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ORIGINAL ARTICLE

Low umbilical artery vascular flow resistance and fetal outcome

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Background. An abnormally high [above mean + 2 standard deviations (SD)] umbilical artery (UA) pulsatility index (PI) indicates impaired fetal outcome, whereas the impact of an "abnormally" low (below mean −2 SD) PI is unknown.
Methods. Perinatal outcome was compared between cases with a UA PI less than mean −2 SD (group A: high-risk cases selected from a database, $n = 330$; group B: unselected cases, $n = 39$) and unselected controls (group C) with a PI within mean ± 2 SD ($n = 863$) at Doppler velocimetry. Groups B and C were retrieved from a population-based sample. The unpaired *t*-test, Mann–Whitney *U*-test, χ^2-test and Fisher's exact probability test were used for statistical comparisons with a two-tailed $p < 0.05$ being significant.
Results. No significant differences were found between group A vs. group C and group B vs. group C regarding perinatal mortality, Apgar scores at 1, 5 or 10 min, or arterial or venous cord blood pH. Postterm pregnancy in group A carried no additional risk. For obvious reasons, operative delivery and neonatal intensive care were more common in group A than in group C, but no such differences were found between groups B and C. The mean birthweight was 3.7% higher in group B than in group C ($p = 0.049$).
Conclusions. Deeming a UA PI below the lower reference limit as "abnormally" low is a statistical definition that was not reflected by a biological imperfection. Instead, a low UA PI promoted fetal growth.

Keywords: Doppler; fetal outcome; low vascular resistance; pregnancy; umbilical

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The vascular flow resistance in the umbilical artery (UA) decreases throughout pregnancy and further postdate (1,2). An increase in flow resistance indicates placental dysfunction associated with intrauterine fetal growth restriction (IUGR) and impaired fetal outcome in cases of an abnormally high flow resistance (3). According to the gaussian distribution, an abnormally high UA pulsatility index (PI) (4) is defined as a PI above the gestational age-corrected mean value plus 2 standard deviations (SD) (1). The impact of the opposite extreme, representing PI values below mean minus 2 SD, has, surprisingly, escaped attention in the medical literature. However, there are indications that a low UA PI may also be associated with an impaired fetal outcome. In a small series of postterm pregnancies, we found a low UA PI to be associated with an increased risk of fetal distress in labor (5). Theoretically, a low UA PI could reflect fetal hypoxia and lactatemia, as lactate has vasodilator properties on placental vessels in response to both acute and chronic hypoxia (6). The present study was conducted to reveal whether an "abnormally" low UA PI is associated with an increased risk of adverse perinatal outcome.

Abbreviations:
CI: confidence interval; IUGR: intrauterine growth restriction; NICU: neonatal intensive care unit; OR: odds ratio; PI: pulsatility index; SD: standard deviation; UA: umbilical artery; WD: weight deviation.

Materials and methods

The study was approved by the Lund University Research Ethics Committee and all participants gave their informed consent. Three groups of singleton pregnancies, two study groups (A and B) and one control group (C) were included. Cases in the study groups A and B all displayed a low umbilical artery PI, defined as a gestational age-corrected PI < (mean − 2 SD). Study group A was selected from consecutive Doppler examinations stored in the computerized database at our Fetal Blood Flow Laboratory. The examinations were carried out because of a clinical indication to perform UA Doppler velocimetry ($n = 330$).

Study group B and the control group C were selected from a prospective population-based study in the Malmö catchment area undergoing longitudinal Doppler velocimetries antenatally as a screening test for the prediction of adverse outcome in labor (unpublished study). Doppler velocimetries in the UA were from 28 gestational weeks and onwards performed every second week until delivery. Group B comprised 39 women with a low UA PI and group C 863 women with a PI within mean ± 2 SD. The last Doppler velocimetry, in all cases performed within 2 weeks before delivery, was used for grouping. Cases with a high PI (>mean ± 2 SD) or absent or reversed end-diastolic flow were not included.

In group A, 114 women (34.5%) were postterm (gestational age at delivery ≥42 completed weeks according to an early midtrimester ultrasound fetometry). Other indications in group A were decreased fetal movements in 44 cases, suspected IUGR 30 cases, gestational hypertension/preeclampsia 33 cases, poor obstetric history 23 cases, fetal supraventricular extrasystolae 18 cases, diabetes mellitus 13 cases, nonreassuring nonstress test eight cases, preterm labor four cases, Rhesus isoimmunization three cases, and miscellaneous indications 40 cases. Five women originally assigned to group B became postterm: two of them were analyzed as belonging to group A as UA Doppler velocimetry was performed according to the routine protocol for surveillance of postterm pregnancy, but in the other three cases the women delivered before postterm Doppler studies were accomplished and they were not included in group A. In group C, 63 women became postterm. Postterm pregnancies were therefore subjected to subanalyses.

The UA Doppler blood flow measurements were performed in group A with a multihertz (3.5 or 5 MHz) pulsed Doppler instrument (Acuson 128 XP, Mountain View, USA) and in groups B and C with a 3.0-MHz pulsed Doppler instrument (Goldline Doppler 6, Vingmed, Horten, Norway). All recordings were performed during fetal quiescence. The UA maximum flow velocity waveforms were recorded in a free loop of the umbilical cord and the PI calculated online from at least 10 successive heart cycles. A group of four experienced Doppler ultrasound technicians performed all the velocimetries.

Data on Doppler flow parameters were extracted manually from the blood flow databases, as an "abnormally low" PI is nominated as normal and not indicated or classified in our system. Cutoff values below mean − 2 SD were identified from the reference curve (1). All fetuses in the study showed a heart rate between 120 and 150 beats/min at examination, *nota bene*, during a regular fetal heart frequency, and also in cases admitted for suspected fetal arrhythmia. Within this limit it is not necessary to adjust UA PI for fetal heart rate variations (1).

Data on pregnancy course and delivery were collected from our computerized obstetric database. Main outcome measures were cesarean section, operative delivery (cesarean section, ventouse or forceps delivery), Apgar scores at 1, 5 and 10 min, umbilical cord arterial and venous blood pH, transfer to the neonatal intensive care unit (NICU), and perinatal death. An Apgar score of <4 at 1 min and/or <7 at 5 or 10 min, and/or arterial pH <7.10 and/or venous pH < 7.15 in umbilical cord blood, were regarded as abnormal. Perinatal mortality was defined as a stillbirth or a neonatal death after 24 weeks of gestation and within 7 days after delivery in liveborns.

Birthweight was expressed in real figures and as weight deviation (WD) from the gestational age-corrected mean, according to reference values (7).

The unpaired *t*-test or the Mann–Whitney *U*-test were used for comparison of continuous variables, and the χ^2-test or Fisher's exact test for comparison of nominal data. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. A two-tailed *p*-value <0.05 was regarded as statistically significant.

Results

Comparisons of outcome variables are shown in Table I. No perinatal deaths occurred in groups A and B. In the control group (group C), three intrauterine and three early neonatal deaths occurred. All but one death in group C occurred preterm, in one case associated with extreme IUGR (WD −36%).

In comparisons between groups A and C, the gestational age at delivery was longer, the operative delivery rates higher, and transfer to the NICU more common in group A. In comparisons between groups B and C the WD from the gestational age-corrected mean value was higher in group B.

Subanalyses were performed for postterm and non-postterm deliveries in group A (data not shown). Comparisons with non-postterm deliveries in group C revealed higher frequencies of operative delivery in both group A subgroups. In addition, transfer to the NICU was higher in the non-postterm subgroup A but not in the postterm subgroup A.

Discussion

This study revealed no evidence of an increased risk of adverse perinatal outcome in pregnancies exhibiting a low UA PI. This was the case whatever Doppler blood flow examinations were performed in a heterogeneous high-risk group or in a sample from an unselected population. For obvious reasons, the operative delivery rate and the need for neonatal intensive care were higher in the high-risk group than in the control group. The slightly longer pregnancy duration in the high-risk group is explained by the fact that one-third of the series comprised postterm pregnancies. Subanalysis for postterm and non-postterm high-risk cases was therefore performed, revealing the same result as for the whole material: a low UA flow resistance *per se* carried no increased risk of fetal compromise, neither in unselected pregnancies nor in high-risk pregnancies, and postterm pregnancy carried no additional risk. This is in

Table I. Outcome in cases with low umbilical artery pulsatility index (groups A and B) and controls (group C). *p*-values were calculated with the *t*-test, Mann–Whitney *U*-test, χ^2-test or Fisher's exact test accordingly. Odds ratios (OR) with 95% confidence interval (CI) are indicated. Values are mean (SD), or number of cases (percentage)

				Significance of difference					
				Group A vs. group C			Group B vs. group C		
	Group A (on indication) (n = 330)	Group B (unselected) (n = 39)	Group C (unselected) (n = 863)	*p*	OR	95% CI	*p*	OR	95% CI
Delivery day (days)	281.1 (19.2)	278.7 (11.2)	278.5 (13.2)	0.008	–	–	0.9	–	–
Birthweight (g)	3474 (773)	3622 (608)	3468 (556)	0.9	–	–	0.09	–	–
WD (%)	−1.7 (16.6)	+3.4 (13.0)	−0.3 (12.4)	0.5	–	–	0.049	–	–
Cesarean section	87 (26.4%)	3 (7.7%)	70 (8.1%)	<0.0005	4.06	2.87–5.73	1.0	0.94	0.28–3.14
Operative delivery	112 (33.9%)	5 (12.8%)	141 (16.3%)	<0.0005	2.63	1.97–3.52	0.7	0.75	0.29–1.96
Apgar score <4 at 1 min*	5 (1.5%)	0	12 (1.2%)	0.8	1.09	0.38–3.11	1.0	–	–
Apgar score <7 at 5 min*	5 (1.5%)	0	13 (1.5%)	1.0	1.00	0.35–2.83	1.0	–	–
Apgar score <7 at 10 min*	1 (0.3%)	0	3 (3.5%)	1.0	0.87	0.09–8.41	1.0	–	–
Cord artery pH <7.10*	18/229 (7.9%)	3/32 (9.4%)	53/535 (9.9%)	0.4	0.78	0.44–1.36	1.0	0.94	0.28–3.19
Cord vein pH <7.15*	10/296 (3.4%)	1/36 (2.8%)	32/703 (4.6%)	0.5	0.73	0.36–1.51	1.0	0.60	0.08–4.51
Transfer to NICU*	56 (17.0%)	2 (5.1%)	57 (6.6%)	<0.0005	2.88	1.94–4.27	1.0	0.76	0.18–3.24
Perinatal mortality	0	0	6 (0.7%)	0.2	–	–	1.0	–	–

WD, weight deviation from the gestational age-adjusted mean birthweight; NICU, neonatal intensive care unit
*Three stillbirths excluded from group C

contrast to our previous finding, indicating a higher risk of fetal distress in labor in postterm pregnancies with a low UA PI (5). However, unlike the present study, all pregnancies in our previous study had passed 43 gestational weeks.

In the sample extracted from the unselected population (group B), a low placental vascular flow resistance indicated a beneficial effect: a higher birthweight was found in the presence of a low UA PI compared with controls. A low placental vascular flow resistance may promote fetal growth, as indicated previously (2). Because of the element of IUGR, this effect was not found in the high-risk group. The mean WD between the groups with a normal and a low UA PI in the unselected population was 3.7%, which corresponds to a 130-g WD at term. In clinical practice, this difference should have little or no impact on the course of pregnancy and delivery.

In conclusion, this study did not indicate that the statistical definition of a low UA PI, that is a PI below the reference interval mean ± 2 SD, should be deemed "abnormally" low, as it was not reflected by a biological imperfection. On the contrary, a low UA PI promoted fetal growth.

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