
Meconium-stained amniotic fluid	2 (13.3%)	1 (3.3%)	NS
NICU admission	2 (13.3%)	0	NS
Birth weight (grams)	2433 ± 228	3306 ± 381	$p < 0.01$

Data are presented as mean ±SD or number (%).
IUGR, intrauterine growth restricted; AGA, appropriate for gestational age; NICU, neonatal intensive care unit.

Table II. Umbilical cord morphometry and umbilical artery Doppler characteristics

Characteristics	First examination			Second examination		
	IUGR fetuses ($n = 15$)	AGA fetuses ($n = 30$)	Significance	IUGR fetuses ($n = 15$)	AGA fetuses ($n = 30$)	Significance
Cord cross-sectional area (mm^2)	124.1 ± 21.8	180.7 ± 44.5	$p < 0.01$	128.6 ± 23.2	176.7 ± 41.3	$p < 0.01$
Arteries cross-sectional area* (mm^2)	10.3 ± 2.2	11.1 ± 3.8	NS	10.7 ± 1.9	11.3 ± 3.4	NS
Vein cross-sectional area (mm^2)	35.5 ± 6.9	43.1 ± 10.2	$p < 0.01$	34.2 ± 7.2	45.3 ± 10.1	$p < 0.01$
Wharton's jelly area (mm^2)	72.4 ± 23.6	115.4 ± 45.7	$p < 0.01$	70.4 ± 21.8	112.6 ± 48.7	$p < 0.01$
Artery pulsatility index	0.94 ± 0.30	0.79 ± 0.19	$p < 0.05$	0.96 ± 0.27	0.71 ± 0.17	$p < 0.05$

Data are presented as mean ±SD. *Both arteries (30 vs. 60).
IUGR, intrauterine growth restricted; AGA, appropriate for gestational age.

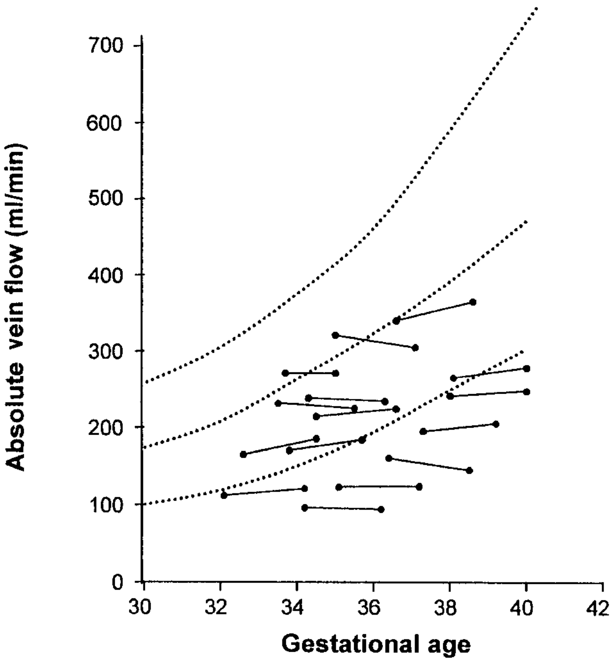

Fig. 1. Absolute umbilical vein blood flow in growth-retarded fetuses at the first and second ultrasonographic examination plotted on previously published reference ranges (8). (Dashed lines represent the 5th, 50th and 95th percentile for gestational age).

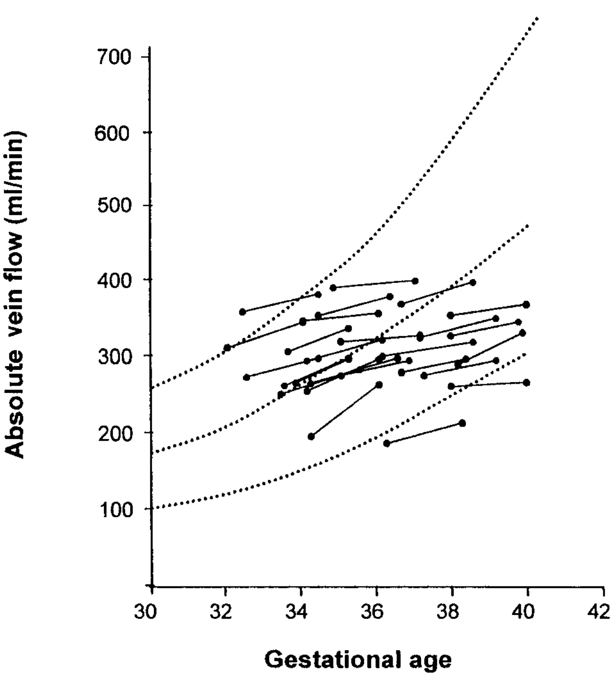

Fig. 2. Absolute umbilical vein blood flow in appropriate for gestational age fetuses at the first and second ultrasonographic examination plotted on previously published reference ranges (8). (Dashed lines represent the 5th, 50th and 95th percentile for gestational age).

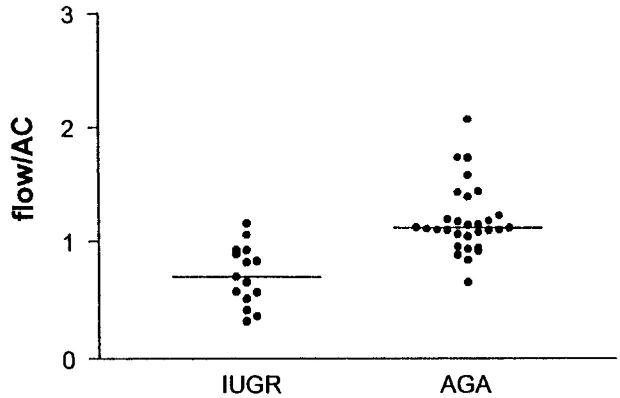

Fig. 3. Umbilical vein blood flow normalized for abdominal circumference at the first examination in growth-retarded and appropriate for gestational age fetuses.

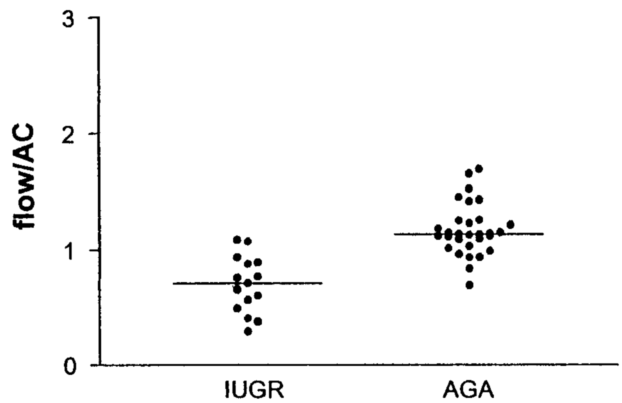

Fig. 4. Umbilical vein blood flow normalized for abdominal circumference at the second examination in growth-retarded and appropriate for gestational age fetuses.

flow normalized for abdominal circumference unit in the IUGR and AGA fetuses. The median (range) umbilical vein blood flow normalized for abdominal circumference was significantly lower in the IUGR fetuses than in the AGA fetuses at the first [0.70 (0.32; 1.15) vs. 1.11 (0.65; 2.07), $p<0.05$] and at the second [0.71 (0.30; 1.09) vs. 1.14 (0.69; 2.05), $p<0.05$] sonographic evaluation. Similarly, the median (range) umbilical vein blood flow normalized for head circumference was significantly lower in the IUGR fetuses than in the AGA fetuses at the first [2.35 (1.12; 3.62) vs. 3.45 (2.41; 6.25), $p<0.05$] and at the second [2.41 (1.04; 3.72) vs. 3.63 (2.71; 6.31), $p<0.05$] sonographic evaluation.

The difference in umbilical vein blood flow normalized for abdominal circumference between the second and first examination was significantly lower in the IUGR than in the AGA fetuses [-0.005 (-0.08; 0.06) vs. 0.02 (-0.08; 0.1), $p<0.05$] (Fig 5). The vein blood flow mean velocity was significantly lower in the IUGR than in the AGA

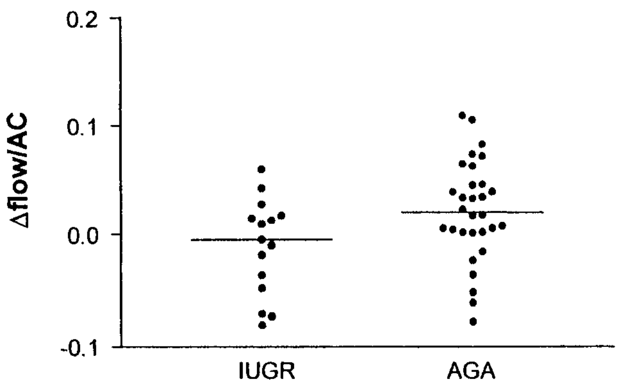

Fig. 5. Difference between the second and first examination (Δ) of the umbilical vein blood flow normalized for abdominal circumference in growth-retarded and appropriate for gestational age fetuses.

fetuses in both the first (7.5 cm/s ± 2.8 vs. 11.7 cm/s ± 3.4, $p < 0.01$) and second examination (7.1 cm/s ± 3.1 vs. 11.2 cm/s ± 2.9, $p < 0.01$).

The umbilical artery pulsatility index was not different between the IUGR and AGA fetuses at both the first and second examination.

Although not statistically significant, two of the seven IUGR fetuses who had an umbilical vein blood flow below the normal range were admitted to the neonatal intensive care unit (NICU) because of respiratory distress syndrome, while none of the IUGR fetuses with normal umbilical vein blood flow were admitted to the NICU.

At delivery, the hematocrit values were obtained in 13 of the IUGR fetuses. Of these, six had an umbilical vein blood flow below the 5th centile for gestational age at the second examination and seven had an umbilical vein blood flow within the normal range. The proportion of fetuses with a hematocrit value greater than 60% was higher in the former than in the latter group (4/6 vs. 0/7, $p = 0.02$).

Discussion

This study shows that the absolute umbilical vein blood flow is significantly lower in IUGR fetuses with normal umbilical artery Doppler parameters compared with AGA fetuses. This is in agreement with the results of Ferrazzi *et al* (11) who measured umbilical vein blood flow in growth-retarded fetuses between 24 and 40 weeks of gestation. Conversely, our results are at variance with those of these authors who did not find a significant reduction in the umbilical vein blood flow of IUGR fetuses with normal pulsatility index of the umbilical artery when the blood flow was expressed per unit abdominal circumference. The reason for this discrepancy might be explained by the higher number of IUGR fetuses with normal Doppler parameters in the present study. Indeed, Ferrazzi *et al* (11) reported that three out of five fetuses with these characteristics presented an umbilical vein blood flow normalized for abdominal circumference below the 5th centile for gestational age.

The important observation of our study is that there is a progressive reduction of the umbilical vein blood flow over time in IUGR fetuses even in the presence of normal umbilical artery Doppler parameters. This supports the observation of previous investigators who reported a poor correlation between umbilical artery Doppler parameters and fetal growth retardation (9,20). Furthermore, animal experiments have shown that when the blood flow is reduced by cord occlusion and placental embolization, significant changes in umbilical artery Doppler values became apparent only when the placental blood flow is severely impaired (5–9,21).

According to Poiseuille's law, the three factors that might influence blood flow are the caliber of the vessel, the blood flow velocity, and the viscosity of the blood. Our group has previously reported that the vein blood flow is lower in fetuses with an umbilical cord cross-sectional area below the 10th centile than in those with an umbilical cord of normal caliber (13). Moreover, Lees *et al* (10) demonstrated that the most important parameter influencing the increase of umbilical vein blood flow in normal fetuses is the umbilical vein cross-sectional area. In the present study the umbilical vein area was significantly lower in IUGR fetuses than in normally grown fetuses. As we and Weissmann (22,23) have previously demonstrated that the umbilical vein size does not change significantly during the third trimester of pregnancy, the reduction of umbilical vein blood flow in IUGR fetuses might be in part explained by variations of the other two parameters: flow velocity and viscosity. Although blood flow velocity measurements are difficult to correctly obtain, it seems that in IUGR fetuses the umbilical blood flow velocity increase normally present in healthy fetuses with advancing gestation does not occur (10). The result of the present study agrees with those of Ferrazzi *et al* (11) and of Jouppila *et al* (24), who found that IUGR fetuses had a lower mean umbilical vein blood flow velocity than AGA fetuses.

A possible explanation for the reduced umbilical vein blood velocity in IUGR fetuses is the different blood viscosity between these fetuses and AGA fetuses. Jouppila *et al* (24) reported that an inverse correlation exists between umbilical vein blood viscosity and both umbilical blood flow volume and velocity. Furthermore, these authors found that umbilical cord blood viscosity is significantly increased in IUGR fetuses without maternal or fetal diseases compared with AGA fetuses. Moreover, Drew *et al* (25) described a significantly higher rate of blood hyperviscosity in IUGR infants than in AGA newborns. Finally, Weiner *et al* (26) noted that, regardless of the etiology, the hematocrit, a major determinant of blood viscosity (27), is increased in IUGR fetuses in comparison with healthy fetuses. Considering that IUGR fetuses with abnormal umbilical artery Doppler parameters have a lower mean umbilical vein blood flow velocity than IUGR fetuses with normal Doppler parameters (7,20), it is reasonable to hypothesize that the viscosity of the umbilical vein blood is correlated with the degree of placental insufficiency.

Another interesting observation of the present study is that umbilical artery Doppler pulsatility indices were not significantly different between the first and the second examination, while this was not the case for the umbilical vein blood flow. This is in keeping with the study by Sutton *et al* (28) who reported that the calculation of the umbilical vein blood flow might provide a better index of placental perfusion than the umbilical artery velocity ratio.

A limitation of the present study is that the umbilical vein blood flow estimation was performed in fetuses that were already growth retarded. Considering that, in IUGR fetuses, umbilical cord morphometric changes are often present in the second trimester (19), further longitudinal studies should be conducted to investigate which is the temporal relationship between umbilical vein blood flow alterations and the overt manifestation of fetal growth restriction.

References

1. Lin CC, Santolaya-Forgas J. Current concepts of fetal growth restriction. Part II Diagnosis Mangement. Obstet Gynecol 1999; 93: 140–6.
2. Madazli R, Uludag S, Ocak V. Doppler assessment of umbilical artery, thoracic aorta and middle cerebral artery in the management of pregnancies with growth restriction. Acta Obstet Gynecol Scand 2001; 80: 702–7.
3. Battaglia C, Artini PG, Galli PA, D'Ambrogio G, Droghino F, Genazzani AR. Absent or reversed end-diastolic flow in umbilical artery and severe intrauterine growth retardation. An ominous association. Acta Obstet Gynecol Scand 1993; 72: 167–71.
4. Todros T, Ronco G, Fianchino O, Rosso S, Gabrielli S, Valsecchi L et al. Accuracy of the umbilical arteries Doppler flow velocity waveforms in detecting adverse perinatal outcomes in a high-risk population. Acta Obstet Gynecol Scand 1996; 75: 113–9.
5. Copel JA, Schlafer D, Wentworth R, Belanger K, Kreitzer L, Hobbins JC, Nathanielsz PW. Does the umbilical artery systolic/diastolic ratio reflect flow or acidosis? Am J Obstet Gynecol 1991; 163: 751–6.
6. Morrow RJ, Adamson SL, Bull SB, Ritchie JWK. Effect of placental embolization on the umbilical artery flow velocity waveform in fetal sheep. Am J Obstet Gynecol 1989; 161: 1055–60.
7. Morrow RJ, Adamson SL, Bull SB, Ritchie JWK. Acute hypoxemia does not affect the umbilical artery flow velocity waveform in fetal sheep. Obstet Gynecol 1990; 75: 590–3.
8. Schmidt KG, di Tommaso M, Silverman NH, Rudolph AM. Evaluation of changes in umbilical blood flow in the fetal lamb by Doppler waveform analysis. Am J Obstet Gynecol 1991; 164: 1118–26.
9. Laurin J, Lingman G, Marsal K, Person PK. Fetal blood flow in pregnancies complicated by intrauterine growth retardation. Obstet Gynecol 1987; 69: 895–902.
10. Lees C, Albaiges G, Deane C, Parra M, Nicolaides KH. Assessment of umbilical arterial and venous flow using color Doppler. Ultrasound Obstet Gynecol 1999; 14: 250–5.
11. Ferrrazzi E, Rigano S, Bozzo M, Bellotti M, Giovannini N, Galan H, Battaglia FC. Umbilical vein blood flow in growth-restricted fetuses. Ultrasound Obstet Gynecol 2000; 16: 432–8.
12. Barbera A, Galan HL, Ferrazzi E, Rigano S, Jozwik M, Battaglia FC, Pardi G. Relationship of umbilical vein blood flow to growth parameters in the human fetus. Am J Obstet Gynecol 1999; 181: 174–9.
13. Di Naro E, Ghezzi F, Raio L, Franchi M, Lanzillotti G, Schneider H. Umbilical vein blood flow in fetuses with normal and lean umbilical cord. Ultrasound Obstet Gynecol 2001; 17: 224–8.
14. Gill RW, Kossoff G, Warren PS, Garrett WJ. Umbilical venous flow in normal and complicated pregnancy. Ultrasound Med Biol 1984; 10: 349–63.
15. Lin CC, Santolaya-Forgas J. Current concepts of fetal growth restriction: Part I: Causes, classification, and pathophysiol. Obstet Gynecol 1998; 92: 1044–55.
16. Raio L, Ghezzi F, Di Naro E, Gomez R, Mueller MD, Maymon E, Mazor M. Sonographic measurements of the umbilical cord and fetal anthropometric parameters. Eur J Obstet Gynecol Reprod Biol 1999; 83: 135–5.
17. Ghezzi F, Raio L, Di Naro E, Franchi M, Balestreri D. D'addario V. Nomogram of Wharton's jelly as depicted in the sonographic cross-section of the umbilical cord. Ultrasound Obstet Gynecol 2001.
18. Raio L, Ghezzi F, Di Naro E, Gomez R, Saile G, Brühwiler H. The clinical significance of antenatal detection of discordant umbilical arteries. Obstet Gynecol 1998; 91: 86–91.
19. Raio L, Ghezzi F, Di Naro E, Franchi M, Maymon E, Mueller MD, Brühwiler H. Prenatal diagnosis of a 'lean' umbilical cord: a simple marker for fetuses at risk of being small for gestational age at birth. Ultrasound Obstet Gynecol 1999; 13: 176–80.
20. Devoe LD, Gardner P, Dear C, Faircloth D. The significance of increasing umbilical artery systolic-diastolic ratio in third-trimester pregnancy. Obstet Gynecol 1992; 80: 684–7.
21. Trudinger BJ, Stevens D, Connelly A, Hales JRS, Alexander G, Bradley L et al. Umbilical artery flow velocity waveform and placental resistance: the effect of embolization of the umbilical circulation. Am J Obstet Gynecol 1987; 157: 1443–8.
22. Raio L, Ghezzi F, Di Naro E, Franchi M, Balestreri D, Bolla D et al. Umbilical cord vessel areas in normal and growth retarded fetuses. Am J Obstet Gynecol 2001; 184: 27, (Abstract) 59.
23. Weissman A, Jakobi P, Bronshtein M, Goldstein I. Sonographic measurements of the umbilical cord and vessels during normal pregnancies. J Ultrasound Med 1994; 13: 11–4.
24. Jouppila P, Kirkinen P, Puukka R. Correlation between um-

bilical vein blood flow and umbilical blood viscosity in normal and complicated pregnancies. Arch Gynecol 1986; 237: 191–7.
25. Drew JH, Guaran RL, Grauer S, Hobbs JB. Cord whole blood hyperviscosity: measurement, definition, incidence and clinical features. J Paediatr Child Health 1991; 27: 363–5.
26. Weiner CP, Williamson RA. Evaluation of severe growth retardation using cordocentesis – hematologic and metabolic alterations by etiology. Obstet Gynecol 1989; 73: 225–9.
27. Buchan BC. Maternal and fetal blood viscosity throughout normal pregnancy. J Obstet Gynaecol 1984; 4: 143–50.
28. Sutton MSJ, Theard MA, Bhatia SJS, Plappert T, Satlzman DH, Doubilet P. Changes in placental blood flow in the normal human fetus with gestational age. Pediatr Res 1990; 28: 383–7.

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