AOGS
Acta Obstetricia et Gynecologica Scandinavica

AOGS ORIGINAL RESEARCH ARTICLE

Placental pulsatility index: a new, more sensitive parameter for predicting adverse outcome in pregnancies suspected of fetal growth restriction

SAEMUNDUR GUDMUNDSSON[1], KARI FLO[2,3], GISELA GHOSH[1], TOM WILSGAARD[4] & GANESH ACHARYA[2,3,5]

[1]Department of Obstetrics and Gynecology, Skane University Hospital, University of Lund, Malmö, Sweden, [2]Women's Health and Perinatology Research Group, Department of Clinical Medicine, Faculty of Health Sciences, University of Tromsø, Tromsø, [3]Department of Obstetrics and Gynecology, University Hospital of North Norway, Tromsø, [4]Department of Community Medicine, Faculty of Health Sciences, UiT – The Arctic University of Norway, Tromsø, Norway, and [5]Department of Clinical Science, Intervention and Technology, Karolinska Institute, Stockholm, Sweden

Key words
Placenta pulsatility index, uterine artery, Doppler, umbilical artery, pregnancy, fetal growth restriction, small for gestational age

Correspondence
Saemundur Gudmundsson, Department of Obstetrics and Gynecology, Skane University Hospital, University of Lund, 205 02 Malmö, Sweden.
E-mail: saemundur.gudmundsson@med.lu.se

Conflict of interest
The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Please cite this article as: Gudmundsson S, Flo K, Ghosh G, Wilsgaard T, Acharya G. Placental pulsatility index: a new, more sensitive parameter for predicting adverse outcome in pregnancies suspected of fetal growth restriction. Acta Obstet Gynecol Scand 2017; 96: 216–222.

Received: 8 July 2016
Accepted: 12 November 2016

DOI: 10.1111/aogs.13060

Abstract

Introduction. The pulsatility indices of the umbilical and uterine arteries are used as the surrogate measures of utero-placental perfusion. Combining the two might simplify the evaluation of total placental vascular impedance, possibly improve prediction of adverse outcomes, and help identify pregnancies with suspected fetal growth restriction that need more intense surveillance. *Material and methods.* Umbilical and uterine blood flow velocities were recorded using pulsed-wave Doppler in a longitudinal study of 53 low-risk pregnancies (248 observations) during 20–40 weeks of gestation. Pulsatility indices was calculated for each of these vessels. A new placental pulsatility index was constructed as: (umbilical artery pulsatility index + mean of the left and right uterine artery pulsatility indices)/2, and mean +2 SD defined as abnormal. Gestational age-specific reference percentiles were calculated for the second half of pregnancy and related to values obtained from 340 pregnancies with suspected intra-uterine growth restriction to test its ability to predict adverse pregnancy outcome. *Results.* The placental pulsatility index was closely associated with gestational age and decreased with advancing gestation in normal pregnancy. The placental pulsatility index had a higher sensitivity and comparable specificity in predicting adverse outcome in pregnancies suspected of intra-uterine fetal growth restriction when compared with conventional umbilical and uterine artery pulsatility indices. *Conclusions.* The new placental pulsatility index, reflecting placental vascular impedance on both the fetal and maternal side of placenta, improves prediction of adverse outcome in pregnancies suspected of intra-uterine fetal growth restriction.

Abbreviations: ARED, absent or reversed end-diastolic blood flow; BFC, blood flow class; EDV, end-diastolic velocity; IUGR, intra-uterine fetal growth restriction; PI, pulsatility index; PPI, placental pulsatility index; PSV, peak systolic velocity; TAMXV, time-averaged maximum velocity; UAS, UtA score; UA, umbilical artery; UtA, uterine artery.

Introduction

Doppler ultrasound has become a valuable tool in the evaluation of fetal and placental circulation and in the prediction of fetal well-being and outcome of pregnancy (1,2).

Doppler signs of increased placental vascular resistance are frequently related to fetal growth restriction and signs of imminent asphyxia (3). Umbilical artery (UA) Doppler velocimetry is presently a routine part of fetal surveillance in high-risk pregnancies. After initial technical difficulties, the uterine artery (UtA) Doppler velocimetry has also proven its value in predicting outcome of high-risk pregnancies, and in recent years it has been reported to be comparable to the UA Doppler in that respect (3). In late pregnancy, abnormal UtA Doppler and reduced umbilical vein volume blood flow are considered to be the surrogates of reduced placental perfusion (4). UtA Doppler screening in the first trimester and mid-gestation has also proven its value in predicting adverse outcome in high-risk pregnancies and choosing cases in need for special surveillance (5,6).

Placental vascular impedance is commonly expressed in terms of pulsatility index (PI), resistance index and systolic/diastolic ratio of the UA and UtA. In some instances, placental location, presence or absence/reversal of end-diastolic flow in the UA and notching in early diastole in UtA are also reported.

The objective of the present study was to construct a new reference chart for placental pulsatility index (PPI), an index reflecting combined vascular impedance of both maternal and fetal sides of the placenta. We compared the new index with conventional UA and UtA Doppler parameters to test the hypothesis that PPI performs better in predicting adverse outcome in pregnancies suspected of intra-uterine fetal growth restriction (IUGR). This information could be of value in identifying pregnancies with a placental vascular cause of fetal growth restriction that may benefit from more intense surveillance.

Material and methods

A total of 393 pregnant women were included after obtaining informed written consent. Fifty-three healthy pregnant women were recruited at the time of routine ultrasound screening at 17–20 weeks of gestation for a longitudinal study of maternal-fetal hemodynamics performed during 2006–2008. Inclusion criteria were normal singleton pregnancy, ultrasound dating before 20 weeks of gestation, absence of any fetal anomalies or any other complication in the current pregnancy. Women with multiple pregnancy, any preexisting medical illness that might affect the current pregnancy or previous history of pregnancy complications were excluded. The study protocol was approved by the Regional Committee for Medical Research Ethics – North Norway (REK Nord 5.2005. 1386).

Doppler ultrasonography in these normal pregnancies was performed at approximately 4-weekly intervals during 22–40 weeks of gestation using a 6-MHz curvilinear transducer (Acuson Sequoia 512, Mountain View, CA, USA). A single investigator (K.F.) performed all the examinations to reduce the variability. The blood flow velocities of the right and the left uterine arteries were measured just proximal to the apparent crossing of the external iliac artery. The peak systolic (PSV), end-diastolic (EDV) and time-averaged maximum (TAMXV) velocities were measured and the PI calculated automatically by the software of the ultrasound system according to the formula: PI = (PSV − EDV)/TAMXV. The UA blood velocity was also recorded in a free-floating loop of the umbilical cord using color-directed pulsed-wave Doppler. The PI values were an average of three consecutive waveforms recorded in the absence of fetal or maternal movements. A mean of three PI measurements of the UA and the mean PI values of both uterine arteries were used for statistical analysis. A new PPI was calculated as: PPI = (UA PI + mean of the left and right UtA PI)/2.

In the high-risk group, 340 singleton pregnancies with fetuses suspected of IUGR were submitted to Doppler examination at Skåne University Hospital. IUGR was suspected during ultrasound fetal biometry performed either as a routine examination at 32–34 weeks of gestation, or on clinical indication during a five-year period (1994–99). Suspected IUGR was defined as an estimated fetal weight of more than 2 SD below the mean for gestational age according to Scandinavian reference growth curve (7), or a decline of more than 1 SD between two ultrasound examinations performed at least two weeks apart. Exclusion criteria for the high-risk pregnancies group were multiple pregnancies, congenital malformations and chromosomal abnormalities known before labor and delivery. All pregnancies were dated by ultrasound examination performed at 1–21 weeks of gestation. The local Ethics Committee approved the study.

The high-risk pregnancies were examined by Acuson 128 XP and Sequoia 512 duplex scanners with power and

Key Message

The new placental pulsatility index has higher sensitivity for predicting adverse outcome in pregnancies suspected of fetal growth restriction compared with conventional umbilical and uterine artery Doppler.

color Doppler options. The uterine and UA blood velocities were recorded in the same way as in the normal controls by ultrasonographers who were only engaged in Doppler recordings and were not involved in patient care. Abnormal placental vascular impedance was defined as: a mean of the two uterine arteries PI > mean +2 SD (PI > 1.20) (8). Abnormal UA Doppler flow spectrum was defined as a PI > mean +2 SD according to Gudmundsson and Marsal (9). Abnormal PPI was defined as >mean +2 SD. The UtA Doppler was also evaluated for UtA score (UAS) taking into account both PI and notching bilaterally (10). Abnormal UAS was defined as UAS > 0.

The results of UA and UtA Doppler obtained at the time of diagnosis of a suspected IUGR were used for analysis. The results of the UA, but not the UtA, were disclosed to the clinician in charge of the patient's care, because the UtA Doppler was not the standard of care during the study period, as its clinical value was not yet established. The women were hospitalized or followed by close outpatient checkups according to the local protocol for the management of pregnancies suspected of an IUGR. The intention of the protocol was to minimize the risk of fetal damage caused by growth restriction without causing unnecessary prematurity. Fetal surveillance included: Doppler examinations of the UA, estimation of amniotic fluid index and non-stress test every second week if UA Doppler was normal. When UA PI was between +2 and 3 SD, control was performed twice weekly. If the UA PI was >+3 SD, control was performed three times weekly, and in the case of absent or reversed end-diastolic blood flow (ARED) the pregnant woman was admitted to the ward for closer monitoring with a non-stress test twice daily and Doppler evaluations daily. Fetal growth was estimated by ultrasound every second week in all cases. If the estimated fetal weight was more than 3 SD below the mean for the gestation age, the woman was hospitalized for closer surveillance and the fetus was further evaluated for congenital malformations by detailed ultrasonography, karyotyping, and screening for viral infection. The decision regarding the time and mode of delivery was made by a senior obstetrician based on gestational age, ultrasound estimation of fetal growth, amniotic fluid index, UA Doppler, non-stress test and/or maternal signs of severe preeclampsia. ARED flow in the UA was regarded as an indication for delivery except in cases of extreme prematurity (<26 weeks) where individual assessment was based on multi-vessel Doppler, non-stress test, amniotic fluid index and fetal growth.

Adverse outcome of high-risk pregnancy was defined as small-for-gestational-age newborns (<10 and 2.3 centiles below the mean birthweight for the given gestational age), premature delivery (<34 weeks and <37 weeks of gestation), and admission of the newborn to the neonatal intensive care unit (NICU). The outcome data were extracted from the local perinatal database. The recorded values of the UA and the UtA Doppler separately were compared with that of the new PPI in relation to these outcome variables.

Statistical analyses

Data obtained from the normal pregnancies were analyzed using the SAS 9.3 (SAS Institute Inc., Cary, NC, USA). The assumption of normality was checked for each variable and logarithmic or power transformations were performed as required to achieve normal distribution of data. The best transformation was chosen using Box-Cox regression. Fractional polynomials were used to obtain best fitting curves in relation to gestational age accommodating for nonlinear associations and repeated measures design. The association between PPI (dependent variable) and the gestational age (independent variable) was investigated using multilevel modeling. Gestational age-specific percentiles were estimated from each fitted model as suggested by Royston and Altman (11) as follows: If Y_i = dependent variable at gestational age T_i, then the mean and variance of a transformed variable Z_i at a transformed time X_i are

$$\mu_i = E(Z_i) = \beta_{0i} + \beta_{1i}X_i$$

$$\sigma_i^2 = \mathrm{Var}(Z_i) = \sigma_{\mathrm{int}}^2 + \sigma_{\mathrm{time}}^2 X_i^2 + 2\sigma_{\mathrm{int,time}} X_i + \sigma_e^2$$

where β_{0i}, β_{1i} are the fixed parameter estimates, and σ^2_{int}, σ^2_{time}, $\sigma_{\mathrm{int,time}}$, σ^2_e are the estimated variance components from the multilevel analysis.

The time-specific reference value for Y_i with 95% coverage is

$$(\mu_i \pm 1.96\sigma_i)^{1/\lambda} \quad \text{if transformed variable } Z_i = Y_i^{\lambda}$$

$$\exp(\mu_i \pm 1.96\sigma_i) \quad \text{if transformed variable } Z_i = \ln(Y_i)$$

The STATISTICA 12.0 computer program (Statsoft Co., Tulsa, OK, USA) was used for the analysis of data obtained from high-risk pregnancies. MEDCALC® version 6.00.014 (MedCalc Software, Mariakerke, Belgium) software was used to calculate receiver operating characteristic (ROC) curves that were drawn for each diagnostic index to evaluate the ability to discriminate the likelihood of developing adverse perinatal outcome. The area under the curve and 95% confidence intervals (CI) were also calculated and used to compare the value of different Doppler parameters in predicting outcome. A p-value of <0.05 was considered statistically significant.

Results

All the participants in the study arm that included low-risk healthy pregnancies completed the study and outcome data were available for all. There were three to five observations per women and a total of 248 recordings were available for analysis. The median maternal age was 28 years (range 18–39), mean body mass index 23.5 ($\pm$3.1 SD) kg/m^2 and the mean arterial blood pressure at inclusion 83 ($\pm$8 SD) mmHg and 68% (36/53) of women were nulliparous. None of these women had any pregnancy complications. Three women were delivered by a cesarean section, two because of slow progress of labor and one because of breech presentation. Six women had vacuum delivery, four due to failure of labor to progress and two due to fetal distress in the second stage of labor. The mean birthweight and placental weight were 3562 ($\pm$470 SD) g and 591 ($\pm$117 SD) g, respectively. The median five-minute Apgar score was 10 (range 7–10), and mean UA pH was 7.24 ($\pm$0.1 SD).

The PPI was transformed as Z = PPI$^{0.2}$, i.e. $\lambda = 0.2$:

$$\mu_i = E(Z_i) = 0.6977 + 1.4279T^{-0.5}$$

$$\sigma_i^2 = \mathrm{Var}(Z_i) = 0.0007187$$

The variance component for time was not estimable, which means that the multilevel model was a random intercept model. The PPI was significantly associated with gestational age ($p < 0.0001$). The mean standard deviation changed with gestation, being 0.16 at 20 weeks and 0.11 at term. Table 1 gives the gestational age-specific PPI values from 20 weeks of gestation to term with a mean and different percentile cut-offs. The reference cut-offs for mean +2 SD, +3 SD and +4 SD are also given in Table 1. Reference curves representing the 2.5th centile, mean and +2, +3 and +4 SD are presented in Figure 1.

The PPI was analyzed in relation to adverse outcome in pregnancies suspected of IUGR. Abnormal PPI defined as > mean +2 SD was found in 170 pregnancies. The results were compared with abnormal UA PI (> mean +2 SD) (n = 96) and mean UtA PI (> +2 SD as >1.2) (n = 79) and presented in Table 2. The PPI had higher sensitivity for predicting adverse outcome of pregnancy compared with abnormal UA and mean UtA PI (Table 3).

Further analysis was performed using the 95th centile for PPI as a definition of abnormal PPI. There were 205 high-risk pregnancies that had PPI above the 95th percentile for the gestational age. The sensitivity to predict adverse outcome was high, but the specificity was much worse.

There were 12 pregnancies with a normal PPI but a slightly increased UA PI. The outcome was fairly good in these cases. Of the 12, five were small for gestational age at birth, and were delivered by a cesarean section. Two were delivered prematurely and one of them had to be admitted to a neonatal intensive care unit.

There were three pregnancies with a normal PPI, but the mean UtA PI was just above 1.2. All these newborns were small for gestational age at birth and two had to be delivered preterm by a cesarean section and required admission to a neonatal intensive care unit.

Table 1. Reference cut-off limits for placental pulsatility index from 20 to 40 weeks of gestation age (ga). The 2.5th centile (cent025), 5th centile, the mean, 95th and 97.5th centiles are given as well as the mean +2 SD, +3 SD and +4 SD limits are given.

ga	cent025	cent05	mean	cent95	cent97.5	+2 SD	+3 SD	+4 SD
22.0	0.77	0.81	1.01	1.25	1.30	1.31	1.49	1.68
23.0	0.75	0.78	0.98	1.21	1.26	1.27	1.44	1.63
24.0	0.72	0.75	0.95	1.18	1.23	1.23	1.40	1.58
25.0	0.70	0.73	0.92	1.14	1.19	1.20	1.36	1.54
26.0	0.68	0.71	0.89	1.11	1.16	1.17	1.33	1.50
27.0	0.66	0.69	0.87	1.09	1.13	1.14	1.29	1.47
28.0	0.64	0.67	0.85	1.06	1.10	1.11	1.26	1.43
29.0	0.63	0.65	0.83	1.04	1.08	1.09	1.24	1.40
30.0	0.61	0.64	0.81	1.01	1.06	1.06	1.21	1.37
31.0	0.60	0.62	0.79	0.99	1.03	1.04	1.19	1.35
32.3	0.58	0.61	0.77	0.97	1.01	1.01	1.16	1.31
33.0	0.57	0.60	0.76	0.95	0.99	1.00	1.14	1.30
34.0	0.56	0.59	0.74	0.94	0.98	0.98	1.12	1.28
35.0	0.55	0.57	0.73	0.92	0.96	0.96	1.10	1.25
36.0	0.54	0.56	0.72	0.90	0.94	0.95	1.08	1.23
37.0	0.53	0.55	0.70	0.89	0.93	0.93	1.07	1.21
38.0	0.52	0.54	0.69	0.87	0.91	0.92	1.05	1.20
39.0	0.51	0.53	0.68	0.86	0.90	0.90	1.03	1.18

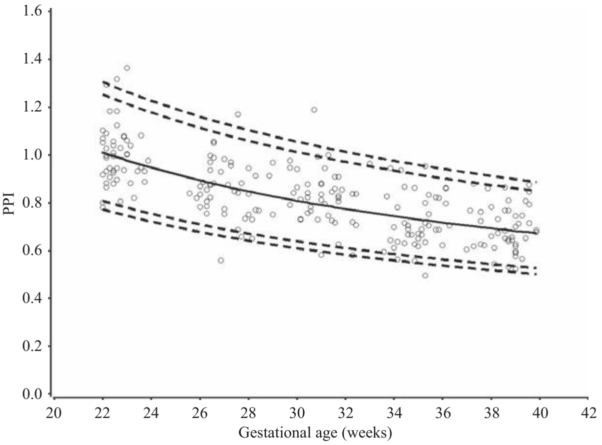

Figure 1. Gestational age-specific longitudinal reference range for placental pulsatility index (PPI) during the second half of pregnancy. The solid line represents the mean and the dashed lines the −2 SD (below) and +2, +3 and +4 SD (above).

There were five mortalities of which three had an abnormal PPI. Two died in utero due to placental abruption and one had a true knot on the cord. Three died in the neonatal period: two had a trisomy 18 and one died due to prematurity after being delivered at 23^{+5} weeks due to severe maternal preeclampsia.

We categorized PPI values into four different classes: 0 – PPI < mean +2 SD; 1 – PPI between +2 and +3 SD; 2 – PPI between +3 and +4 SD; 3 – PPI > mean +4SD, and calculated the proportions of adverse outcomes for each class (Table 4). The proportion of pregnancies with adverse outcomes increased with increasing PPI class.

Table 2. Placental Doppler results and outcome in 340 high-risk pregnancies where the fetus was suspected of intrauterine growth restriction (<2.3 centile).

	n	PPI > +2 SD	UA PI > +2 SD	Mean ute PI > 1.2
Number		170	96	79
Mean gestational age at detection (weeks)		33.8 ± 3.3	33.6 ± 3.4	32.9 ± 3.2
Mean gestational age at birth (weeks)		35.5 ± 3.3	34.5 ± 3.4	34.3 ± 3.3
Birthweight (g)		1978.3 ± 611	1794.6 ± 594	1688.5 ± 538
Birthweight deviation in %		−28.3 ± 11.7	−30.7 ± 11	−33.4 ± 9.7
Placental weight (g)		391.0 ± 143	361.9 ± 166	348.4 ± 138
SGA < 2.3 centiles, *n* (%)	191	127 (74.7)	77 (80.2)	71 (89.9)
SGA < 10 centiles, *n* (%)	273	154 (90.6)	90 (93.7)	78 (98.7)
Birth < 34 weeks, *n* (%)	51	45 (26.4)	35 (36.5)	30 (38.0)
Birth < 37 weeks, *n* (%)	115	94 (55.3)	61 (63.5)	55 (69.6)
Birth > 36 weeks, *n* (%)	225	76 (44.7)	35 (36.5)	24 (30.4)
Admission to NICU, *n* (%)	144	107 (62.9)	70 (72.9)	67 (84.8)
Mortality, *n* (%)	5	3 (1.7)	3 (3.1)	2 (2.5)

Birthweight deviation in %, birthweight deviation from the population mean in percent; Mean ute PI, mean of the two uterine artery pulsatility indices; NICU, neonatal intensive care unit; PPI, placental pulsatility index; SGA, small for gestational age at birth; UA PI, umbilical artery pulsatility index.

Discussion

We present a new Doppler index, PPI, that appears to be useful in predicting outcome of pregnancies with suspected of IUGR. The PPI values decreased with increasing gestational age in the second half of normal pregnancy. Abnormal PPI had higher sensitivity for the prediction of adverse pregnancy outcome in suspected IUGR compared with conventional UA and UtA PIs separately. Using this new index instead of UA and UtA PIs separately, might thus improve detection of fetal growth restriction associated with increased placental vascular impedance and assist in planning surveillance of these pregnancies.

We have previously included the presence of a notch in the spectrum of UtA blood velocity waveform in the evaluation of vascular impedance on the maternal side of the placenta. This has been expressed as UAS of 0–4 based on UtA PI values and the presence or absence of a notch on one or both sides (10). The UAS was constructed to make it easier for the clinicians to understand the information on both UtA blood velocities in one figure. When compared with PPI, UAS had lower sensitivity. Abnormal UAS (>0, was seen in 97 pregnancies) predicted adverse outcome slightly better than the UA PI and the mean UtA PI. However, we believe that the mean UtA PI is a better choice than the UAS because of the problems associated with the definition of a notch and its interobserver reproducibility.

Another scoring system, the blood flow class (BFC), has been widely applied in Scandinavia for assessing UA blood flow velocity waveforms. The BFC is a simple system for expressing the degree of abnormal feto-placental vascular impedance: BFC 0 – when the UA PI is normal; BFC 1 – when the PI is above mean +2 SD and below +3 SD; BFC 2 – when the PI is above +3 SD and there is still forward flow in diastole; BFC 3 – when there is absent or reversal of flow in diastole. This system has gained wide popularity and continues to be used.

Table 3. Sensitivity, specificity, positive and negative predictive value for adverse outcome of pregnancy in relation to abnormal placental pulsatility index (PPI), abnormal umbilical artery (UA) PI, abnormal mean uterine artery (UtA) PI and abnormal uterine artery score (UAS). Receiver operating characteristic (ROC) curve area with 95% confidence intervals (CI) are also presented for each Doppler index or score.

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	ROC area and CI
PPI > mean +2 SD					
SGA <2.3 centile	66.5	71.1	74.7	62.4	0.719 (0.668–0.767)
SGA <10 centile	56.4	76.1	90.6	30.0	0.705 (0.653–0.753)
<34 weeks	27.6	29.4	26.5	30.6	0.875 (0.835–0.908)
<37 weeks	39.7	26.2	55.3	15.9	0.842 (0.799–0.879)
NICU	74.3	67.9	62.9	78.2	0.801 (0.754–0.842)
UAPI > mean +2 SD					
SGA <2.3 centile	40.3	87.2	80.2	53.3	0.671 (0.618–0.721)
SGA <10 centile	33.0	91.0	93.8	25.0	0.653 (0.600–0.703)
<34 weeks	21.5	65.5	36.5	47.5	0.869 (0.828–0.903)
<37 weeks	25.7	66.0	63.5	27.9	0.809 (0.763–0.849)
NICU	48.6	86.7	72.9	69.7	0.764 (0.715–0.809)
UtA PI mean >1.20					
SGA <2.3 centile	37.1	94.6	89.9	54.0	0.716 (0.665–0.763)
SGA <10 centile	28.6	98.5	98.7	25.3	0.710 (0.659–0.758)
<34 weeks	18.4	72.3	38.0	49.0	0.793 (0.746–0.835)
<37 weeks	23.2	76.7	69.6	30.3	0.769 (0.720–0.812)
NICU	46.5	93.9	84.8	70.5	0.762 (0.712–0.807)
UAS > 0					
SGA <2.3 centile	49.7	98.7	97.9	60.5	0.673 (0.621–0.723)
SGA <10 centile	53.9	99.4	99.0	66.3	0.664 (0.611–0.714)
<34 weeks	22.7	66.1	38.1	48.1	0.746 (0.696–0.791)
<37 weeks	30.8	76.7	75.3	32.5	0.726 (0.676–0.773)
NICU	61.1	95.4	90.7	77.0	0.743 (0.693–0.790)

Table 4. Outcome of pregnancies suspected of intrauterine growth restriction depending on the degree of increase in placental pulsatility index (PPI) value and related to PPI class defined as different levels of SD from the mean.

	PPI class 0 (PPI < +2 SD)	PPI class 1 (PPI +2–3 SD)	PPI class 2 (PPI +3–4 SD)	PPI class 3 (PPI > +4 SD)
Number	170	58	32	80
Mean gestational age at detection (weeks)	35.2 ± 3.0	35.0 ± 3.1	33.8 ± 2.3	32.9 ± 3.4
Mean gestational age at birth (weeks)	38.5 ± 2.2	37.6 ± 2.2	35.6 ± 2.5	33.8 ± 3.3
Birthweight (g)	2676.0 ± 454	2464.7 ± 460	1981.3 ± 471	1624.4 ± 508
Birthweight deviation in %	−19.4 ± 9.2	−21.2 ± 11.0	−28.6 ± 7.6	−33.4 ± 9.4
Placental weight (g)	518.0 ± 206	457.9 ± 149	396.2 ± 83	328.1 ± 132
SGA < 2.3 centiles, *n* (%)	64 (37.6)	29 (50.0)	26 (81.3)	72 (90.0)
SGA < 10 centiles, *n* (%)	119 (70.0)	43 (74.1)	31 (96.9)	80 (100)
Birth < 34 weeks (n%)	7 (4.1)	4 (6.9)	7 (31.2)	34 (42.5)
Birth < 37 weeks, *n* (%)	21 (12.4)	17 (29.3)	20 (62.5)	57 (71.3)
NICU, *n* (%)	37 (21.8)	20 (34.5)	18 (56.3)	69 (86.3)
Mortality, *n* (%)	2 (1.2)	1 (1.7)	1 (3.1)	1 (1.3)

Birthweight deviation in %, weight deviation in percent from the population mean; SGA, small for gestational age at birth; NICU, admission to the neonatal intensive care unit.

However, we found that PPI is a better predictor of adverse outcome than the UA PI. Moreover, the new PPI can also be categorized into classes, again reducing the time the clinician needs to plot the PPI figure on a graph. We found that the frequency of adverse outcome increased with increasing PPI class (Table 4).

We have previously tried to combine the BFC (0–3) and UAS (0–4) to create a single score representing placental vascular impedance. The placental score (PLS), which gives figures from 0 to 7, produced interesting results (12), but was never used in clinical practice because a case with BFC of 3 (absent or reversal of flow in the UA) might theoretically have a normal flow in the uterine arteries (UAS 0), although we have never seen this. If that were the case, the PLS would be low, giving an incorrect impression of lower placental vascular impedance. All cases of ARED blood flow in the UA in the present study had a PPI above mean +4 SD.

The main limitation of our study is that it is based on patient material collected in two different hospital settings more than 10 years apart, although using the same technique. The results on the high-risk pregnancies were based on retrospective data of pregnancies suspected of fetal growth restriction between 1994 and 1999, whereas the reference values were based on prospectively collected longitudinal data from low-risk pregnancies during 2006–2008. The clinician in charge was not blinded to the results of UA Doppler. This knowledge might have affected the outcome results. However, the UA Doppler was not the only parameter used in deciding the mode and time of delivery. It also included gestational age, ultrasound estimation of fetal growth, amniotic fluid index, NST, and/or maternal signs of severe preeclampsia. The mean UtA PI was, however, not supplied to the clinician as there was no evidence to support its clinical benefit at the time of the study. Another limitation is that we did not investigate the correlation between PPI and fetal/neonatal acid-base status, and thus its value in predicting/diagnosing fetal hypoxia is not known.

In summary, we propose a new index (PPI), expressing vascular impedance on both sides of the placenta, and established reference ranges for the second half of pregnancy. The reference chart was tested on 340 pregnancies with suspected IUGR. The PPI had a higher sensitivity in predicting adverse outcome of these pregnancies compared with either UA PI/BFC or the mean UtA PIs separately. The new PPI might therefore simplify and improve the decision-making process in the management of pregnancies suspected of IUGR.

Acknowledgments

The authors are grateful to Pia Soikkeli, Maria Nilsson, Lena Berg and Åse Vårtun for their help in the recruitment of participants and data collection.

Funding

Financial support for this study was obtained from Medical Faculty at the University of Lund, the Swedish Society of Medicine, University Hospital Malmö funds, Region Skåne and the Northern Norway Regional Health Authority (SFP934-10).

References

1. Marsal K. Obstetric management of intrauterine growth restriction. Best Pract Res Clin Obstet Gynaecol. 2009;23:857–70.
2. Figueras F, Gratacos E. Update on the diagnosis and classification of fetal growth restriction and proposal of a stage-based management protocol. Fetal Diagn Ther. 2014;36:86–98.
3. Ghosh GS, Gudmundsson S. Uterine and umbilical artery Doppler are comparable in predicting perinatal outcome of growth-restricted fetuses. Br J Obstet Gynecol. 2009;116:424–30.
4. Parra-Saavedra M, Crovetto F, Triunfo S, Savchev S, Peguero A, Nadal A, et al. Association of Doppler parameters with placental signs of underperfusion in late-onset small-for-gestational-age pregnancies. Ultrasound Obstet Gynecol. 2014;44:330–7.
5. Velauthar L, Plana MN, Kalidindi M, Zamora J, Thilaganathan B, Illanes SE, et al. First-trimester uterine artery Doppler and adverse pregnancy outcome: a meta-analysis involving 55,974 women. Ultrasound Obstet Gynecol. 2014;43:500–7.
6. Li Na, Ghosh G, Gudmundsson S. Uterine artery Doppler in high-risk pregnancies at 23–24 weeks of gestation is of value in predicting adverse outcome of pregnancy and select cases for more intense surveillance. Acta Obstet Gynecol Scand. 2014;93:1276–81.
7. Marsal K, Persson P-H, Larsen T, Lilja H, Selbing A, Sultan B. Intrauterine growth curves based on ultrasonically estimated foetal weights. Acta Paediatr. 1996;85:843–8.
8. Hofstaetter C, Dubiel M, Gudmundsson S, Marsal K. Uterine artery color Doppler assisted velocimetry and perinatal outcome. Acta Obstet Gynecol Scand. 1996;75:612–9.
9. Gudmundsson S, Marsal K. Umbilical and uteroplacental blood flow velocity waveforms in normal pregnancy – a cross-sectional study. Acta Obstet Gynecol Scand. 1988;67:347–54.
10. Hernandez-Andrade E, Brodszki J, Lingman G, Gudmundsson S, Molin J, Marsal K. Uterine artery score and perinatal outcome. Ultrasound Obstet Gynecol. 2002;19:438–42.
11. Royston P, Altman DG. Regression using fractional polynomials of continuous covariates: parsimonious parametric modeling. Appl Statist. 1994;43:429–67.
12. Gudmundsson S, Korszun P, Olofsson P, Dubiel M. New score indicating placental vascular resistance. Acta Obstet Gynecol Scand. 2003;82:807–12.

