OBSTETRICS

Is fetal cerebroplacental ratio an independent predictor of intrapartum fetal compromise and neonatal unit admission?

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OBJECTIVE: We sought to evaluate the association between fetal cerebroplacental ratio (CPR) and intrapartum fetal compromise and admission to the neonatal unit (NNU) in term pregnancies.

STUDY DESIGN: This was a retrospective cohort study in a single tertiary referral center over a 14-year period from 2000 through 2013. The umbilical artery pulsatility index, middle cerebral artery pulsatility index, and CPR were recorded within 2 weeks of delivery. The birthweight (BW) values were converted into centiles and Doppler parameters converted into multiples of median (MoM), adjusting for gestational age using reference ranges. Logistic regression analysis was performed to identify, and adjust for, potential confounders.

RESULTS: The study cohort included 9772 singleton pregnancies. The rates of operative delivery for presumed fetal compromise and neonatal admission were 17.2% and 3.9%, respectively. Doppler CPR MoM was significantly lower in pregnancies requiring operative delivery or admission to NNU for presumed fetal compromise ($P < .01$). On multivariate logistic regression, both CPR MoM and BW centile were independently associated with the risk of operative delivery for presumed fetal compromise (adjusted odds ratio [OR], 0.67; 95% confidence interval [CI], 0.52–0.87; $P = .003$ and adjusted OR, 0.994; 95% CI, 0.992–0.997; $P < .001$, respectively). The latter associations persisted even after exclusion of small-for-gestational-age cases from the cohort. Multivariate logistic regression also demonstrated that CPR MoM was an independent predictor for NNU admission at term (adjusted OR, 0.55; 95% CI, 0.33–0.92; $P = .021$), while BW centile was not (adjusted OR, 1.00; 95% CI, 0.99–1.00; $P = .794$). The rates of operative delivery for presumed fetal compromise were significantly higher for appropriate-for-gestational-age fetuses with low CPR MoM (22.3%) compared to small-for-gestational-age fetuses with normal CPR MoM (17.3%).

CONCLUSION: Lower fetal CPR, regardless of the fetal size, was independently associated with the need for operative delivery for presumed fetal compromise and with NNU admission at term. The extent to which fetal hemodynamic status could be used to predict perinatal morbidity and optimize the mode of delivery merits further investigation.

Key words: cerebroplacental ratio, Doppler, fetal compromise, neonatal unit admission, small for gestational age

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Approximately 10-15% of cerebral palsy cases result from intrapartum hypoxia.[1,2] Despite the clinical importance of intrapartum hypoxia, the antenatal identification of the fetus at risk of cerebral palsy and other hypoxia-related outcomes remains challenging. The widespread use of intrapartum cardiotocography (CTG) has not led to a reduction in the incidence of cerebral palsy.[3,4] Likewise, admission CTG in early labor and amniotic fluid volume assessment have been shown to be of limited value in identifying fetuses at risk of intrapartum compromise.[5,6] Adverse events related to fetal hypoxia, such as cerebral palsy and stillbirth, are known to be more frequent in fetal growth restriction (FGR) secondary to placental insufficiency.[7,8] In clinical practice where fetal size is often used as a proxy for FGR, small-for-gestational-age (SGA) babies have 4 times the incidence of cesarean delivery for nonreassuring fetal status.[9] This approach is limited by the inaccuracy of ultrasound in the detection of SGA fetuses and the finding that the majority of cerebral palsy cases are, in fact, born with a birthweight (BW) appropriate for gestational age (AGA).[10] Antenatal fetal Doppler assessment also appears to be able to predict those SGA pregnancies

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likely to have cesarean delivery for nonreassuring fetal status.[9] We have recently reported that fetal Doppler assessment might also be of value in detecting pregnancies that are AGA, yet complicated by placental insufficiency.[11] Consistent with these results, Prior et al[12] recently demonstrated in a small prospective study that, independent of fetal size, fetal cerebroplacental ratio (CPR) measured within 72 hours of delivery could identify those likely to require obstetric intervention for intrapartum fetal compromise. The main aim of this study was to investigate the association in term pregnancies between fetal CPR and both intrapartum fetal compromise and admission to the neonatal unit (NNU).

Materials and Methods

This was a retrospective cohort study (retrospective analysis of prospectively collected data) in a single tertiary referral center over a 14-year period from 2000 through 2013. Cases were identified by searching the ViewPoint database (ViewPoint 5.6.8.428; ViewPoint Bildverarbeitung GmbH, Weßling, Germany) in the Fetal Medicine Unit, St. George's Hospital, London, United Kingdom. The inclusion criteria were singleton morphologically normal fetuses born at term (≥37 weeks' gestation) that had an ultrasound scan within 2 weeks of delivery. Pregnancies complicated by fetal abnormality, aneuploidy, or stillbirth were excluded from the analysis. Elective cesarean delivery cases were also excluded from the analysis of operative delivery for intrapartum fetal compromise. Gestational age was calculated from the crown-rump length measurement at 11-13 weeks and only one (the last) examination per pregnancy was included in the analysis.[13] For the pregnancies where the first ultrasound performed was in the second trimester (>14 weeks' gestation), the pregnancy was dated according to the head circumference. Routine fetal biometry was performed according to a standard protocol and the estimated fetal weight (EFW) calculated using the formula of Hadlock et al.[14] The umbilical artery (UA) and middle cerebral artery (MCA) Doppler waveforms were recorded using color Doppler, and the pulsatility index (PI) was calculated according to a standard protocol.[15,16] The CPR was calculated as the simple ratio between the MCA PI and the UA PI.[17] All Doppler indices were converted into multiples of median (MoM), correcting for gestational age using reference ranges and BW values were converted into centiles.[11,18,19] The study cohort was divided into 4 groups according to a combination of a BW cutoff of the 10th centile and a CPR cutoff of 0.6765 MoM[11] to assess the difference between the SGA model, which relies on fetal biometry, and the placental insufficiency model, which relies on fetal hemodynamic assessment.

Intrapartum data included whether the labor was induced or spontaneous, presence or absence of meconium-stained liquor (grade 2 or 3), CTG abnormalities (classified according to National Institute for Health and Clinical Excellence guidelines),[20] ST analysis abnormalities,[21] use of oxytocin for slow progress of labor, intrapartum pyrexia, intrapartum hemorrhage, use of epidural analgesia for labor, and mode of delivery. Data on maternal baseline characteristics and pregnancy outcomes were collected from hospital obstetric and neonatal records. The main outcome in this study was operative delivery for presumed fetal compromise. Operative delivery for fetal compromise included both cesarean delivery and instrumental delivery. The second outcome was admission to the NNU. The diagnosis of fetal compromise was based on CTG abnormalities, ST analysis abnormalities, abnormal fetal scalp blood sample pH, or a combination of these. Pregnancies that had an elective cesarean delivery were excluded from the analysis. The study was exempt from review by Wandsworth Research Ethics Committee.

Statistical analysis

Categorical data were presented as number (%) and were compared using the Fisher exact test or χ^2 test. Continuous data were presented as median (interquartile range). The D'Agostino and Pearson omnibus test was used to assess the normality of the data. Nonparametric analysis using Mann-Whitney *U* test was then used to compare continuous data between the study groups. Logistic regression analysis was performed to identify, and adjust for, potential confounders. We considered both maternal and intrapartum risk factors as important confounders for the 2 outcomes investigated in this study. As

FIGURE 1
Flowchart of pregnancies included in study according to outcome investigated

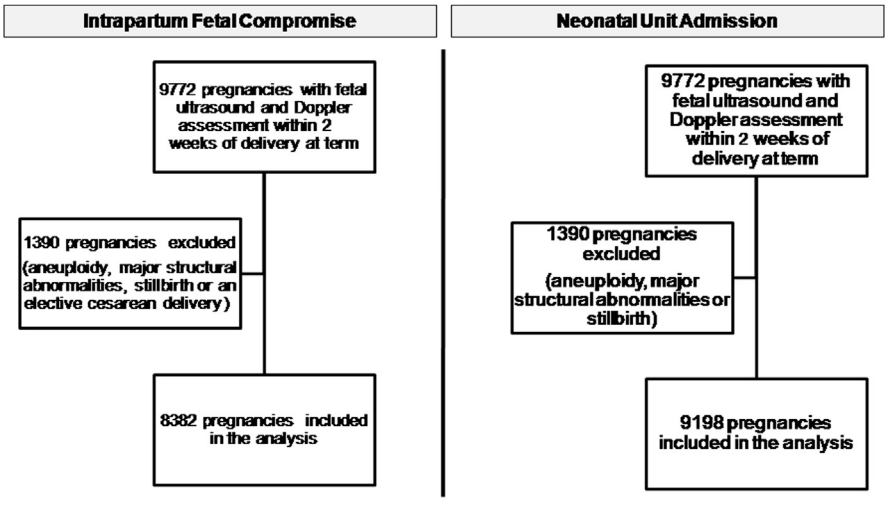

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TABLE 1
Characteristics of study cohort according to need for operative delivery for fetal compromise

Pregnancy variables	No operative delivery for fetal compromise, n = 6941	Operative delivery for fetal compromise, n = 1441	*P* value
Antenatal variables			
Maternal age, y, median (IQR)	31.0 (27.0–35.0)	32.0 (28.0–35.0)	.003
Body mass index, kg/m^2, median (IQR)	24.10 (21.70–27.60)	24.10 (21.70–27.20)	.714
Nulliparous, n (%)	3564 (51.3)	1169 (81.1)	< .001
Ethnicity, n (%)			.135
Caucasian	4211 (60.7)	928 (64.4)	
African	1167 (16.8)	225 (15.6)	
South Asian	1180 (17.0)	217 (15.1)	
East Asian	77 (1.1)	18 (1.3)	
Mixed	247 (3.6)	41 (2.9)	
Other	59 (0.9)	12 (0.8)	
Smoker, n (%)	474 (6.8)	66 (4.6)	.002
Alcohol use, n (%)	104 (1.5)	15 (1.04)	.182
Drug use, n (%)	47 (0.7)	8 (0.6)	.602
Ultrasound and Doppler variables			
Gestational age at ultrasound, wk, median (IQR)	40.4 (38.4–41.4)	41.3 (39.6–41.4)	< .001
Interval between scan and delivery, d, median (IQR)	4.0 (2.0–7.0)	5.0 (2.0–7.0)	.367
Umbilical artery pulsatility index, median (IQR)	0.82 (0.71–0.93)	0.81 (0.71–0.93)	.948
Umbilical artery pulsatility index MoM, median (IQR)	1.00 (0.88–1.13)	1.01 (0.89–1.16)	.003
Middle cerebral artery pulsatility index, median (IQR)	1.32 (1.12–1.55)	1.23 (1.05–1.44)	< .001
Middle cerebral artery pulsatility index MoM, median (IQR)	1.30 (1.13–1.51)	1.29 (1.12–1.50)	.237
Cerebroplacental ratio, median (IQR)	1.63 (1.35–1.95)	1.53 (1.26–1.84)	< .001
Cerebroplacental ratio MoM, median (IQR)	0.96 (0.81–1.15)	0.93 (0.77–1.11)	< .001
Cerebroplacental ratio <0.6765 MoM, n (%)	649 (9.4)	188 (13.1)	< .001
Intrapartum variables			
Induction of labor, n (%)	2549 (40.0)	755 (52.4)	< .001
Meconium-stained liquor (grade 2 or 3), n (%)	137 (2.0)	71 (4.9)	< .001
Oxytocin use for slow progress in labor, n (%)	1613 (23.2)	708 (49.1)	< .001
Intrapartum hemorrhage, n (%)	16 (0.2)	10 (0.7)	.006
Intrapartum pyrexia, n (%)	98 (1.5)	114 (7.9)	< .001
Epidural use, n (%)	2297 (34.8)	1094 (75.9)	< .001
Variables at birth			
Gestational age at delivery, wk, median (IQR)	41.1 (39.4–41.9)	41.6 (40.4–42.1)	< .001
Fetal sex male, n (%)	3517 (50.7)	815 (56.6)	< .001
Birthweight, g, median (IQR)	3420 (3020–3800)	3460 (3100–3820)	.01
Birthweight centile, median (IQR)	44.39 (18.59–73.17)	45.0 (17.72–74.45)	.941
Small for gestational age, n (%)	1033 (14.9)	236 (16.4)	.15
Admission to neonatal unit, n (%)	194 (2.8)	139 (10.0)	< .001

IQR, interquartile range; *MoM*, multiples of median.

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year was not found to be a significant confounder, we decided not to include it as a covariate. Both unadjusted and adjusted odds ratios were calculated. *P* values < .05 were considered statistically significant. All *P* values were 2-tailed. We did not perform a sample size calculation a priori as this was a retrospective study. We included all the pregnancies that fit the inclusion criteria and excluded those that fit the exclusion criteria. However, as the sample size was large, we thought that the analysis was adequately powered to address the outcomes chosen. The analysis was performed using the statistical software packages SPSS 18.0 (IBM Corp, Armonk, NY); Stata 11, Release 11.2 (StataCorp LP, College Station, TX); and GraphPad Prism 5.0 for Windows (GraphPad Software Inc, San Diego, CA).

RESULTS

We identified 9772 pregnancies with fetal ultrasound and Doppler assessment within 2 weeks of delivery at term. We excluded 1390 pregnancies because they had aneuploidy, major structural abnormalities, stillbirth, or an elective cesarean delivery, leaving 8382 for the analysis of data related to operative delivery for fetal distress (Figure 1). The prevalence of SGA in this cohort, defined as BW <10th centile, was 15.3%. The overall operative delivery for presumed fetal compromise was 17.2%, which was divided into emergency cesarean delivery (n = 757, 9.0%) and instrumental delivery (n = 684, 8.2%). Women who had operative delivery for presumed fetal compromise were significantly older and more likely to be nulliparous ($P < .01$) (Table 1). The rate of admission to NNU for presumed fetal compromise was significantly higher in the operative delivery group (10.0% vs 2.8%, $P < .001$).

Doppler ultrasound UA PI MoM was significantly higher and CPR MoM significantly lower in pregnancies requiring operative delivery for presumed fetal compromise ($P < .01$) (Table 1). The BW centile and prevalence of SGA were not significantly different between the 2 study groups ($P = .941$ and $P = .15$, respectively). According to the multivariate logistic regression, both CPR MoM and BW centile were independently associated with the risk of operative delivery for presumed fetal compromise ($P < .05$) (Table 2). The latter associations persisted even after exclusion of SGA cases from the cohort (Table 3). The overall neonatal admission rate in the study cohort was 3.9% (Table 3). The admission to the NNU was significantly higher in nullipara, smokers, non-Caucasian ethnic origin, and those with larger body mass index ($P < .05$) (Table 4). UA PI MoM was significantly higher, while MCA PI and CPR MoM were significantly lower, in pregnancies where the newborn was admitted to the NNU ($P < .05$) (Table 4). The BW centile was not significantly different between the 2 groups ($P = .064$), while the prevalence

TABLE 2
Factors associated with operative delivery for presumed fetal compromise

Risk factor	Unadjusted OR	95% CI	*P* value	Adjusted OR	95% CI	*P* value
Maternal age, y	1.02	1.01–1.03	.001	1.04	1.02–1.05	< .001
Body mass index, kg/m^2	1.00	0.98–1.01	.49	1.01	0.96–1.02	.182
Multiparous	0.25	0.21–0.28	< .001	0.38	0.31–0.45	< .001
Ethnicity	0.94	0.89–0.99	.016	1.08	1.02–1.16	.013
Smoking	0.65	0.50–0.85	.002	0.83	0.61–1.13	.229
Drug abuse	0.82	0.39–1.74	.602	0.73	0.29–1.82	.501
Alcohol use	0.69	0.40–1.19	.184	0.78	0.41–1.49	.449
Cerebroplacental ratio MoM	0.59	0.48–0.74	< .001	0.67	0.52–0.87	.003
Gestational age at delivery, wk	1.30	1.25–1.36	< .001	1.18	1.12–1.25	< .001
Birthweight centiles	0.99	0.998–1.002	.941	0.994	0.992–0.997	< .001
Intrapartum factors						
Induction of labor	1.88	1.67–2.10	< .001	1.28	1.12–1.47	< .001
Epidural use	5.92	5.19–6.75	< .001	4.00	3.38–4.70	< .001
Intrapartum pyrexia	5.71	4.33–7.52	< .001	2.66	1.94–3.63	< .001
Intrapartum hemorrhage	2.88	1.30–6.36	.009	4.34	1.64–11.53	.003
Oxytocin used for slow progress	3.19	2.84–3.59	< .001	1.02	0.87–1.19	.838
Meconium grade 2/3	2.53	1.89–3.38	< .001	3.31	2.32–4.73	< .001

CI, confidence interval; *MoM*, multiples of median; *OR*, odds ratio.

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TABLE 3
Factors associated with operative delivery for presumed fetal compromise (AGA)

Risk factor	Unadjusted OR	95% CI	*P* value	Adjusted OR	95% CI	*P* value
Maternal age, y	1.02	1.01–1.03	.001	1.04	1.02–1.05	< .001
Body mass index, kg/m^2	1.00	0.98–1.01	.535	1.01	1.00–1.03	.145
Multiparity	0.24	0.21–0.28	< .001	0.39	0.32–0.47	< .001
Ethnicity	0.92	0.87–0.98	.011	1.08	1.01–1.16	.031
Smoking	0.68	0.50–0.92	.013	0.86	0.61–1.22	.394
Drug abuse	0.56	0.20–1.58	.271	0.54	0.18–1.59	.262
Alcohol use	0.86	0.50–1.50	.603	0.89	0.46–1.71	.721
Cerebroplacental ratio MoM	0.61	0.48–0.77	<.001	0.68	0.52–0.91	.009
Gestational age at delivery, wk	1.40	1.33–1.48	< .001	1.21	1.14–1.29	< .001
Birthweight centiles	1.00	0.999–1.003	.24	0.996	0.993–0.999	.007
Intrapartum factors						
Induction of labor	1.86	1.64–2.11	< .001	1.24	1.07–1.44	.005
Epidural use	6.21	5.37–7.19	< .001	4.03	3.34–4.85	< .001
Intrapartum pyrexia	5.66	4.23–7.57	< .001	2.67	1.92–3.72	< .001
Intrapartum hemorrhage	2.20	0.89–5.40	.86	3.12	1.00–9.75	.05
Oxytocin used for slow progress	3.33	2.93–3.79	< .001	1.03	0.87–1.21	.761
Meconium grade 2/3	2.62	1.83–3.47	< .001	2.87	1.94–4.24	< .001

AGA, appropriate for gestational age, after exclusion of small-for-gestational-age newborns (defined as birthweight <10th centile); *CI*, confidence interval; *MoM*, multiples of median; *OR*, odds ratio.

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of SGA was ($P < .001$) (Table 4). According to the multivariate logistic regression, CPR MoM was an independent predictor for neonatal admission at term ($P = .021$), while BW centile was not ($P = .794$) (Table 5).

When divided into 4 groups according to a combination of a BW cutoff of 10th centile and a CPR cutoff of 0.6765 MoM (Appendix; Supplementary Figure), the rates of operative delivery for presumed fetal compromise were significantly higher for AGA with low CPR MoM compared to SGA with normal CPR MoM (22.3% vs 17.3%, $P < .001$) (Figure 2). The corresponding rates of NNU admission were significantly different among the groups ($P < .001$) (Figure 2). The proportion of delivery for fetal compromise in the group with low CPR was significantly higher than in those with normal CPR (22.5% vs 16.9%, $P < .001$). We also performed a subanalysis according to the mode of operative delivery for fetal compromise (cesarean or instrumental delivery). The rates of both cesarean delivery and instrumental delivery for presumed fetal compromise were significantly higher for AGA with low CPR MoM compared to AGA with normal CPR MoM (11.0% vs 8.7%, $P = .043$ and 11.2% vs 7.8%, $P = .003$, respectively) (Figure 3).

Comment

The results of this study demonstrate that fetal CPR measured at term is associated with the need for emergency operative delivery for abnormal fetal heart rate patterns and risk of admission to the NNU. These associations remained significant even after adjustment for possible confounding variables that are known to increase the risk of operative delivery for presumed fetal compromise, such as BW. Importantly, the rate of operative delivery for presumed fetal compromise was higher in AGA fetuses with low CPR than in SGA fetuses with normal CPR, indicating that CPR is more strongly associated with fetal compromise due to placental insufficiency than is BW. Only SGA with abnormal CPR were significantly more likely to be admitted to the NNU. This finding could be explained by the fact that the neonatologists are more likely to admit a newborn to the NNU for observation or monitoring of blood sugar levels if it is small (simply based on the size alone). The neonatologists were not blinded to the size, while they were to CPR values.

Association of BW and CPR with presumed fetal compromise

To date, the evidence for the value of fetal Doppler assessment in predicting adverse neonatal outcome, such as the need for operative delivery for presumed fetal compromise or admission to NNU, has been demonstrated mainly in SGA fetuses.[9,22-26] Our findings demonstrate that when fetal CPR is low at term, the risks of operative delivery for fetal compromise and NNU admission are significantly increased in both SGA and

TABLE 4
Characteristics of study cohort and need for neonatal unit admission

Pregnancy variables	No neonatal admission n = 8842	Neonatal admission n = 356	*P* value
Antenatal criteria			
Maternal age, y, median (IQR)	31.0 (27.0–35.0)	30.0 (26.0–33.8)	.001
Body mass index, kg/m^2, median (IQR)	24.10 (21.70–27.70)	24.95 (21.90–28.63)	.033
Nulliparous, n (%)	4829 (54.6)	232 (65.2)	< .001
Ethnicity, n (%)			.014
Caucasian	5450 (61.6)	197 (55.3)	
African	1452 (16.4)	77 (21.6)	
South Asian	1462 (16.5)	70 (19.7)	
East Asian	102 (1.2)	4 (1.1)	
Mixed	301 (3.4)	8 (2.3)	
Other	75 (0.9)	0	
Smoker, n (%)	547 (6.2)	32 (9.0)	.033
Alcohol use, n (%)	132 (1.5)	2 (0.6)	.151
Drug use, n (%)	51 (0.6)	4 (1.1)	.19
Ultrasound and Doppler criteria			
Gestational age at ultrasound, wk, median (IQR)	40.4 (38.3–41.4)	40.3 (37.7–41.4)	.203
Interval between scan and delivery, d, median (IQR)	4.0 (2.0–8.0)	5.0 (2.0–8.0)	.049
Umbilical artery pulsatility index, median (IQR)	0.82 (0.71–0.93)	0.84 (0.73–0.96)	.018
Umbilical artery pulsatility index MoM, median (IQR)	1.00 (0.88–1.13)	1.01 (0.90–1.15)	.038
Middle cerebral artery pulsatility index, median (IQR)	1.32 (1.12–1.55)	1.30 (1.10–1.52)	.385
Middle cerebral artery pulsatility index MoM, median (IQR)	1.29 (1.13–1.50)	1.26 (1.08–1.47)	.033
Cerebroplacental ratio, median (IQR)	1.63 (1.35–1.95)	1.54 (1.30–1.89)	.005
Cerebroplacental ratio MoM, median (IQR)	0.96 (0.80–1.15)	0.92 (0.77–1.10)	.003
Cerebroplacental ratio <0.6765 MoM, n (%)	857 (9.7)	51 (14.3)	.004
Intrapartum criteria			
Induction of labor, n (%)	3163 (39.4)	146 (44.1)	.087
Meconium-stained liquor (grade 2 or 3), n (%)	177 (2.0)	31 (8.7)	< .001
Oxytocin use for slow progress in labor, n (%)	2200 (24.9)	124 (34.8)	< .001
Intrapartum hemorrhage, n (%)	23 (0.3)	3 (1.0)	.037
Intrapartum pyrexia, n (%)	177 (2.3)	34 (11.2)	< .001
Epidural use, n (%)	2297 (34.8)	1094 (75.9)	< .001
Criteria at birth			
Gestational age at delivery, wk, median (IQR)	41.1 (39.3–41.9)	41.1 (38.5–42.0)	.526
Fetal sex male, n (%)	4524 (51.2)	213 (59.8)	.001
Birthweight (g), median (IQR)	3420 (3012–3800)	3400 (2860–3780)	.052
Birthweight centile, median (IQR)	44.33 (18.66–73.28)	40.37 (12.56–71.99)	.064
Small for gestational age, n (%)	1328 (15.0)	78 (21.9)	< .001

IQR, interquartile range; *MoM*, multiples of median.

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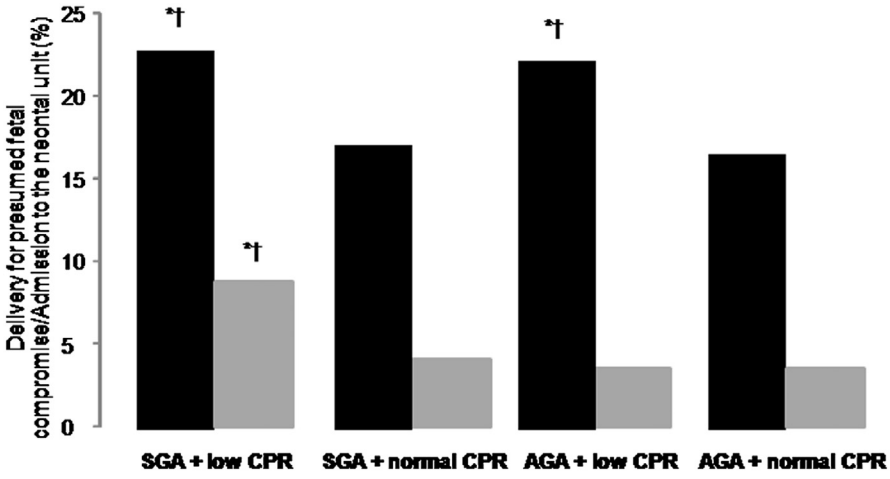
FIGURE 2
Outcomes according to birthweight and cerebroplacental ratio group



Operative delivery for presumed fetal compromise (*black bars*) and admission to the neonatal unit (*gray bars*) in 4 study groups according to combination of birthweight cutoff of 10th centile and cerebroplacental ratio (CPR) cutoff of 0.6765 multiples of median (MoM).

*$P < .05$ when compared to group 4 (appropriate for gestational age [AGA] and normal CPR MoM); †$P < .05$ when compared to group 2 (small for gestational age [SGA] and normal CPR MoM).

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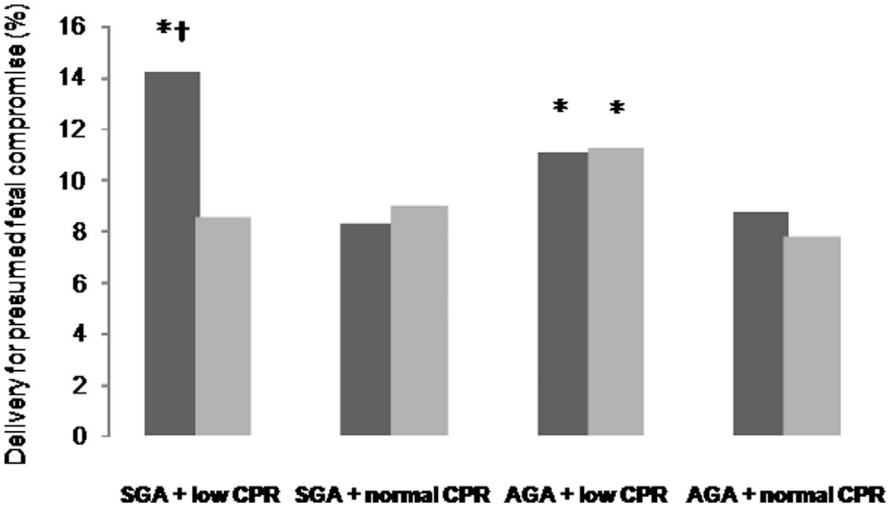
AGA fetuses. This association supports the concept that even AGA infants could suffer from placental insufficiency and fail to meet their genetic growth potential at term.[11,27,28] Furthermore, studies demonstrate placental histological abnormalities typical of FGR in about 25% of term AGA pregnancies, suggesting the presence of occult chronic placental insufficiency.[29]

FIGURE 3
Delivery for presumed fetal compromise according to birthweight and CPR group



Cesarean delivery (*dark gray bars*) and instrumental delivery (*light gray bars*) for presumed fetal compromise in 4 study groups according to combination of birthweight cutoff of 10th centile and cerebroplacental ratio (CPR) cutoff of 0.6765 multiples of median (MoM).

*$P < .05$ when compared to group 4 (appropriate for gestational age [AGA] and normal CPR MoM); †$P < .05$ when compared to group 2 (small for gestational age [SGA] and normal CPR MoM).

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The antenatal diagnosis of FGR using fetal biometry alone has recently been challenged and the use of fetal Doppler assessment has been proposed as a potentially better marker.[11,28,30,31] These authors argue that a normally sized (AGA) fetus at term exposed to hypoxemia from placental insufficiency invariably has a short latency to delivery, and is therefore unlikely to manifest SGA as a feature. In contrast, Doppler-detectable cerebral redistribution, a fundamental physiological response to hypoxemia in preterm FGR and postnatal life, should be no less likely with placental insufficiency at term. We have previously demonstrated that current UA and MCA Doppler normal ranges at term are significantly influenced by the inclusion of AGA pregnancies suffering from occult placental insufficiency. By using the concept of optimal CPR established from fetuses on the upper BW centiles, we have revealed a stronger relationship between umbilical cord pH and CPR compared to BW. These findings together challenge the convention of using EFW to assess the at-risk fetus at term and suggest that fetal arterial Doppler assessment may have a more important role here.

CPR influences birth outcome more than any other antenatal confounder, including BW

Multiple factors were found to be independently associated with the risk of operative delivery for fetal distress and admission to the NNU, including maternal age, nulliparity, ethnicity, induction of labor, intrapartum pyrexia, meconium-stained liquor, and epidural use. These findings are consistent with a recent study, where the investigators developed a clinical prediction model to assess the risk of operative delivery for suspected fetal distress or failure to progress, using data from 5667 singleton pregnancies.[32] Importantly, in our study cohort, CPR had the strongest association with adverse labor outcomes among all the antenatally determinable

TABLE 5
Factors associated with neonatal unit admission at term

Risk factor	Unadjusted OR	95% CI	*P* value	Adjusted OR	95% CI	*P* value
Maternal age, y	2.13	1.69–2.70	< .001	0.98	0.95–0.99	.042
Body mass index, kg/m^2	1.02	0.99–1.24	.139	1.02	1.00–1.05	.110
Multiparous	0.64	0.52–0.80	< .001	0.85	0.62–1.16	.310
Ethnicity	1.02	0.93–1.12	.669	1.03	0.92–1.16	.580
Smoking	1.50	1.03–2.18	.034	1.19	0.73–1.93	.495
Drug abuse	1.96	0.70–5.45	.198	0.54	0.07–3.96	.541
Alcohol use	0.37	0.09–1.51	.167	1.19	0.05–2.45	.283
Birthweight centiles	1.00	0.99–1.00	.142	1.00	0.99–1.00	.794
Cerebroplacental ratio MoM	0.54	0.35–0.81	.003	0.55	0.33–0.92	.021
Induction of labor	1.21	0.97–1.51	.088	1.19	0.92–1.54	.195
Epidural use	0.98	0.96–0.99	.009	1.70	1.24–2.32	.001
Intrapartum pyrexia	5.41	3.67–7.96	< .001	3.78	2.42–5.92	< .001
Intrapartum hemorrhage	3.36	1.00–11.25	.049	2.84	0.64–12.55	.167
Gestational age at delivery, wk	0.94	0.88–1.00	.070	0.93	0.85–1.02	.128
Oxytocin used for slow progress	1.61	1.29–2.02	< .001	1.06	0.78–1.45	.697
Meconium grade 2/3	4.54	3.06–6.73	< .001	4.64	2.90–7.43	< .001

CI, confidence interval; *MoM*, multiples of median; *OR*, odds ratio.

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characteristics. The association between BW centiles and admission to the NNU at term was not significant. These findings reinforce again the relative importance of CPR to BW for the identification of pregnancies at risk of fetal compromise from placental insufficiency. This supposition is lent weight by the report of a lower CPR in pregnancies requiring operative delivery for fetal distress.[12] In this prospective study of 400 singleton pregnancies at term, the investigators assessed fetal well-being within 72 hours of delivery and reported promising results for the value of CPR, even in AGA fetuses.[12] Even though CPR >90th centile had a very high negative predictive value for cesarean delivery for presumed fetal compromise, the area under the curve was 0.69, which suggests that CPR, as a single marker, is not a strong predictor of intrapartum fetal compromise.[12] Although the latter study did not investigate the relationship between CPR and admission to the NNU, other investigators have demonstrated a correlation between fetal pulse oximetry, MCA, and UA Doppler velocimetry during active labor and fetal morbidity.[33]

Study limitations

The data of this retrospective study are influenced by the biases of selective assessment of a population referred for scan assessment at term—a nonroutine procedure in the United Kingdom. This explains the slightly higher than expected proportion of SGA in the study cohort. The latter is mitigated by the relatively large set of prospectively collected data and because the majority of women were, in fact, assessed routinely in an unselected fashion for a postdates scan as per local protocol. Furthermore, the results of the ultrasound and Doppler assessment were not blinded, giving rise to the possibility of subsequent clinical intervention and a 'treatment effect.' However, during the study period, intervention in the form of induction of labor was only undertaken for EFW of <5th centile or UA PI >95th centile, as per local protocol. Hence the relations among fetal Doppler findings, BW, and labor outcomes should be relatively uninfluenced by these interventions. Moreover, the study cohort will have been scanned by a large number of different operators, highlighting the risk of interobserver variability in the measurements. The threshold for the diagnosis of fetal compromise is also likely to have been influenced by changing personnel and attitudes toward intrapartum management over the 14-year period. The strengths of our study include the large number of pregnancies, the short interval between ultrasound and delivery, ascertainment of the outcome data and adjusting for possible confounding variables including BW centiles. Furthermore, the CPR values were not calculated before the analysis for this study. Therefore, the health care professionals providing the intrapartum care were effectively blinded to this value.

In conclusion, lower CPR at term was independently associated with increased need for operative delivery for presumed fetal compromise and admission to the

NNU. Even though BW at term was also independently associated with adverse birth outcomes, the rate of operative delivery for presumed fetal compromise was higher in AGA fetuses with low CPR than in SGA fetuses with normal CPR. These findings highlight the relative importance of Doppler indices of fetal hypoxemia compared to fetal size in the risk stratification for birth and neonatal outcome. It has long been accepted that the majority of SGA fetuses are not growth restricted as a consequence of placental insufficiency. These data support the credo that even normal-weight babies may be compromised by placental insufficiency and provides a potential tool for their identification using fetal Doppler assessment. Most national guidance documents recommend the assessment of fetal Doppler only in pregnancies complicated by SGA, but not in AGA fetuses.[34,35] Our results suggest that the categorization of the at-risk fetus according to size alone is inadequate and that prospective studies are required to evaluate the role of fetal Doppler assessment of CPR for this purpose. ■

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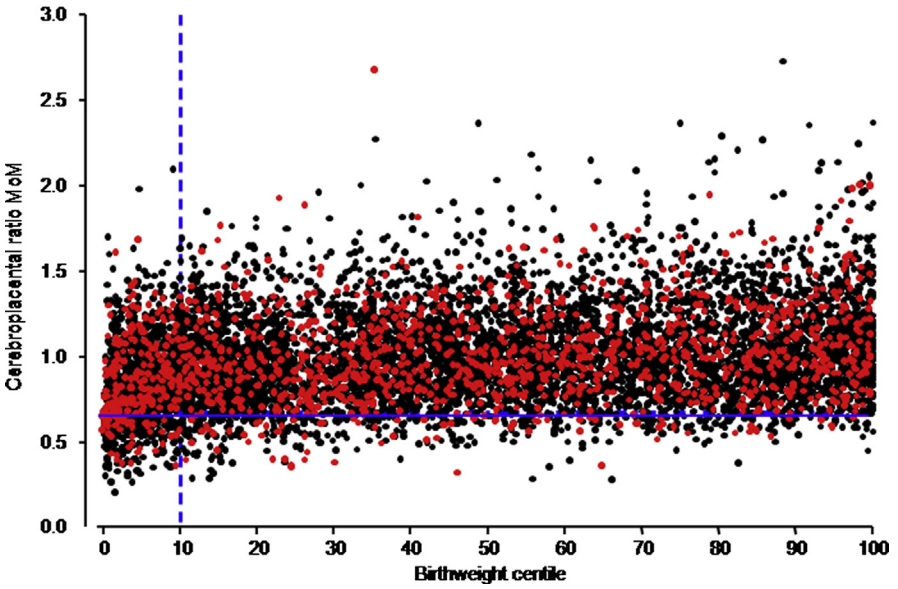
Appendix

SUPPLEMENTARY FIGURE

Scatter plot of relationship between BW centile and CPR MoM



Study cohort was divided into 4 groups according to combination of BW cutoff of 10th centile and CPR cutoff of 0.6765 MoM to assess difference between small-for-gestational-age model, which relies on fetal biometry, and failure to reach growth potential model, which relies on fetal hemodynamic assessment. Cases that had operative delivery for presumed fetal compromise are shown as *red dots* on scatter plot.

BW, birthweight; *CPR*, cerebroplacental ratio; *MoM*, multiples of median.

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