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Poor neonatal acid–base status in term fetuses with low cerebroplacental ratio

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KEYWORDS: cerebroplacental ratio; cord pH; failure to reach growth potential; fetal acid–base status; fetal Doppler; fetal growth restriction

ABSTRACT

Objective *To determine whether small- and appropriate-for-gestational-age (SGA and AGA) term fetuses with a low cerebroplacental ratio (CPR) have worse neonatal acid–base status than those with normal CPR.*

Methods *This was a retrospective study of 2927 term fetuses divided into groups according to birth-weight centile and CPR multiple of the median. The acid–base status at birth as determined by arterial and venous umbilical cord blood pH was compared between weight-centile groups with and without low CPR.*

Results *CPR was better correlated with umbilical cord blood pH (arterial pH,* $r^2 = 0.008$, $P < 0.0001$ *and venous pH,* $r^2 = 0.01$, $P < 0.0001$*) than was birth weight (arterial pH,* $r^2 = 0.001$, $P = 0.180$ *and venous pH,* $r^2 = 0.005$, $P < 0.001$*). AGA fetuses with low CPR were more acidemic than were those with normal CPR (*$P = 0.0359$ *and 0.0006, respectively, for arterial and venous pH).*

Conclusions *The findings of this study demonstrate that low CPR in AGA fetuses is an equally important marker of low neonatal pH secondary to placental underperfusion as is being SGA. Although the relative importance of low CPR and birth weight in identifying pregnancies at risk of placental hypoxemia and adverse fetal and neonatal outcome remains to be determined, this finding may be of particular value in the prediction and prevention of stillbirth and long-term neurodevelopmental disability.*

INTRODUCTION

Term fetuses with birth weight above the 10th centile are labeled appropriate for gestational age (AGA) and considered to be healthy[1–3]. However, it is generally accepted that some of these AGA fetuses suffer from placental insufficiency and fail to reach their genetic growth potential[4–6]. Calculation of estimated fetal weight centiles using either population-specific or customized charts has proved to be ineffective in prospectively identifying these AGA fetuses, which are at increased risk of adverse pregnancy outcome[7–9]. An alternative approach is the use of the cerebroplacental ratio (CPR) to suggest placental insufficiency and failure to reach their growth potential, regardless of their absolute birth-weight centile[4]. If the use of CPR at term improves fetal surveillance, then low CPR might be able to indicate which AGA fetuses would present with a higher risk of adverse outcome. The main aim of this study was to evaluate to what extent arterial and venous umbilical cord blood pH at birth is associated with birth weight and fetal CPR.

METHODS

This was a retrospective cohort study performed in two tertiary centers, including singleton term fetuses that had an ultrasound scan within 14 days of delivery. The umbilical (UA) and fetal middle cerebral (MCA) arteries were examined using color Doppler ultrasound according to a standard protocol[10,11], and CPR was calculated as the ratio between the MCA and UA pulsatility indices[12]. Only the last examination per fetus was included.

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Ultrasound examinations were performed with Voluson E8/E6/730 ultrasound machines (GE Medical Systems, Zipf, Austria) using 2–8-MHz convex probes, during fetal quiescence, in the absence of fetal tachycardia and keeping the insonation angle with respect to the examined vessels as small as possible. Gestational age (GA) was determined according to first-trimester crown–rump length. Pregnancies complicated by congenital fetal abnormalities or stillbirth were excluded.

Birth weights were converted into centiles using the method described by Yudkin *et al.*[13], and CPR values were converted into multiples of the median (MoM), correcting for GA. CPR medians (50^{th} percentile) were those used in a recent study[4] and were represented by the equation:

$$\text{CPR } 50^{th} \text{ percentile} = -1.3841 + (0.22659 \times GA) - (0.003743 \times GA^2),$$ where GA is in weeks.

A pregnancy with a fetal CPR below 0.6765 MoM was considered more likely to have placental insufficiency[4]. We used this threshold together with birth weight to classify fetuses into small-for-gestational-age (SGA), AGA and large-for-gestational-age (LGA), with their homonymous subgroups with normal and abnormal CPR. LGA was defined as birth weight $>90^{th}$ percentile, SGA was defined as birth weight $<10^{th}$ percentile and AGA was defined as birth weight between the 10^{th} and 90^{th} percentiles.

The acid–base status represented by the arterial and venous umbilical cord pH obtained at birth was correlated with CPR and birth weight using scattergrams, calculating the correlation coefficient r^2 and *P*-value. Subsequently, arterial and venous pH were compared between the subgroups with and without low CPR using the Mann–Whitney *U*-test. The pH measurements were obtained using Radiometer ABL80-FLEX and ABL800-FLEX pH meters (Radiometer Medical ApS, Åkandevej 21, DK-2700, Brønshøj, Denmark). Statistical analysis was carried out and graphs were constructed using the software GraphPad Prism® version 5a, for Apple Macintosh (GraphPad Software Inc., San Diego, CA, USA) and R-software® version 3.1.0 (Institute for Statistics and Mathematics of WU, Wirtschaftsuniversität Wien). Statistical significance was set at $P < 0.05$.

RESULTS

The study included 2927 pregnancies, of which 1580 (54%) were male and 1347 (46%) female. The mean maternal age was 31.1 ± 5.5 (range, 14–52) years and the mean birth weight was 3471 ± 533 (range, 1645–5730) g. The mean GA at ultrasound examination was 40.2 ± 1.3 (range, 37–41.9) weeks, and at delivery it was 40.9 ± 1.2 (range, 37–43.3) weeks. The mean interval between ultrasound and delivery was 5.1 ± 3.5 (range, 0–14) days.

There was a significant correlation between birth weight and venous-blood pH ($r^2 = 0.005$, $P < 0.001$), but not between birth weight and arterial-blood pH (Figure 1a; $r^2 = 0.001$, $P = 0.180$). CPR was significantly correlated with both arterial-blood and venous-blood pH (Figure 1b; $r^2 = 0.008$, $P < 0.0001$ and $r^2 = 0.01$, $P < 0.0001$, respectively). For all these associations, the best fit was achieved using linear regression. For the association between birth weight and CPR, the best fit

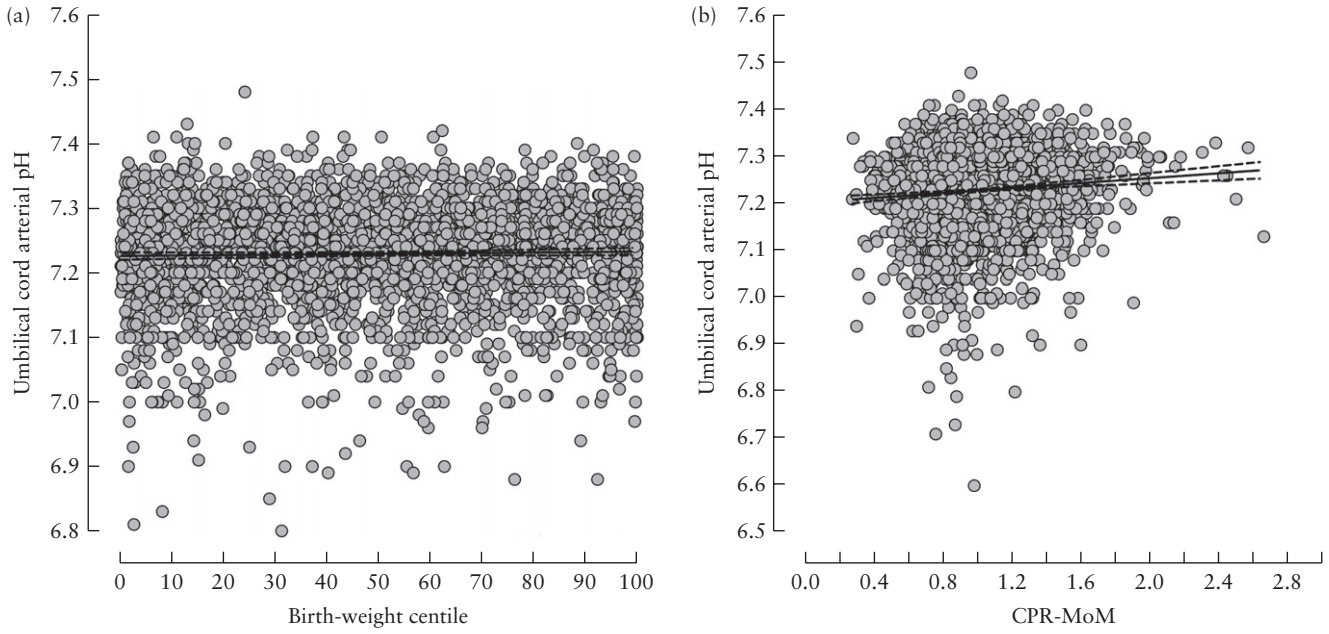

Figure 1 Scattergrams for 2927 term fetuses of umbilical cord arterial-blood pH at birth against: (a) birth weight ($r^2 = 0.001$, $P = 0.180$) and (b) cerebroplacental ratio multiples of the median (CPR-MoM); ($r^2 = 0.008$, $P < 0.0001$). Solid lines represent best fit with linear regression; dashed lines are 95% CIs.

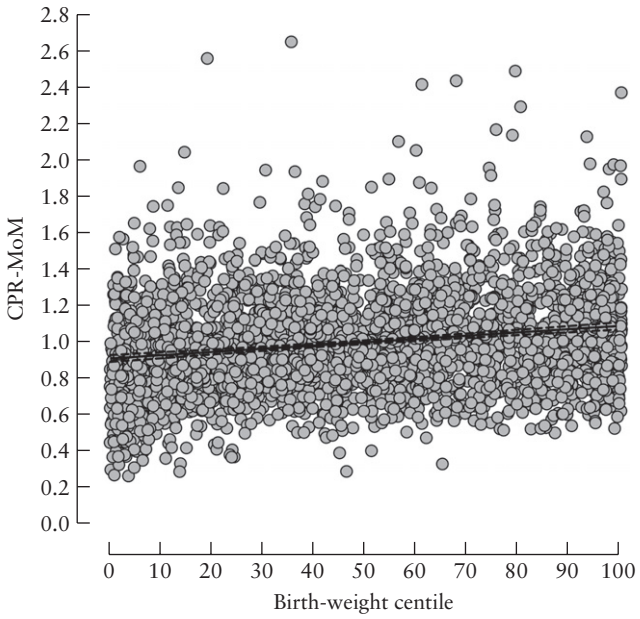

Figure 2 Scattergram for 2927 term fetuses of cerebroplacental ratio multiples of the median (CPR-MoM) against birth weight ($r^2 = 0.037$, $P < 0.001$). Solid line represents best fit with linear regression; dashed lines are 95% CI.

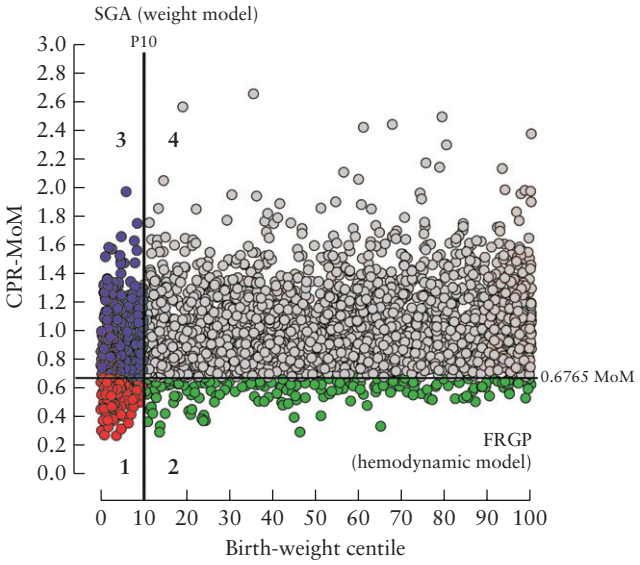

Figure 4 Scattergram showing distribution of 2927 fetuses according to birth weight and cerebroplacental ratio multiples of the median (CPR-MoM). Group 1, small-for-gestational-age (SGA) fetuses with abnormal CPR; Group 2, appropriate-for-gestational-age (AGA) and large-for-gestational-age (LGA) fetuses with abnormal CPR; Group 3, SGA fetuses with normal CPR; Group 4, AGA and LGA fetuses with normal CPR. FRGP, failure to reach growth potential (i.e. abnormal CPR).

was achieved using spline regression (Figure S1; $r^2 = 0.05$, $P < 0.0001$), which showed a slightly higher r^2 than did linear regression ($r^2 = 0.037$, $P < 0.001$; Figure 2). The AGA and LGA subgroups with normal CPR had higher arterial- and venous-blood pH than did their respective subgroups with low CPR (Figure 3). These differences in umbilical cord pH were statistically significant in AGA fetuses for both arterial and venous pH ($P = 0.0359$, $P = 0.0006$, respectively), but not for LGA fetuses ($P = 0.052$ and $P = 0.057$, respectively). No significant differences were found in the SGA subgroups with and without abnormal CPR ($P = 0.319$ and $P = 0.198$, respectively).

Comparison of groups according to the different classifications of birth weight or CPR are shown in Figure 4 and Table 1.

DISCUSSION

The main finding of this study demonstrates that just before term birth, fetal CPR is better correlated with umbilical cord blood pH than is birth weight, and that AGA fetuses with low CPR present with significantly lower neonatal pH than do AGA fetuses with normal CPR.

The fact that fetal CPR correlates with pH better than does birth weight is a novel finding. Previous studies have investigated the importance of fetal Doppler indices before birth and suggested that fetuses with lower impedance in the MCA or low CPR are at increased risk of adverse pregnancy outcome[14,15]. These studies assessed CPR as a continuous rather than as a categorical variable to diagnose placental insufficiency, although they did not

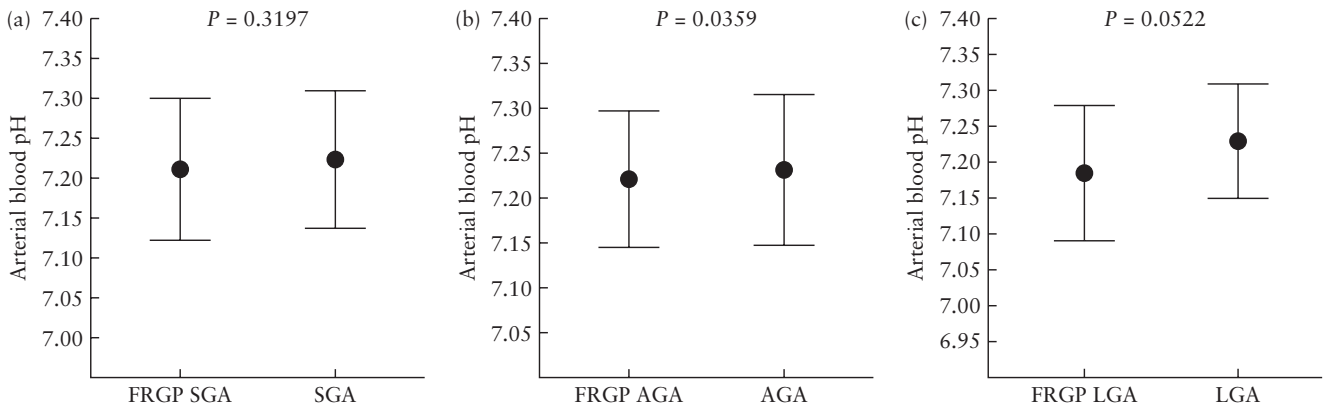

Figure 3 Mean (with 95% CI) arterial-blood pH in small-for-gestational-age (SGA) (a), appropriate-for-gestational-age (AGA) (b) and large-for-gestational-age (LGA) (c) fetuses, with and without abnormal cerebroplacental ratio (i.e. failure to reach growth potential (FRGP)).

Table 1 Arterial-blood* and venous-blood† pH among birth-weight centile and cerebroplacental ratio (CPR) groups for 2927 pregnancies (as shown in Figure 4)

	Group 1 (n = 92)	*Group 2 (n = 192)*	*Group 3 (n = 312)*	*Group 4 (n = 2331)*
Group 1	—	$P = 0.403$†	$P = 0.165$†	$P < 0.001$†
Group 2	$P = 0.704$*	—	$P = 0.436$†	$P < 0.001$†
Group 3	$P = 0.420$*	$P = 0.492$*	—	$P < 0.001$†
Group 4	$P = 0.032$*	$P = 0.012$*	$P = 0.074$*	—

Group 1, SGA–low CPR; Group 2, AGA–low CPR; Group 3, SGA–normal CPR; Group 4, AGA–normal CPR. Only comparisons with Group 4 were statistically significant. Comparison of Groups 1 + 2 (abnormal CPR fetuses, hemodynamic model) with Groups 1 + 3 (SGA fetuses, birth-weight model) was not statistically significant for either venous- or arterial-blood pH ($P = 0.456$ and $P = 0.443$, respectively). AGA, appropriate for gestational age; SGA, small for gestational age.

directly compare CPR with birth weight in this evaluation. Other studies have concluded that abnormal Doppler impedance in the MCA, in isolation or combined with abnormal UA Doppler indices, was a risk factor for low cord pH at birth and abnormal postnatal neurobehavioral performance in childhood[16–18]. These findings are in accordance with those of the current study, which also demonstrates that fetal Doppler indices (namely low CPR) are capable of identifying term AGA pregnancies at the same risk as SGA term neonates for acidemia secondary to placental insufficiency.

Current definitions of AGA and SGA are based on fetal weight population models, which do not take into account fetal Doppler changes indicative of fetal hypoxemia. Even though different weight thresholds and customized charts have been applied, these birth-weight centile models perform relatively poorly in identifying fetuses at risk of adverse outcome at term[7–9,19–25]. In contrast, the use of birth-weight models in placental insufficiency of preterm onset has good predictive ability[26]. Small preterm fetuses have lower metabolic demands and may survive for many weeks after the onset of placental insufficiency, thereby permitting a clinically recognizable fall across birth-weight centiles as the pregnancy progresses. Importantly, these babies also demonstrate characteristic changes in MCA and UA Doppler impedances that are directly related to their perinatal mortality and morbidity[26–28]. The onset of placental insufficiency near term, in general precludes the development of an SGA fetus, as the baby has usually already attained a good weight. Furthermore, the time lag between the onset of term placental insufficiency and either delivery or demise is inevitably short, making a fall across weight centiles unlikely.

It is important to acknowledge that even term fetuses should demonstrate classical Doppler-detectable hemodynamic changes characteristic of fetal hypoxemia secondary to placental insufficiency. However, to date, the use of fetal Doppler reference ranges that included AGA cases affected by placental insufficiency has hindered the recognition of these compromised fetuses. In the absence of fetal Doppler reference standards, which are difficult to construct, the use of an 'optimal CPR' standard of 0.6765 MoM based on fetuses with birth weight > 90th centile for GA has been proposed for the identification of placental insufficiency, fetal hypoxemia and failure to reach growth potential[4]. The data of this study support the assertion that CPR may be just as good at predicting AGA fetuses at risk of compromise as it is at predicting SGA fetuses at risk. Previous studies have demonstrated that the presence of abnormal MCA Doppler indices (with or without abnormal UA Doppler) in SGA is a risk factor for low cord pH at birth[16,29–33]. Our results indicate that this risk is also present in AGA fetuses with low CPR, presumably as a consequence of placental insufficiency and fetal hypoxemia.

Importantly, pH differences in SGA fetuses with normal and abnormal CPR were found not to be significant. It seems that small fetuses tend to present with lower pH at birth, independently of their CPR status, most probably owing to the scarcity of metabolic reserves needed to overcome the stress of labor[34]. This finding is in line with earlier work indicating that SGA fetuses *per se* and independently of fetal Doppler indices are at risk of adverse outcome[35–38]. Another intriguing finding of this study is the stronger association of both birth weight and CPR with umbilical cord venous-blood pH compared with that of arterial-blood pH. Venous pH measurements reflect metabolism and O_2/CO_2 exchange in the placenta, while arterial pH values represent acid–base metabolism and O_2/CO_2 exchange in fetal tissues. Although low arterial pH is the better indicator of neonatal outcome, it is logical to suppose that in this mainly healthy cohort of pregnancies, venous pH is a better reflection of placental underperfusion[39,40].

As a retrospective cohort study, this analysis is prone to the biases of data collection. However, this limitation is mitigated to a certain extent by the size of the population studied and the prospective data collection of fetal Doppler indices and umbilical cord blood pH. Furthermore, local protocols indicated delivery on the basis of fetal size but not CPR, favoring an unbiased assessment of the relationship between the latter and umbilical cord blood pH. Even though umbilical cord blood pH at birth is likely to be influenced by multiple maternal characteristics and intrapartum confounders, these should not have a disproportionate effect on the influence of either birth weight or CPR on cord pH. Thus, we feel that the study findings and subsequent discussion make a worthwhile contribution to this area of research.

Low birth weight and being SGA are well established risk factors for low neonatal pH as a consequence

of placental insufficiency. The findings of this study demonstrate that low CPR in AGA fetuses is an equally important marker of low neonatal pH secondary to placental underperfusion. This finding may be of value in risk assessment for stillbirth at term and long-term neurodevelopmental disability. However, the relative importance of low CPR and birth weight in identifying pregnancies at risk of placental hypoxemia and adverse fetal and neonatal outcomes remains to be determined.

REFERENCES

1. American College of Obstetricians and Gynecologists. Intrauterine growth restriction. ACOG practice bulletin. Number 12, January 2000. *Int J Gynecol Obstet* 2001; **72**: 85–96.
2. Nicolaides KH, Economides DL, Soothill PW. Blood gases, pH, and lactate in appropriate- and small-for-gestational-age fetuses. *Am J Obstet Gynecol* 1989; **161**: 996–1001.
3. Cetin I, Marconi AM, Bozzetti P, Sereni LP, Corbetta C, Pardi G, Battaglia FC. Umbilical amino acid concentrations in appropriate and small for gestational age infants: a biochemical difference present *in utero*. *Am J Obstet Gynecol* 1988; **158**: 120–126.
4. Morales-Roselló J, Khalil A, Morlando M, Papageorghiou A, Bhide A, Thilaganathan B. Fetal Doppler changes as a marker of failure to reach growth potential at term. *Ultrasound Obstet Gynecol* 2014; **43**: 303–310.
5. Stratton JF, Scanail SN, Stuart B, Turner MJ. Are babies of normal birth weight who fail to reach their growth potential as diagnosed by ultrasound at increased risk? *Ultrasound Obstet Gynecol* 1995; **5**: 114–118.
6. Danielian PJ, Allman AC, Steer PJ. Is obstetric and neonatal outcome worse in fetuses who fail to reach their own growth potential? *Br J Obstet Gynaecol* 1992; **99**: 452–454.
7. Carberry AE, Raynes-Greenow CH, Turner RM, Jeffery HE. Customized versus population-based birth weight charts for the detection of neonatal growth and perinatal morbidity in a cross-sectional study of term neonates. *Am J Epidemiol* 2013; **178**: 1301–1308.
8. Costantine MM, Lai Y, Bloom SL, Spong CY, Varner MW, Rouse DJ, Ramin SM, Caritis SN, Peaceman AM, Sorokin Y, Sciscione A, Mercer BM, Thorp JM, Malone FD, Harper M, Iams JD; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Population versus customized fetal growth norms and adverse outcomes in an intrapartum cohort. *Am J Perinatol* 2013; **30**: 335–341.
9. Larkin JC, Hill LM, Speer PD, Simhan HN. Risk of morbid perinatal outcomes in small-for-gestational-age pregnancies: customized compared with conventional standards of fetal growth. *Obstet Gynecol* 2012; **119**: 21–27.
10. Acharya G, Wilsgaard T, Berntsen GK, Maltau JM, Kiserud T. Reference ranges for serial measurements of umbilical artery Doppler indices in the second half of pregnancy. *Am J Obstet Gynecol* 2005; **192**: 937–944.
11. Bahlmann F, Reinhard I, Krummenauer F, Neubert S, Macchiella D, Wellek S. Blood flow velocity waveforms of the fetal middle cerebral artery in a normal population: reference values from 18 weeks to 42 weeks of gestation. *J Perinat Med* 2002; **30**: 490–501.
12. Baschat AA, Gembruch U. The cerebroplacental Doppler ratio revisited. *Ultrasound Obstet Gynecol* 2003; **21**: 124–127.
13. Yudkin PL, Aboualfa M, Eyre JA, Redman CW, Wilkinson AR. New birthweight and head circumference centiles for gestational ages 24 to 42 weeks. *Early Hum Dev* 1987; **15**: 45–52.
14. Hecher K, Spernol R, Stettner H, Szalay S. Potential for diagnosing imminent risk to appropriate- and small-for-gestational-age fetuses by Doppler sonographic examination of umbilical and cerebral arterial blood flow. *Ultrasound Obstet Gynecol* 1992; **2**: 266–271.
15. Prior T, Mullins E, Bennett P, Kumar S. Prediction of intrapartum compromise using the cerebroumbilical ratio: a prospective observational study. *Am J Obstet Gynecol* 2013; **208**: 124.e1–6.
16. Eixarch E, Meler E, Iraola A, Illa M, Crispi F, Hernandez-Andrade E, Gratacos E, Figueras F. Neurodevelopmental outcome in 2-year-old infants who were small-for-gestational age term fetuses with cerebral blood flow redistribution. *Ultrasound Obstet Gynecol* 2008; **32**: 894–899.
17. Cruz-Martinez R, Figueras F, Oros D, Padilla N, Meler E, Hernandez-Andrade E, Gratacos E. Cerebral blood perfusion and neurobehavioral performance in full-term small-for-gestational-age fetuses. *Am J Obstet Gynecol* 2009; **201**: 474.e1–7.
18. Mula R, Savchev S, Parra M, Arranz A, Botet F, Costas-Moragas C, Gratacos E, Figueras F. Increased fetal brain perfusion and neonatal neurobehavioral performance in normally grown fetuses. *Fetal Diagn Ther* 2013; **33**: 182–188.
19. Ott WJ. Small for gestational age fetus and neonatal outcome: reevaluation of the relationship. *Am J Perinatol* 1995; **12**: 396–400.
20. Chard T, Costeloe K, Leaf A. Evidence of growth retardation in neonates of apparently normal weight. *Eur J Obstet Gynecol Reprod Biol* 1992; **45**: 59–62.
21. Larsen T, Larsen JF, Petersen S, Greisen G. Detection of small-for-gestational-age fetuses by ultrasound screening in a high risk population: a randomized controlled study. *Br J Obstet Gynaecol* 1992; **99**: 469–474.
22. Maulik D. Fetal growth compromise: definitions, standards, and classification. *Clin Obstet Gynecol* 2006; **49**: 214–218.
23. Frøen JF, Gardosi JO, Thurmann A, Francis A, Stray-Pedersen B. Restricted fetal growth in sudden intrauterine unexplained death. *Acta Obstet Gynecol Scand* 2004; **83**: 801–807.
24. Kase BA, Carreno CA, Blackwell SC. Customized estimated fetal weight: a novel antenatal tool to diagnose abnormal fetal growth. *Am J Obstet Gynecol* 2012; **207**: 218.e1–5.
25. Hutcheon JA, Walker M, Platt RW. Assessing the value of customized birth weight percentiles. *Am J Epidemiol* 2011; **173**: 459–467.
26. Lees C, Marlow N, Arabin B, Bilardo CM, Brezinka C, Derks JB, Duvekot J, Frusca T, Diemert A, Ferrazzi E, Ganzevoort W, Hecher K, Martinelli P, Ostermayer E, Papageorghiou AT, Schlembach D, Schneider KT, Thilaganathan B, Todros T, van Wassenaer-Leemhuis A, Valcamonico A, Visser GH, Wolf H; TRUFFLE Group. Perinatal morbidity and mortality in early-onset fetal growth restriction: cohort outcomes of the trial of randomized umbilical and fetal flow in Europe (TRUFFLE). *Ultrasound Obstet Gynecol* 2013; **42**: 400–408.
27. Turan OM, Turan S, Gungor S, Berg C, Moyano D, Gembruch U, Nicolaides KH, Harman CR, Baschat AA. Progression of Doppler abnormalities in intrauterine growth restriction. *Ultrasound Obstet Gynecol* 2008; **32**: 160–167.
28. Baschat AA. Arterial and venous Doppler in the diagnosis and management of early onset fetal growth restriction. *Early Hum Dev* 2005; **81**: 877–887.
29. Hata T, Aoki S, Manabe A, Kanenishi K, Yamashiro C, Tanaka H, Yanagihara T. Subclassification of small-for-gestational-age fetus using fetal Doppler velocimetry. *Gynecol Obstet Invest* 2000; **49**: 236–239.
30. Roza SJ, Steegers EA, Verburg BO, Jaddoe VW, Moll HA, Hofman A, Verhulst FC, Tiemeier H. What is spared by fetal brain-sparing? Fetal circulatory redistribution and behavioral problems in the general population. *Am J Epidemiol* 2008; **168**: 1145–1152.
31. Severi FM, Bocchi C, Visentin A, Falco P, Cobellis L, Florio P, Zagonari S, Pilu G. Uterine and fetal cerebral Doppler predict the outcome of third-trimester small-for-gestational

age fetuses with normal umbilical artery Doppler. *Ultrasound Obstet Gynecol* 2002; **19**: 225–228.
32. Hershkovitz R, Kingdom JC, Geary M, Rodeck CH. Fetal cerebral blood flow redistribution in late gestation: identification of compromise in small fetuses with normal umbilical artery Doppler. *Ultrasound Obstet Gynecol* 2000; **15**: 209–212.
33. Hecher K, Spernol R, Stettner H, Szalay S. Potential for diagnosing imminent risk to appropriate- and small-for-gestational-age fetuses by Doppler sonographic examination of umbilical and cerebral arterial blood flow. *Ultrasound Obstet Gynecol* 1992; **2**: 266–271.
34. Boehm G, Müller DM, Teichmann B, Krumbiegel P. Influence of intrauterine growth retardation on parameters of liver function in low birth weight infants. *Eur J Pediatr* 1990; **149**: 396–398.
35. Savchev S, Sanz-Cortes M, Cruz-Martinez R, Arranz A, Botet F, Gratacos E, Figueras F. Neurodevelopmental outcome of full-term small-for-gestational-age infants with normal placental function. *Ultrasound Obstet Gynecol* 2013; **42**: 201–206.
36. Savchev S, Figueras F, Cruz-Martinez R, Illa M, Botet F, Gratacos E. Estimated weight centile as a predictor of perinatal outcome in small-for-gestational-age pregnancies with normal fetal and maternal Doppler indices. *Ultrasound Obstet Gynecol* 2012; **39**: 299–303.
37. Arcangeli T, Thilaganathan B, Hooper R, Khan KS, Bhide A. Neurodevelopmental delay in small babies at term: a systematic review. *Ultrasound Obstet Gynecol* 2012; **40**: 267–275.
38. Figueras F, Eixarch E, Meler E, Iraola A, Figueras J, Puerto B, Gratacos E. Small-for-gestational-age fetuses with normal umbilical artery Doppler have suboptimal perinatal and neurodevelopmental outcome. *Eur J Obstet Gynecol Reprod Biol* 2008; **136**: 34–38.
39. Sebire NJ. Detection of fetal growth restriction at autopsy in non-anomalous stillborn infants. *Ultrasound Obstet Gynecol* 2014; **43**: 241–244.
40. Parra-Saavedra M, Crovetto F, Triunfo S, Savchev S, Peguero A, Nadal A, Parra G, Gratacos E, Figueras F. Placental findings in late-onset SGA births without Doppler signs of placental insufficiency. *Placenta* 2013; **34**: 1136–1141.

SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Figure S1 Scattergram showing cerebroplacental ratio multiples of the median (MoM) plotted against birth weight. In this case correlation (in red) was performed using spline regression; $r^2 = 0.05$, $P < 0.0001$.