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Review article

Re-evaluating the role of cerebroplacental ratio in predicting adverse perinatal outcome

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ABSTRACT

Aim: This meta-analysis evaluates the use of cerebroplacental ratio (CPR) in predicting adverse perinatal outcome.

Methods: An electronic search of PubMed, Embase, Google scholar, Cochrane Library and Up-to-Date was done using variations of 'cerebroplacental ratio' and 'cerebroumbilical ratio'. We included studies where CPR was measured and postpartum outcomes were available. Selected articles were evaluated for quality of study methodology using the Newcastle-Ottawa Scale, and aggregate statistics for relative risks, odds ratios and 95% confidence interval were calculated.

Results: Data from 66,392 patients in 47 studies was extracted. There were 25 prospective, 17 retrospective and 5 case-control studies. Data on each obstetric or perinatal outcome was separately analysed. When analysing the prospective data, it showed abnormal CPR can predict the need for operative delivery due to foetal distress [RR: 2.52, 95%CI: 2.10–3.02; $I^2 = 65.78$, $P < 0.001$], low pH [RR: 2.19, 95%CI: 1.01–4.75; $I^2 = 70.26$, $P = 0.005$] and low Apgar score [RR: 2.05, 95%CI: 1.39–3.03; $I^2 = 37.15$, $P = 0.10$], foetal or neonatal demise [RR: 2.49, 95%CI: 1.00–6.20], as well as NICU admission [RR: 2.23, 95% CI: 1.84–2.70; I^2 48.53, $P = 0.14$].The retrospective data showed a statistically significant correlation in all outcomes but the low pH.

Conclusion: Our meta-analysis shows that CPR can be used to identify foetuses with higher risk of operative delivery due to foetal distress, low Apgar score, NICU admission, neonatal morbidity as well as stillbirth and neonatal death rates.

Contents

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Introduction

Predicting which pregnancies are at risk of developing adverse perinatal outcome remains one of the major challenges obstetricians face. Ultrasound can aid in the detection of these at-risk pregnancies by, for example, identifying growth restriction. However, foetal growth alone cannot detect all foetuses who are at risk and can miss those who are normally grown but are not reaching their growth potential [1]. Doppler flow can provide useful information about the foetal hemodynamic status which can be used to aid in the distinction between constitutionally small children and those who are growth restricted due to placental insufficiency [2]. The foetal brain in uncomplicated pregnancies has a high resistance circulation. With progressive hypoxia, blood flow increases to compensate for the decrease in available oxygen, the so called 'brain-sparing effect'. This results in a reduction in the Doppler parameters used to assess blood flow through the middle cerebral artery (MCA): the peak systolic to end diastolic blood flow velocity ratio (S/D), resistance index (RI), and pulsatility index (PI) [3]. The cerebroplacental ratio (CPR) is a measure that quantifies the brain-sparing effect and provides information on how foetal cardiac output is distributed. It is calculated by dividing the middle cerebral artery (MCA) Doppler flow by the umbilical artery (UA) Doppler flow. Either the pulsatility index (PI), resistance index (RI) or the systolic/diastolic ratio (S/D) can be used for the calculation. More recently the PI has been the computation of choice [4–9]. The cerebroplacental ratio was first described by Arbeille et al. in 1983 [10]. It was then theorised that the CPR would improve the sensitivity of Doppler methods for detecting foetal growth retardation and provide a better understanding of the foetal vascular regulation [3]. Since then many studies have investigated the role of CPR as a predictor for small for gestational age neonates as well as adverse perinatal outcome [7,11–13], with a recent systematic review and meta-analysis reporting on their outcomes [14]. This study showed that CPR appeared better than UA Doppler flow in terms of sensitivity and specificity. However, sensitivity and specificity are considered inappropriate for meta-analyses, as they do not behave independently when they are pooled from various primary studies to generate separate averages [15].

We set out to quantify and qualify the data available on the correlation between CPR and adverse perinatal outcome in the growth restricted as well as the appropriately grown foetuses. Our aim was to evaluate whether the CPR is an adequate predictor of adverse perinatal outcome, and if so, should be used as such in regular clinical practice.

Methods

Study protocol

We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [16]. A systematic search of the databases MEDLINE, PubMed, Google Scholar and EMBASE, was performed up to July 2017, to identify relevant articles. Our search items included (cerebroplacental) AND ("Ratio") OR (cerebro-placental) AND ("Ratio") OR (cerebro AND ("placenta"[MeSH Terms] OR placenta) OR

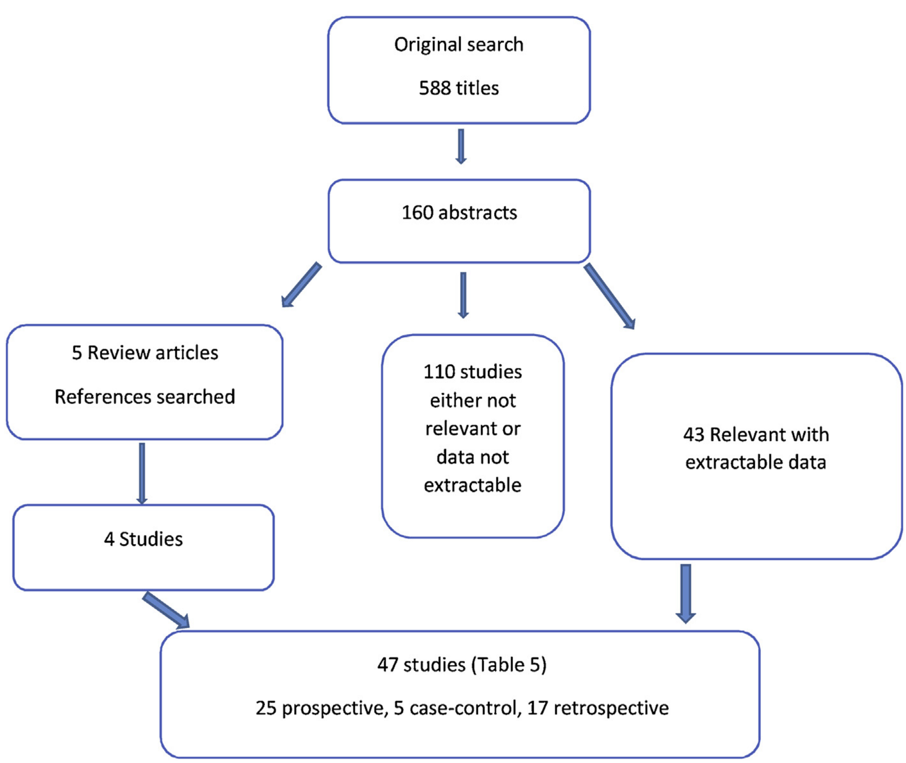


Fig. 1. PRISMA flow diagram leading to final 47 studies used for statistical analysis.

Table 1
Study characteristics.

First author	Year	Title	Type Study	N
Adiga, P	2015	Predictive value of middle cerebral artery to uterine artery pulsatility index ratio in hypertensive disorders of pregnancy	Prospective	95
Akolekar	2015	Umbilical and fetal middle cerebral artery Doppler at 35-37 weeks' gestation in the prediction of adverse perinatal outcome	Prospective	6038
Arias	1994	Accuracy of the middle-cerebral-to-umbilical-artery resistance index ratio in the prediction of neonatal outcome in patients at high risk for fetal an	Case control	135
Bahado-S	1999	The Doppler cerebroplacental ratio and perinatal outcome in intrauterine growth restriction	Prospective 2	203
Bakalis	2015	Umbilical and foetal middle cerebral artery Doppler at 30-34 weeks' gestation in the prediction of adverse perinatal outcome	Prospective	30780
Bano	2010	Color doppler evaluation of cerebral-umbilical pulsatility ratio and its usefulness in the diagnosis of intrauterine growth retardation and prediction	Case control	90
Bligh	2017	Cerebroplacental ratio thresholds measured within two weeks of birth and the risk of Cesarean section for intrapartum fetal compromise and adverse neo	Prospective	483
Casillas	2007	Correlación entre la flujometría Doppler de la arteria cerebral media/umbilical y la prueba sin estrés como métodos de vigilancia fetal antesdel p	Prospective	161
Cruz-Mar	2011	Fetal brain Doppler to predict cesarean delivery for nonreassuring fetal status in term small-for-gestational-age fetuses	Case control	420
D'Antoni	2013	Role of cerebroplacental ratio for fetal assessment in prolonged pregnancy	Retrospective	320
Devine	1994	Middle cerebral to umbilical artery Doppler ratio in post-date pregnancies	Retrospective	49
El-Sokka	2011	Ratio of middle cerebral artery/umbilical artery Doppler velocimetry and status of newborn in postterm pregnancy	Case control	100
Figueras	2015	An integrated model with classification criteria to predict small-for-gestational-age fetuses at risk of adverse perinatal outcome	Prospective	509
Flood	2014	The role of brain sparing in the prediction of adverse outcomes in intrauterine growth restriction: results of the multicenter PORTO Study	Prospective	881
Fu	2011	Relations between fetal brain-sparing circulation, oxytocin challenge test, mode of delivery and fetal outcome in growth-restricted term fetuses	Prospective	126
Garcia-S	2015	Cervical condition and fetal cerebral Doppler as determinants of adverse perinatal outcome after labor induction for late-onset small-for-gestational-	Prospective	164
Gibbons	2017	The fetal cerebro-placental ratio in diabetic pregnancies is influenced more by the umbilical artery rather than middle cerebral artery pulsatility in	Retrospective	1281
Gramelli	1992	Cerebral-umbilical Doppler ratio as a predictor of adverse perinatal outcome	Retrospective	90
Habek	2003	Fetal Biophysical Profile and Cerebro-Umbilical Ratio in Assessment of Perinatal Outcome in Growth-Restricted Fetuses	Prospective	87
Josephin	2016	Doppler Ultrasound Study of Umbilical Artery and Middle Cerebral Artery in Clinically Suspected Iugr Pregnancies	Prospectve	50
Jugovic	2007	New Doppler index for prediction of perinatal brain damage in growth-restricted and hypoxic fetuses	Prospective	29
Karlsen	2016	Use of conditional centiles of middle cerebral artery pulsatility index and cerebroplacental ratio in the prediction of adverse perinatal outcomes	Prospective	220
Khalil	2015	Is fetal cerebroplacental ratio an independent predictor of intrapartum fetal compromise and neonatal unit admission?	Retrospective	9772
Laltjamt	2015	Study on role of obstetrical Doppler in pregnancies with hypertensive disorders of pregnancy	Prospective	100
Liu	2016	The Value of the Cerebroplacental Ratio for the Prediction of Intrapartum Fetal Monitoring in Low-Risk Term Pregnancies	Retrospective	476
Lobmaier	2014	Angiogenic factors vs Doppler surveillance in the prediction of adverse outcome among late-pregnancy small-for-gestational-age fetuses	Prospective	198
Luzi	1996	Doppler velocimetry of different sections of the fetal middle cerebral artery in relation to perinatal outcome	Case control	70
Makhseed	2000	Middle cerebral artery to umbilical artery resistance index ratio in the prediction of neonatal outcome	Prospective	70
Morales-	2015	Neonatal Acid-Base Status in Fetuses with Abnormal Vertebro- and Cerebro-Placental Ratios	Retrospective	1059
Morales-	2017	The vertebroplacental ratio as an alternative to the cerebroplacental ratio in the evaluation of the fetus at the end of pregnancy	Prospective	1470
Najam	2016	Predictive Value of Cerebroplacental Ratio in Detection of Perinatal Outcome in High-Risk Pregnancies	Retrospective	150
Odibo	2005	Cerebroplacental Doppler ratio and adverse perinatal outcomes in intrauterine growth restriction: evaluating the impact of using gestational age-speci	Retrospective	183
Ott	1999	Comparison of the non-stress test with the evaluation of centralization of blood flow for the prediction of neonatal compromise	Prospective	447
Peixoto	2016	Assessment of ultrasound and Doppler parameters in the third trimester of pregnancy as predictors of adverse perinatal outcome in unselected pregnancy	Retrospective	700
Prior	2015	Are fetuses that fail to achieve their growth potential at increased risk of intrapartum compromise?	Prospective	775
Ropacka-	2015	Cerebroplacental ratio in prediction of adverse perinatal outcome and fetal heart rate disturbances in uncomplicated pregnancy at 40 weeks and beyond	Prospective	148
Sabdia	2015	Predicting intrapartum fetal compromise using the fetal cerebro-umbilical ratio	Retrospective	1381
Shaheen	2014	Doppler cerebroplacental ratio and adverse perinatal outcome.	Retrospective	62
Simanavi	2006	Fetal middle cerebral to uterine artery pulsatility index ratios in normal and pre-eclamptic pregnancies	Prospective	113
Simeone	2017	Doppler velocimetry and adverse outcome in labor induction for late IUGR	Retrospective	100
Singh	2013	Role of Doppler indices in the prediction of adverse perinatal outcome in Preeclampsia	Prospective	50
Sirico	2017	Prediction of adverse perinatal outcome by cerebroplacental ratio adjusted for estimated fetal weight	Retrospective	3515
Sjahinaj	2010	The value of the middle cerebral to umbilical artery Doppler ratio in the prediction of neonatal outcome in patient with preeclampsia and gestational	Retrospective	738
Triunfo	2016	Prediction of delivery of small for gestational age neonates and adverse perinatal outcomes by feto-placental Doppler at 37 weeks' gestation	Prospective	946
Twomey	2016	The association between a low cerebro-umbilical ratio at 30-34 weeks gestation, increased intrapartum operative intervention and adverse perinatal out	Retrospective	1224
Vimalraj	2016	CORRELATION OF CEREBROPLACENTAL RATIO WITH PERINATAL OUTCOME IN INTRAUTERINE GROWTH RESTRICTION	Prospective	180
Warshak	2015	Doppler for growth restriction: the association between the cerebroplacental ratio and a reduced interval to delivery:	Retrospective	154
				Total: 66392

Table 2
CPR cut-off used between studies.

Abnormal CPR defined as		Frequency
Valid	CPR < 1	14
	CPR in MoM	7
	CPR < p5	6
	CPR < p10	5
	CPR < 1.08	7
	CPR < 1.05	2
	CPR Z score	1
	CPR < 0.85	1
	CPR < 1.23	1
	CPR < 1.1	1
	CPR PI < 1.5 and CPR R I< 1	1
	Total	46
Missing		1
Total		47

(placental) AND ("Ratio") OR (cerebroumbilical AND ratio). The reference lists of relevant articles as well as the Cochrane library and Uptodate were also searched for appropriate studies. No language restrictions were used in either the search, however in the study selection only English and Spanish articles were used. No search for unpublished literature was performed.

Study selection

We included studies that met the following inclusion criteria: CPR was measured and postpartum outcomes were available. The neonatal and obstetric outcomes analysed were; the need for intervention based on presence of foetal distress, neonatal pH, Apgar score, Neonatal Intensive Care Unit (NICU) admission as well as stillbirth and neonatal death rates or a composite score on the combinations of these adverse outcomes. Only articles available in full-text were used that were written in English or Spanish. Studies that were small (n<10) or those looking exclusively at multiple pregnancies, or congenital anomalies, as well as looking at the effect of certain medications or therapy on Doppler flows, were excluded. The search was carried out by one reviewer (DM) who analysed all the available abstracts for usability and gathered all the available full-text on the subject. Two independent reviewers (DM and SV) analyzed all the articles that were found through the above mentioned search on their usability for the study. If there was disagreement on the usability of the study the reviewers met to discuss the study and the data derived from it and came to a consensus.

Data extraction

The data extraction was performed using a standardized data extraction form, collecting information on the publication year, study design, number of cases, number of controls, total sample size, case control matching, the risk estimates or data used to calculate the risk estimates, CIs or data used to calculate CIs. Adjusted ratios were extracted in preference to non-adjusted ratios, however, where adjusted ratios were not provided, unadjusted ORs and CIs were calculated. Where more than one adjusted ratio was reported, the ratio with the highest number of adjusted variables was used.

Quality assessment

Quality assessment of the included studies was performed by two independent reviewers (DM and SV) using the Newcastle-Ottawa Scale [17]. This scale judges the article on selection of the study groups, comparability of the groups and ascertainment of the outcome of interest. Agreement regarding the marking of each study was reached by consensus.

Statistical analysis

Pooled odds ratios (OR) and 95% confidence intervals were calculated separately for the effect of each obstetric or perinatal

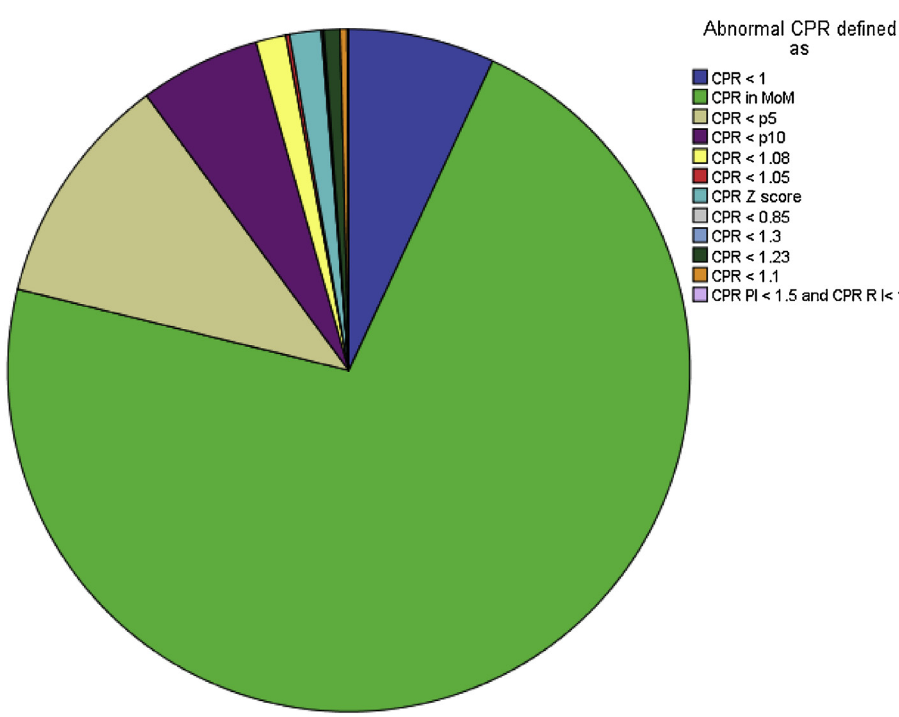


Fig. 2. CPR cut-off per total patients.

outcome using a random effects model [18]. We tested heterogeneity with Cochran's Q statistic, with $P < 0.10$ indicating heterogeneity, and quantified the degree of heterogeneity using the I^2 statistic, which represents the percentage of the total variability across studies which is due to heterogeneity. I^2 values of 25, 50 and 75% corresponded to low, moderate and high degrees of heterogeneity respectively [19]. We quantified publication bias using the Egger's regression model with the effect of bias assessed using the fail-safe number method [20]. The fail-safe number was the number of studies that we would need to have missed for our observed result to be nullified to statistical non-significance at the $p < 0.05$ level. Publication bias is generally regarded as a concern if the fail-safe number is less than 5n+10, with n being the number of studies included in the meta-analysis [21]. All analyses were performed with Comprehensive Meta-analysis (version 3.0), Biostat, Englewood, NJ (2014) as well as IBM SPSS statistics version 24. In the outcome for perinatal mortality where it was expected to have 0 cases in most normal CPR group a Yates correction was used to analyze the additional data [22–24].

Results

The search yielded 588 titles with abstracts, from which 160 abstracts were found to be relevant to our stated clinical question (Fig. 1). After independent review, 47 studies, 25 prospective, 5 case-control and 17 retrospective, could be included in the analysis. No randomised controlled trials were found. The publication dates of these 47 studies ranged from 1992-2017. All data was extracted for the different outcomes from the 66,392 patients and combined depending on the type of study (Table 1).

The variations of CPR cut-offs used between studies are defined in Table 2. Fig. 2 defines the distribution among the number of patients used. The cut-off of 1 was used in the largest percentage of studies, however most data is from studies were MoM were used to define the cut-off.

When analysing the gestation at inclusion, most studies had an inclusion of gestation before 32 weeks, however most patients were between 32 and 40 weeks pregnant at inclusion (Fig. 3). Publication bias was regarded as a concern only in the retrospective data on operative delivery for foetal distress.

Most studies reported on the operative delivery due to foetal distress outcome, with the prospective data showing an RR of 2.52 [95%CI: 2.10–3.02; $I^2 = 65.78$, $P < 0.001$], the retrospective showed a combined OR of 2.62 [95%CI: 1.02–6.72, $p = 0.045$].

The combined prospective data showed CPR to be correlated with low Apgar score [RR: 2.05, 95%CI: 1.39–3.03; $I^2 = 37.15$, $P = 0.10$], low pH [RR: 2.19, 95%CI: 1.01–4.75; $I^2 = 70.26$, $P = 0.005$], foetal and/or neonatal demise [RR: 2.49, 95%CI: 1.00–6.20; $I^2 = 37.27$, $p = 0.21$], as well as NICU admission [RR: 2.23, 95%CI: 1.84–2.70; I^2 48.53, $P = 0.14$]. All the prospective data on the different perinatal outcomes is depicted in Table 3, and the combined prospective and retrospective data in Table 4. Table 3 also differentiates between appropriately grown (AGA), combination or IUGR cohorts. When analysing the data specifically on the appropriately grown cohort, a comparable correlation of CPR with adverse outcomes was found compared to the total risk ratio and isolated IUGR cohorts on most outcomes. For example a risk ratio of 3.26 for operative delivery for foetal distress with 95%CI of 2.36–4.51 was found, compared to a risk ratio of 2.22, 95%CI 1.76–2.79 for IUGR cohorts. The stronger correlation of CPR with adverse outcomes in the AGA cohorts compared to IUGR was found for all outcomes except NICU admission.

With regards to gestational age at inclusion, an abnormal CPR diagnosed early on in the pregnancy had a stronger correlation with adverse outcomes compared to at a more advanced gestational age (Table 5). This table also highlights the post term group as having an even stronger correlation with adverse

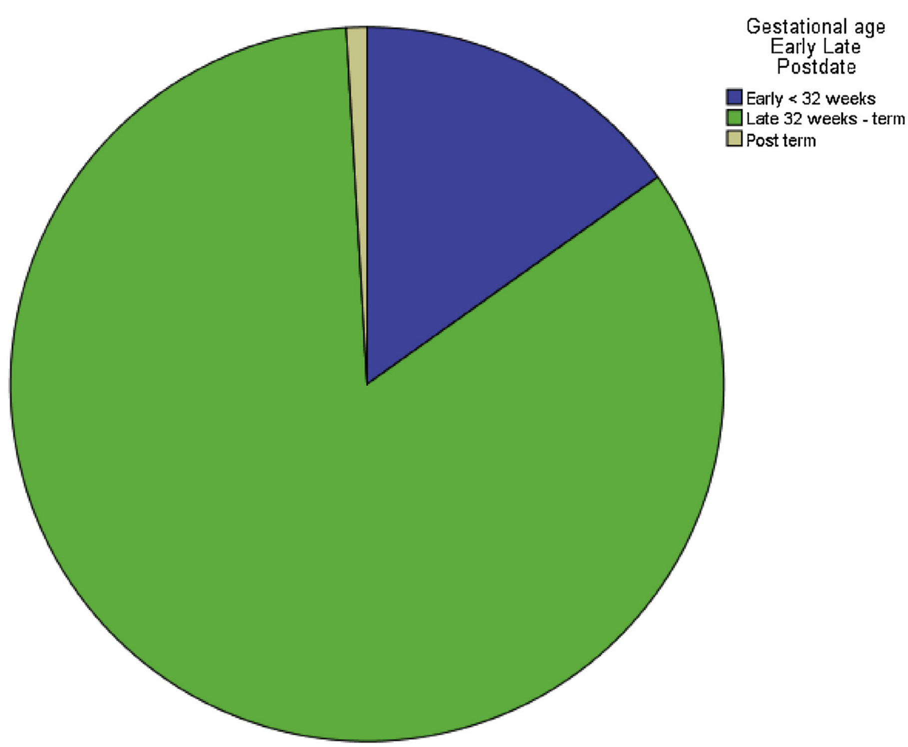


Fig. 3. Gestational age per total patients.

outcomes, however this group consists only of two article which makes this data difficult to interpret.

The Newcastle-Ottawa scale for the various studies can be found in Table 6. It was noted that only a few articles adjusted for confounders when analysing their results as can be seen in the discrepancy between studies in Table 6 on the comparability item, while selection and outcome were comparable between studies.

Discussion

Main findings

The findings from the systematic review and meta-analysis show that CPR can be used to predict which pregnancies are at higher risk of developing adverse perinatal outcomes for all the outcomes analysed. It provides a clear overview of the available data on the subject and shows a statistically significant effect on all the adverse perinatal outcomes studied.

Study limitations

Half of the data used in this meta-analysis was collected from retrospective studies, none of the studies had a randomized design, and some smaller studies were used. In only a few studies the treating physicians were known to be blinded to the CPR value. The heterogeneity of the study data, as shown by the I^2 calculation, is the major limitation of our study. Most adverse perinatal outcomes showed high heterogeneity in the prospective data, except for low Apgar score and NICU admission, which showed low to moderate heterogeneity. The use of different CPR cut-offs used between the studies might also have contributed to the increased heterogeneity of the data. Based on our analysis publication bias was only found to have influenced the findings in the retrospective data on operative delivery due to foetal distress, when assessed by the Egger's regression model.

Most of the observed outcomes were reported by only a limited proportion of the included studies. Most studies collected data on the need for operative delivery due to foetal distress and within this group most studies only recorded the caesarean rate and not the instrumental rate for foetal distress which might give an under representation of the predicting ability of the CPR.

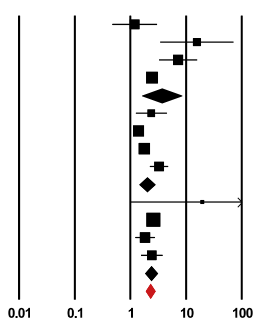
The Newcastle-Ottawa scale was used to analyse the quality of the data and showed that only a few articles corrected for confounders when calculating the odds ratios and relative risks, therefore mostly crude odds ratios and relative risks were used which might also skew the data.

Table 3
Prospective data as grouped by cohort type. (AGA = appropriately grown for gestational age, IUGR = intrauterine growth retardation).

Composite adverse events (n=2477)

Group by Type of Cohort	Study name	Risk ratio	Lower limit	Upper limit	p-Value
AGA	D'Antoni 2013	1.19	0.47	3.01	0.710
AGA	Devine 1994	15.60	3.41	71.30	0.000
AGA	El-Sokka 2011	7.17	3.23	15.94	0.000
AGA	Laltjamt 2015	2.44	2.16	2.76	0.000
AGA		3.65	1.61	8.26	0.002
Combination	Adiga 2015	2.38	1.24	4.54	0.009
Combination	Ebrashy 2005	1.40	1.15	1.70	0.001
Combination	Gibbons 2017	1.78	1.51	2.10	0.000
Combination	Kant 2016	3.27	2.21	4.83	0.000
Combination		1.98	1.44	2.73	0.000
IUGR	Josephin 2016	19.59	1.00	383.99	0.050
IUGR	Karlsen 2016	2.59	1.99	3.37	0.000
IUGR	Lobmaier 2014	1.83	1.22	2.75	0.004
IUGR	Odibo 2005	2.42	1.54	3.80	0.000
IUGR		2.35	1.83	3.02	0.000
Overall		2.26	1.87	2.74	0.000

Risk ratio and 95%CI

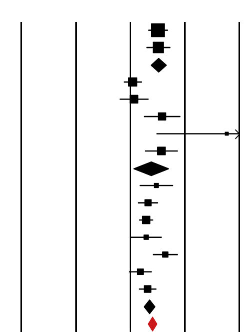


AGA I^2=79.83, P=0.002, Combination I^2=80.97, P<0.001, IUGR I^2=23.65, P=0.27, Total I^2=82.64, p<0.001

Operative delivery for foetal distress (n= 17.198)

Group by Type of Cohort	Study name	Risk ratio	Lower limit	Upper limit	p-Value
AGA	Prior 2015	3.25	2.14	4.94	0.000
AGA	Ropacka- 2015	3.28	1.97	5.46	0.000
AGA		3.26	2.36	4.51	0.000
Combination	Akolekar 2015	1.11	0.75	1.64	0.591
Combination	Bakalis 2015	1.17	0.64	2.17	0.608
Combination	Luzi 1996	3.85	1.77	8.38	0.001
Combination	Bano 2010	59.50	3.01	1175.08	0.007
Combination	Ott 1999	3.75	1.87	7.51	0.000
Combination		2.38	1.14	4.98	0.021
IUGR	Bahado 1999	3.02	1.48	6.17	0.002
IUGR	Cruz-Mar 2011	2.12	1.38	3.26	0.001
IUGR	Figueras 2015	1.96	1.45	2.66	0.000
IUGR	Garcia-S 2015	1.97	1.02	3.79	0.043
IUGR	Karlsen 2016	4.41	2.58	7.52	0.000
IUGR	Makhseed 2000	1.53	0.94	2.49	0.085
IUGR	Fu 2011	2.08	1.43	3.03	0.000
IUGR		2.22	1.76	2.79	0.000
Overall		2.52	2.10	3.02	0.000

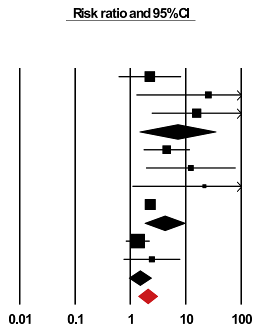
Risk ratio and 95%CI



AGA I^2=0.00, P=0.97, Combination I^2=80.55, P<0.001, IUGR I^2=40.71, P=0.12, Total I^2=65.78, p<0.001

Low Apgar score (n=26.069)

Group by Type of Cohort	Study name	Risk ratio	Lower limit	Upper limit	p-Value
AGA	Makhseed 2000	2.25	0.61	8.28	0.222
AGA	Najam 2016	25.67	1.28	514.26	0.034
AGA	Bano 2010	15.75	2.42	102.60	0.004
AGA		7.10	1.46	34.53	0.015
Combination	Adiga 2015	4.54	1.73	11.89	0.002
Combination	Habek 2003	12.40	1.92	80.21	0.008
Combination	Ropacka- 2015	21.75	1.09	435.98	0.044
Combination	Sjahinaj 2010	2.29	1.85	2.82	0.000
Combination		4.17	1.81	9.63	0.001
IUGR	Bakalis 2015	1.36	0.82	2.24	0.232
IUGR	Singh 2013	2.45	0.75	7.99	0.137
IUGR		1.49	0.94	2.36	0.092
Overall		2.05	1.39	3.03	0.000

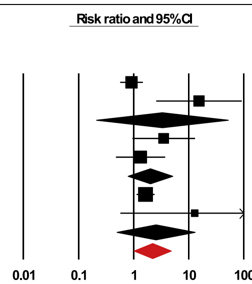


AGA I^2=5

0.27, P=0.13, Combination I^2=56.56, P=0.08, IUGR I^2=0.00, P=0.37, Total I^2=37.15, p=0.10

Low pH (n=3.115)

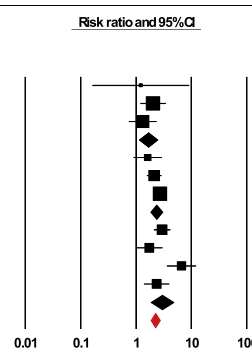
Group by Type of Cohort	Study name	Risk ratio	Lower limit	Upper limit	p-Value
AGA	Prior 2015	0.92	0.57	1.49	0.734
AGA	Ropacka- 2015	15.46	2.56	93.21	0.003
AGA		3.28	0.21	51.45	0.397
Combination	Adiga 2015	3.53	0.95	13.12	0.060
Combination	Akolekar 2015	1.34	0.48	3.78	0.576
Combination		1.99	0.79	5.05	0.146
IUGR	Garcia-S 2015	1.65	1.13	2.42	0.010
IUGR	Habek 2003	12.92	0.57	291.35	0.108
IUGR		2.52	0.50	12.85	0.265
Overall		2.19	1.01	4.75	0.048



AGA I^2=88.68, P=0.003, Combination I^2=22.06, P=0.26, IUGR I^2=39.31, P=0.20, Total I^2=70.26, p=0.005

NICU admission (n=38.729)

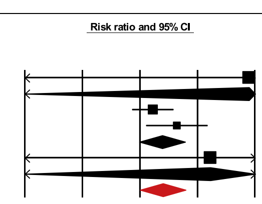
Group by Type of Cohort	Study name	Risk ratio	Lower limit	Upper limit	p-Value
AGA	Prior 2015	1.22	0.16	9.21	0.847
AGA	Laltjamt 2015	2.04	1.19	3.48	0.009
AGA	Simanavi 2006	1.33	0.74	2.39	0.343
AGA		1.66	1.12	2.44	0.011
Combination	Akolekar 2015	1.63	0.90	2.96	0.110
Combination	Bakalis 2015	2.13	1.57	2.89	0.000
Combination	Ott 1999	2.71	2.28	3.22	0.000
Combination		2.33	1.81	2.99	0.000
IUGR	Bahado-S 1999	2.97	2.10	4.18	0.000
IUGR	Garcia-S 2015	1.74	1.00	3.02	0.050
IUGR	Karlsen 2016	6.65	3.59	12.30	0.000
IUGR	Makhseed 2000	2.36	1.39	4.03	0.002
IUGR		2.95	1.84	4.75	0.000
Overall		2.23	1.84	2.70	0.000



AGA I^2=0.00, p=0.55, Combination I^2=48.53, p=0.14, IUGR I^2=72.31, p=0.01, Total I^2=58.61, p=0.01

Fetal and Neonatal demise* (n=31.164)

Group by Type of Cohort	Study name	Risk ratio	Lower limit	Upper limit	p-Value
AGA	Warshak 2015	78.27	0.00	42991612.27	0.518
AGA		78.27	0.00	42991612.27	0.518
Combination	Bakalis 2015	1.68	0.73	3.88	0.221
Combination	Laltjamt 2015	4.40	1.28	15.16	0.019
Combination		2.43	0.97	6.07	0.057
IUGR	Bahado-S 1999	16.65	0.00	9975639.57	0.679
IUGR		16.65	0.00	9975639.57	0.679
Overall		2.49	1.00	6.20	0.049



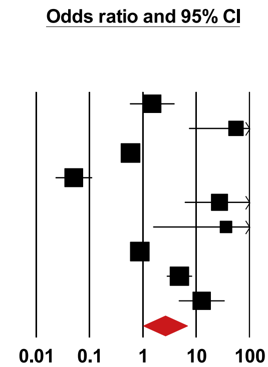
AGA I^2=0.00, p=1.00, Combination I^2=37.27, p=0.21, IUGR I^2=0.00, p=1.00, Total I^2=0.00, p=0.61,

*Yates correction used

Table 4
Retrospective data on CPR and perinatal outcome.

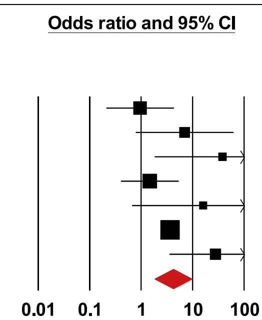
Operative delivery due to foetal distress (n=11.911)

Study name	Odds ratio	Lower limit	Upper limit	p-Value
Gibbons 2017	1.50	0.57	3.94	0.410
Gramelli 1992	56.00	7.34	427.38	0.000
Khalil 2015	0.59	0.48	0.73	0.000
Liu 2016	0.05	0.02	0.11	0.000
Najam 2016	27.41	6.09	123.39	0.000
Shaheen 2014	36.36	1.56	846.46	0.025
Sjahinaj 2010	0.88	0.65	1.20	0.432
Twomey 2016	4.87	2.81	8.45	0.000
Warshak 2015	12.71	4.70	34.36	0.000
	2.62	1.02	6.72	0.045



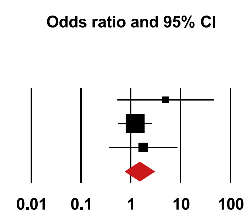
Low Apgar score (n=3.584)

Study name	Odds ratio	Lower limit	Upper limit	p-Value
Gibbons 2017	0.96	0.21	4.33	0.952
Gramelli 1992	7.00	0.78	62.47	0.081
Najam 2016	38.00	1.83	790.57	0.019
Sabdia 2015	1.48	0.40	5.38	0.555
Shaheen 2014	16.00	0.67	383.88	0.087
Sjahinaj 2010	3.64	2.62	5.07	0.000
Bano 2010	27.82	3.55	218.02	0.002
	4.16	1.82	9.53	0.001



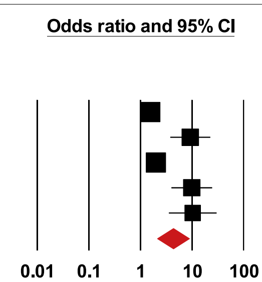
Low pH (n=2.680)

Study name	Odds ratio	Lower limit	Upper limit	p-Value
Cruz-Mar 2011	5.00	0.53	46.90	0.159
Gibbons 2017	1.23	0.56	2.70	0.609
Sabdia 2015	1.77	0.36	8.69	0.482
	1.49	0.76	2.92	0.247



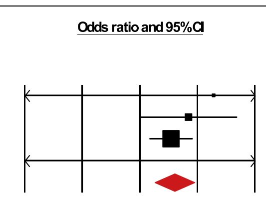
NICU admission (n=10.194)

Study name	Odds ratio	Lower limit	Upper limit	p-Value
Khalil 2015	1.56	1.14	2.14	0.006
Najam 2016	9.29	3.78	22.79	0.000
Sjahinaj 2010	2.00	1.47	2.73	0.000
Twomey 2016	9.92	3.98	24.73	0.000
Warshak 2015	10.35	3.55	30.15	0.000
	4.30	2.12	8.72	0.000



Fetal demise (n=1.573)

Study name	Odds ratio	Lower limit	Upper limit	p-Value
Arias 1994	19.22	0.00	11650841.32	0.664
Najam 2016	7.03	1.00	49.41	0.050
Twomey 2016	3.49	1.46	8.32	0.005
Warshak 2015	114.33	0.00	64487415.11	0.483
	3.99	1.81	8.80	0.001



The correlation between CPR and perinatal death rates was likely to be stronger as 5 out of the 10 studies reporting on this outcome could not provide OR nor RR as there were no perinatal deaths in the normal CPR group. Yates correction was used to analyse this and found an increased risk ratio from 2.30 (95%CI 1.15–4.59 p = 0.018) to 3.04 (95% CI 1.80–5.16 p = 0.000).

Our meta-analysis included one large study which theoretically could have skewed our data. We analysed the effect of this study on our findings. Outcomes from this study were operative delivery due to foetal distress, low Apgar score, NICU admission and perinatal demise. If we removed this study these outcomes showed a stronger predictive value of CPR [7].

Implications for clinical practice

CPR and intrauterine growth restriction or small for gestational age foetuses

When analysing our data on early growth restriction. The data derived from relatively large prospective studies showed CPR to be a good predictor of operative delivery due to foetal distress [2,25,26]. Data on late growth restricted cohorts also showed CPR to be able to predict a higher risk for foetal distress [27–29]. The value of CPR as a predictor of foetal distress during labour has been proven. UA and MCA Doppler flows should be measured in all pregnancies complicated by growth restriction and CPR calculated. It is useful in predicting those foetuses that might require careful surveillance and should be taken into consideration when looking after these high risk pregnancies in the antenatal period and during labour.

CPR and appropriately grown foetuses and predicting foetal distress at term

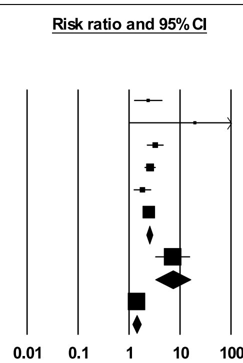
We selected some larger studies to specifically focus on the role of CPR in predicting the need for intervention based on presence of foetal distress. CPR at term in appropriately grown foetuses has been shown by Prior et al. to be a predictor for intrapartum foetal compromise and the need for emergency caesarean delivery [30]. Similarly Khalil et al used multivariate logistic regression analysis on the 8382 patients scanned after 37 weeks and found that CPR was associated with the risk of emergency operative delivery in both SGA as well as AGA patient, this finding was independent of birthweight [31]. Bligh conducted a prospective blinded study of 437 participants assessing the value of term CPR as a screening test for Caesarean section for intrapartum foetal distress in normally grown foetuses and found that a low CPR measured within two weeks of birth in clinically 'low risk' women is associated with emergency Caesarean section [32]. Ropacka-Lesiak examined 148 uncomplicated post-term pregnancies comparing selected Doppler blood flow indices to CPR revealed a significantly higher emergency caesarean section rate in the abnormal CPR group, CPR also showed the highest sensitivity in prediction of both the intrapartum suspected foetal distress (74.1%) and the adverse neonatal outcome (87.8%) [33].

Our study combined these studies and found relative risk of 2.52 (95%CI: 2.10–3.02) for operative delivery due to foetal distress in the appropriately grown cohorts. This supports DeVore's suggestion to assess CPR as part of a screening test at the time of admission to delivery suite for labour. The ability to risk stratify women prior to labour would allow decisions regarding timing and

Table 5
Data as grouped by gestation.

Composite adverse events (n=913) prospective

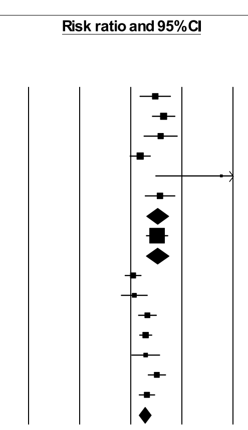
Group by Gestation	Study name	Risk ratio	Lower limit	Upper limit	p-Value
Early	Adiga 2015	2.38	1.24	4.54	0.009
Early	Josephin 2016	19.59	1.00	383.99	0.050
Early	Kant 2016	3.27	2.21	4.83	0.000
Early	Karlsen 2016	2.59	1.99	3.37	0.000
Early	Lobmaier 2014	1.83	1.22	2.75	0.004
Early	Laltjamt 2015	2.44	2.16	2.76	0.000
Early		2.49	2.16	2.86	0.000
Post-Term	El-Sokka 2011	7.17	3.23	15.94	0.000
Post-Term		7.17	3.23	15.94	0.000
Term	Ebrashy 2005	1.40	1.15	1.70	0.001
Term		1.40	1.15	1.70	0.001



Early I^2=17.80, p=0.30, PT I^2=0.00, p=1.00, Term I^2=0.00, p=1.00

Operative delivery for foetal distress (n=39.994) prospective

Group by Gestation	Study name	Risk ratio	Lower limit	Upper limit	p-Value
Early	Bahado 1999	3.02	1.48	6.17	0.002
Early	Karlsen 2016	4.41	2.58	7.52	0.000
Early	Luzi 1996	3.85	1.77	8.38	0.001
Early	Makhseed 2000	1.53	0.94	2.49	0.085
Early	Bano 2010	59.50	3.01	1175.08	0.007
Early	Ott 1999	3.75	1.87	7.51	0.000
Early		3.29	2.00	5.39	0.000
Post-Term	Ropacka- 2015	3.28	1.97	5.46	0.000
Post-Term		3.28	1.97	5.46	0.000
Term	Akolekar 2015	1.11	0.75	1.64	0.591
Term	Bakalis 2015	1.17	0.64	2.17	0.608
Term	Cruz-Mar 2011	2.12	1.38	3.26	0.001
Term	Figueras 2015	1.96	1.45	2.66	0.000
Term	Garcia-S 2015	1.97	1.02	3.79	0.043
Term	Prior 2015	3.25	2.14	4.94	0.000
Term	Fu 2011	2.08	1.43	3.03	0.000
Term		1.87	1.43	2.45	0.000

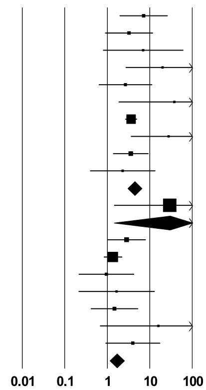


Early I^2=64.17, p=0.02, PT I^2=0.00, p=1.00, Term I^2=63.70, p=0.01

Low Apgar score (n=38.047) all data combined

Group by Gestation	Study name	Odds ratio	Lower limit	Upper limit	p-Value
Early	Adiga 2015	7.19	1.93	26.76	0.003
Early	Bahado-S 1999	3.26	0.88	12.06	0.077
Early	Gramelli 1992	7.00	0.78	62.47	0.081
Early	Habek 2003	20.00	2.68	149.22	0.003
Early	Makhseed 2000	2.68	0.63	11.51	0.184
Early	Najam 2016	38.00	1.83	790.57	0.019
Early	Sjahinaj 2010	3.64	2.62	5.07	0.000
Early	Bano 2010	27.82	3.55	218.02	0.002
Early	Laltjamt 2015	3.58	1.36	9.45	0.010
Early	Simanavi 2006	2.31	0.39	13.73	0.358
Early		4.36	2.99	6.37	0.000
Post-Term	Ropacka- 2015	29.64	1.43	612.87	0.028
Post-Term		29.64	1.43	612.87	0.028
Term	Akolekar 2015	2.85	1.00	8.14	0.050
Term	Bakalis 2015	1.36	0.82	2.27	0.232
Term	Gibbons 2017	0.96	0.21	4.33	0.952
Term	Prior 2015	1.66	0.21	13.23	0.632
Term	Sabdia 2015	1.48	0.40	5.38	0.555
Term	Shaheen 2014	16.00	0.67	383.88	0.087
Term	Singh 2013	4.00	0.90	17.79	0.069
Term		1.67	1.13	2.46	0.010

Odds ratio and 95% CI

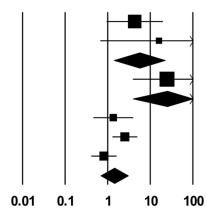


Early I^2=10.89, p=0.34, Post-term I^2=0.00, p=1.00, Term I^2=0.00, p=0.49

Low pH (n=7.307) prospective

Group by Gestation	Study name	Risk ratio	Lower limit	Upper limit	p-Value
Early	Adiga 2015	4.32	0.93	20.09	0.062
Early	Habek 2003	16.05	0.67	387.00	0.087
Early		5.54	1.39	22.10	0.015
Post-Term	Ropacka- 2015	24.75	3.86	158.68	0.001
Post-Term		24.75	3.86	158.68	0.001
Term	Akolekar 2015	1.36	0.46	4.03	0.584
Term	Garcia-S 2015	2.53	1.28	5.01	0.008
Term	Prior 2015	0.82	0.40	1.64	0.566
Term		1.42	0.67	2.99	0.357

Risk ratio and 95% CI

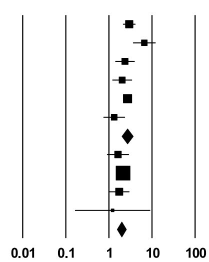


Early I^2=0.00, p=0.47, PT I^2=0.00, p=1.00, Term I^2=61.24, p=0.08

NICU admission (n=38.910) prospective

Group by Gestation	Study name	Risk ratio	Lower limit	Upper limit	p-Value
Early	Bahado-S 1999	2.97	2.10	4.18	0.000
Early	Karlsen 2016	6.65	3.59	12.30	0.000
Early	Makhseed 2000	2.36	1.39	4.03	0.002
Early	Laltjamt 2015	2.04	1.19	3.48	0.009
Early	Ott 1999	2.71	2.28	3.22	0.000
Early	Simanavi 2006	1.33	0.74	2.39	0.343
Early		2.64	1.96	3.56	0.000
Term	Akolekar 2015	1.63	0.90	2.96	0.110
Term	Bakalis 2015	2.13	1.57	2.89	0.000
Term	Garcia-S 2015	1.74	1.00	3.02	0.050
Term	Prior 2015	1.22	0.16	9.21	0.847
Term		1.95	1.53	2.48	0.000

Risk ratio and 95% CI

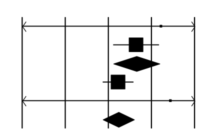


Early I^2=67.62, p=0.009, Term I^2=0.00, p=0.79

Fetal and Neonatal demise* (n=31.244) prospective

Group by Gestation	Study name	Risk ratio	Lower limit	Upper limit	p-Value
Early	Bahado-S 1999	16.65	0.00	9975639.57	0.679
Early	Laltjamt 2015	4.40	1.28	15.16	0.019
Early		4.45	1.30	15.25	0.017
Term	Bakalis 2015	1.68	0.73	3.88	0.221
Term	Casillas 2007	27.56	0.00	19267574.81	0.629
Term		1.70	0.74	3.91	0.211

Risk ratio and 95% CI



Early I^2=0.00, p=0.85, Term I^2=0.00, p=0.68

*Yates correction used

Table 6
Newcastle- Ottawa scale.

First author	Year	Selection	Comparability	Outcome
Adiga	2015	★★★	★	★★★
Akolekar	2015	★★½	★★	★★★
Arias	1994	★★		★★★
Bahado-Singh	1999	★★★	★	★★★
Bakalis	2015	★★	★★	★★★
Bano	2010	★★★		★★★
Bligh	2017	★★★	★	★★★
Casillas	2007	★★★		★★★
Cruz-Mar	2011	★★★	★	★★★
D'Antonio	2013	★★★		★★★
Devine	1994	★★★	★★	★★
Ebrashy	2005	★★		★★
El-Sokkary	2011	★★	★	★★
Figueras	2015	★★★		★★★
Flood	2014	★★★		★★★
Fu	2011	★★★		★★★
Garcia-Simon	2015	★★★	★★	★★★
Gibbons	2017	★★		★★★
Gramelli	1992	★		★★★
Habek	2003	★★★		★★★
Josephin	2016	★★★		★★★
Jugovic	2007	★★★		★★★
Karlsen	2016	★★★	★★	★★★
Khalil	2015	★★★	★★	★★★
Lalthantluanga	2015	★★★		★★
Liu	2016	★★★	★★	★★★
Lobmaier	2014	★★★	★	★★★
Luzi	1996	★★		★★★
Makhseed	2000	★★★		★★★
Morales-Rosello	2015	★★★		★★★
Morales-Rosello	2017	★★	★	★★
Najam	2016	★★★		★★★
Odibo	2005	★★		★★
Ott	1999	★★★	★	★★★
Peixoto	2016	★★★		★★★
Prior	2015	★★★	★	★★★
Ropacka-Lesiak	2015	★★		★★
Sabdia	2015	★★★	★★	★★★
Shaheen	2014	★★★		★★
Simanavi	2006	★★★	★	★★★
Simeone	2017	★★★	★★	★★★
Singh	2013	★★		★★★
Sirico	2017	★★★	★★	★★
Sjahinaj	2010	★★★		★★★
Triunfo	2016	★★★	★★	★★★
Twomey	2016	★★★	★★	★★★
Vimalraj	2016	★★		★★
Warshak	2015	★★★	★★	★★★

mode of delivery to be made in a non-emergent situation, decreasing the risk of adverse perinatal outcome [5,32,34].

The optimal threshold

There was a large variance in the definition of abnormal CPR, the largest amount of studies used 1 as the threshold. Flood et al performed a secondary analysis on data derived from the prospective multicentre PORTO study to evaluate the role of CPR calculation with respect to the prediction of adverse perinatal outcome. They compared CPR calculated using both the PI and RI with a result less than 1 considered as well as a categorical cut-off of less than 1.08 and gestational age specific reference values (less than the fifth centile). The data from 881 early growth restricted foetuses was used and found a strong agreement between CPR calculations based on PI and RI, neither of the computations outperformed the other, either showing a lowering of the specificity when using the 5th centile cut-off or lowering of the sensitivity by using 1 as a cut-off [13]. Bligh et al. also investigated the performance of three of the most widely reported thresholds, CPR $\leq$ 1, CPR <5th centile and CPR <10th centile, recognising that the 0.6765 multiples of the median (MoM) value equates to the 5th centile [32,35]. They found that the CPR <10th centile has a sensitivity and specificity of 55.6% and 87.9% respectively, for Caesarean section due to foetal compromise, outperforming other previously suggested CPR thresholds [30,32]. For the benefit of future research, one threshold for abnormal CPR should be used and we propose the 10th centile to be that threshold.

Conclusion

Our meta-analysis shows that CPR can be used to identify foetuses with higher risk of operative delivery due to foetal distress, low Apgar score, NICU admission, neonatal morbidity as well as stillbirth and neonatal death rates, both in the appropriately grown as well as the growth restricted cohorts. CPR appears to be an independent marker for adverse perinatal outcome and should be measured, calculated and reported on during basic ultrasound examinations in the second and third trimester.

Declaration of Competing Interest

The authors report no conflicts of interest.

References

[1] Buck Louis GM, et al. Racial/ethnic standards for fetal growth: the NICHD fetal growth studies. Am J Obstet Gynecol 2015;213(4):449 e1–449 e41.
[2] Bahado-Singh RO, et al. The Doppler cerebroplacental ratio and perinatal outcome in intrauterine growth restriction. Am J Obstet Gynecol 1999;180(3 Pt 1):750–6.
[3] Arbeille P, et al. Fetal cerebral circulation assessment by Doppler ultrasound in normal and pathological pregnancies. Eur J Obstet Gynecol Reprod Biol 1988;29(4):261–73.
[4] Muresan D, Rotar IC, Stamatian F. The usefulness of fetal Doppler evaluation in early versus late onset intrauterine growth restriction. Review of the literature. Med Ultrason 2016;18(1):103–9.
[5] DeVore GR. The importance of the cerebroplacental ratio in the evaluation of fetal well-being in SGA and AGA fetuses. Am J Obstet Gynecol 2015;213(1):5–15.
[6] Arbeille P, et al. Doppler examination of the umbilical and cerebral arterial circulation of the fetus. J de gynecologie, obstetrique et biologie de la reproduction 1987;16(1):45–51.
[7] Bakalis S, et al. Umbilical and fetal middle cerebral artery Doppler at 30-34 weeks' gestation in the prediction of adverse perinatal outcome. Ultrasound Obstet Gynecol 2015;45(4):409–20.
[8] Sirico A, et al. Prediction of adverse perinatal outcome by cerebroplacental ratio adjusted for estimated fetal weight. Ultrasound Obstet Gynecol 2017 p. n/a-n/a.
[9] Twomey S, Flatley C, Kumar S. The association between a low cerebro-umbilical ratio at 30-34 weeks gestation, increased intrapartum operative intervention and adverse perinatal outcomes. Eur J Obstet Gynecol Reprod Biol 2016;203:89–93.
[10] Arbeille P, et al. Nouvelle technique dans la surveillance de la grossesse: l'étude de la circulation foetale et placentaire par les ultrasons. J Gynecol Obstet Biol Reprod (Paris) 1983;12:851–9.
[11] Morales-Rosello J, et al. Poor neonatal acid-base status in term fetuses with low cerebroplacental ratio. Ultrasound Obstet Gynecol 2015;45(2):156–61.
[12] Akolekar R, et al. Umbilical and fetal middle cerebral artery Doppler at 35-37 weeks' gestation in the prediction of adverse perinatal outcome. Ultrasound Obstet Gynecol 2015;46(1):82–92.
[13] Flood K, et al. The role of brain sparing in the prediction of adverse outcomes in intrauterine growth restriction: results of the multicenter PORTO Study. Am J Obstet Gynecol 2014;211(3) p. 288 e1-5.
[14] Vollgraff Heidweiller-Schreurs CA, De Boer MA, Heymans MW, Schoonmade LJ, et al. Prognostic accuracy of cerebroplacental ratio and middle cerebral artery Doppler for adverse perinatal outcome: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2018;51(March 3):313–22.
[15] Shapiro DE. Issues in combining independent estimates of the sensitivity and specificity of a diagnostic test. Acad Radiol 1995;2:S37–47.

[16] Moher D, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6(7):e1000097.
[17] Wells G, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses. 2009 Epub Available from: URL: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm [cited 2009 Oct 19], 2013.
[18] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7(3):177–88.
[19] Higgins J, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21(11):1539–58.
[20] Egger M, et al. Bias in meta-analysis detected by a simple, graphical test. Bmj 1997;315(7109):629–34.
[21] Orwin RG. A fail-safe N for effect size in meta-analysis. J Educ Stat 1983;8 (2):157–9.
[22] Fates F. Contingency tables involving small numbers and the X 2 test. J. Roy. Statist. Soc 1934.
[23] Haviland MG. Yates's correction for continuity and the analysis of 2× 2 contingency tables. Stat Med 1990;9(4):363–7.
[24] Walter S. Point estimation of the odds ratio in sparse 2× 2 contingency tables. Biostatistics 1987;71–102.
[25] Makhseed M, et al. Middle cerebral artery to umbilical artery resistance index ratio in the prediction of neonatal outcome. Int J Gynaecol Obstet 2000;71 (2):119–25.
[26] Karlsen HO, et al. Use of conditional centiles of middle cerebral artery pulsatility index and cerebroplacental ratio in the prediction of adverse perinatal outcomes. Acta Obstet Gynecol Scand 2016;95(6):690–6.
[27] Garcia-Simon R, et al. Cervical condition and fetal cerebral Doppler as determinants of adverse perinatal outcome after labor induction for late-onset small-for-gestational-age fetuses. Ultrasound Obstet Gynecol 2015;46 (6):713–7.
[28] Cruz-Martinez R, et al. Fetal brain Doppler to predict cesarean delivery for nonreassuring fetal status in term small-for-gestational-age fetuses. Obstet Gynecol 2011;117(3):618–26.
[29] Figueras F, et al. An integrated model with classification criteria to predict small-for-gestational-age fetuses at risk of adverse perinatal outcome. Ultrasound Obstet Gynecol 2015;45(3):279–85.
[30] Prior T, et al. Prediction of intrapartum fetal compromise using the cerebroumbilical ratio: a prospective observational study. Am J Obstet Gynecol 2013;208(2) p. 124 e1-6..
[31] Khalil A, et al. IS cerebroplacental ratio a marker of impaired fetal growth velocity and adverse pregnancy outcome? Am J Obstet Gynecol 2017.
[32] Bligh L, et al. Cerebroplacental ratio thresholds measured within two weeks of birth and the risk of Cesarean section for intrapartum fetal compromise and adverse neonatal outcome. Ultrasound Obstet Gynecol 2017 p. n/a-n/a.
[33] Ropacka-Lesiak M, et al. Cerebroplacental ratio in prediction of adverse perinatal outcome and fetal heart rate disturbances in uncomplicated pregnancy at 40 weeks and beyond. Arch Med Sci 2015;11(1):142–8.
[34] Gibbons A, et al. The fetal cerebro-placental ratio in diabetic pregnancies is influenced more by the umbilical artery rather than middle cerebral artery pulsatility index. Eur J Obstet Gynecol Reprod Biol 2017;211:56–61.
[35] Morales-Rosello J, et al. Changes in fetal Doppler indices as a marker of failure to reach growth potential at term. Ultrasound Obstet Gynecol 2014;43(3):303–10.