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Diagnostic accuracy of Doppler ultrasound in predicting perinatal outcome in pregnancies at term: A prospective longitudinal study

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Abstract

Introduction: To explore the strength of association and the diagnostic accuracy of umbilical (UA), middle cerebral (MCA), uterine arteries pulsatility index (PI) and the cerebroplacental ratio in predicting an adverse outcome when applied to singleton pregnancies at term.

Material and methods: Prospective study carried out in a dedicated research ultrasound clinic. Attended clinicians were blinded to Doppler findings. Inclusion criteria were consecutive singleton pregnancies between 36^{+0} and 37^{+6} weeks of gestation. The primary outcome was a composite score of adverse perinatal outcome. Logistic regression and ROC curve analyses were used to analyze the data.

Results: In all, 600 consecutive singleton pregnancies from 36 weeks of gestation were included in the study. Mean MCA PI (1.1 ± 0.2 vs 1.5 ± 0.4, $P < 0.001$) and cerebroplacental ratio (1.4 ± 0.4 vs 1.9 ± 0.6, $P < 0.001$) were lower, whereas uterine arteries PI (0.8 ±0.2 vs 0.7 ±0.3, $P = 0.001$) was higher in pregnancies experiencing than in those not experiencing composite adverse outcome. Conversely, there was no difference in either UA PI ($P = 0.399$) or estimated fetal weight centile ($P = 0.712$) between the two groups, but AC centile was lower in fetuses experiencing composite adverse outcome (45.4 vs 53.2, $P = 0.040$). At logistic regression analysis, MCA PI (odds ratio [OR] 0.1, 95% CI 0.01-.2, $P = 0.001$), uterine arteries PI (OR 1.4, 95% CI 1.2-1.6, $P = 0.001$), abdominal circumference centile (OR 1.12, 95% CI 1.1-1.4, $P = 0.001$) and gestational age at birth (OR 1.6, 95% CI 1.2-2.1, $P = 0.004$) were independently associated with composite adverse outcome. Despite this, the diagnostic accuracy of Doppler in predicting adverse pregnancy outcome at term was poor.

Conclusions: MCA PI and cerebroplacental ratio are associated with adverse perinatal outcome at term. However, their predictive accuracy for perinatal compromise is poor, and thus their use as standalone screening test for adverse perinatal outcome in singleton pregnancies at term is not supported.

Abbreviations: CI, confidence interval; CPR, cerebroplacental ratio; MCA, middle cerebral artery; MoM, multiple of the medians; OR, odds ratio; PI, pulsatility index; SGA, small for gestational age; UA, umbilical artery.

KEYWORDS
cerebroplacental ratio, Doppler, middle cerebral artery, outcome pregnancies at term, perinatal outcome, umbilical artery

1 | INTRODUCTION

Prediction of perinatal compromise in pregnancies close to or at term is challenging. Impendence to blood flow in the umbilical artery (UA), which reflects the magnitude of impaired placental function in fetuses affected by early placental insufficiency, is common in pregnancies beyond 34 weeks of gestation, thus making it impossible objectively to identify those fetuses at higher risk of chronic hypoxemia and adverse perinatal outcome.[1-4] Small for gestational age (SGA) has been used a proxy of fetal growth restriction and impaired placental function. However, not all SGA fetuses are growth-restricted and the diagnostic accuracy of SGA alone in predicting perinatal outcome at term is poor.[5-7]

Reduced impendence to blood flow in the middle cerebral artery has been shown to identify a sub-set of small fetuses at higher risk of short- and long-term adverse outcome, such as abnormal acid-base status, need for cesarean section (CS) and impaired cognitive function.[8,9] More recently, the cerebroplacental ratio, a ratio between the middle cerebral artery (MCA) and UA pulsatility index (PI), has been proposed as a reliable proxy of impaired placental function, irrespective of fetal weight, suggesting its usefulness as a screening test for perinatal compromise.[10-16]

Despite this, the actual role of Doppler ultrasound in predicting perinatal outcome in pregnancies at term remains to be ascertained as well as whether such assessment should be undertaken in the general population as a screening tool for perinatal compromise. The large majority of these studies are retrospective and come from countries where third trimester ultrasound is not routinely performed, thus potentially including cases at high-risk of perinatal compromise.[11,17-19]

The primary aim of this study was to explore the strength of association between Doppler ultrasound and perinatal outcome in singleton pregnancies at term; the secondary aim was to elucidate its predictive accuracy as a screening test for perinatal morbidity.

Key message

The findings from this study do not support the use of either umbilical artery, middle cerebral artery, uterine arteries or cerebroplacental ratio as a standalone screening test for perinatal compromise in uncomplicated pregnancies at term, unless a specific indication, such as small for gestational age, is provided.

2 | MATERIAL AND METHODS

This prospective study was carried out in a dedicated research ultrasound clinic in a single tertiary referral center (University Hospital of Chieti, Italy) over a 1-year period from January to December 2017. Inclusion criteria were consecutive singleton pregnancies between 36^{+0} and 37^{+6} weeks of gestation. Exclusion criteria were multiple gestations, pregnancies affected by structural or chromosomal anomalies, maternal medical complications or drugs intake and abnormal Doppler waveform in the UA, defined as PI > 95^{th} or absent/end diastolic flow.[20] All women were pre-screened at 28-32 weeks of gestation to rule out signs of early fetal growth restriction.

The primary outcome was a composite adverse perinatal outcome including either:

- An adverse intrapartum outcome, defined as the occurrence of either instrumental delivery or emergency cesarean section for fetal distress or non-reassuring fetal status, defined as the presence of suspicious or pathological cardiotocography tracings according to the FIGO consensus guidelines on cardiotocography interpretation.[22]
- Abnormal acid-base status, defined as the presence of arterial cord pH <7.15 and a base excess of <11 mEq/L.[23]

The Doppler parameters explored were:

- UA pulsatility index (PI)
- MCA PI
- Uterine artery PI
- CPR, defined as MCA PI divided UA PI

Gestational age was defined according to the crown-rump length during the first trimester ultrasound scan. All the examinations were carried out in a dedicated ultrasound research clinic and clinicians in the delivery suite were blinded to the ultrasound findings. All women underwent induction of labor at $41^{+6/7}$ if spontaneous onset of labor did not occur.

Pulsed Doppler parameters were performed automatically from three or more consecutive waveforms using a Samsung HS40 (Samsung Healthcare, Italy) ultrasound machine equipped with a 3.5 MHz convex probe, during fetal quiescence, in the absence of fetal tachycardia, with the insonation angle kept as close to 0° as possible. MCA was examined at the point at which it passes the sphenoid wing, close to the circle of Willis, and the UA was examined at a free loop of the umbilical cord. To record the uterine artery Doppler, the transducer was placed over the iliac fossa and the course of the uterine arteries was followed from the lateral pelvic wall across external iliac artery using color Doppler. Pulsed Doppler was then applied 1 cm medial to the crossover point.

When three similar consecutive waveforms were obtained, the PI was measured, and the mean value of the left and right uterine artery PI calculated.[21]

Continuous variables were presented as medians with interquartile ranges, and categorical variables as numbers and percentages. The distribution assumptions were tested with Shapiro-Wilk test. The group comparison of the variables was performed using t-test, Mann Whitney U test or Chi square test where appropriate. We first examined potential differences in maternal, ultrasound and neonatal parameters in pregnancies complicated by adverse perinatal outcome compared with those not complicated. The potential independent predictors of the risk of the primary outcome of the study were then evaluated using binary logistic regression. All covariates were included a priori in the final model. The goodness-of-fit was checked using Hosmer-Lemeshow test, and the predictive accuracy assessed through C-statistics (area under the receiving operator curve).[24] Standard post-estimation tests were used to check the final model validity, performing multicollinearity and influential observation analyses (using standardized residuals, change in Pearson and deviance chi square). There were no missing values and therefore no missing imputation technique was adopted. All the analyses adjusted for parity, ethnicity, gestational age at ultrasound evaluation and birthweight.

Finally, we assessed the predictive accuracy of different Doppler parameters for the risk of adverse perinatal outcome receiver operating characteristic curve (ROC) analysis and reporting the area under the curve (AUC) for each Doppler parameter explored.[25,26]

According to the previously published literature, the incidence of composite adverse outcome among unselected, low-risk pregnancies has been reported to be 18%.[27] Based upon these data, and assuming: (1) a sensitivity and a specificity of CPR to detect composite outcome of 45 and 75%, respectively, and (2) an alpha-error of 0.05, a minimum of 540 women would be required to achieve a 80% statistical power to detect an increase in the values of sensitivity and specificity ≥10%. To be conservative, we enrolled 600 women.

The statistical significance was defined as a two-sided P <0.05, and all analyses were carried out using STAT DIRECT, version 13.1 (Stata Corp., College Station, Texas, USA) and SPSS version 24 (SPSS Inc., Chicago, IL, USA).

2.1 | Ethical approval

The study was approved by the local IRB (November 2016, Approval number: rich5j7v9). STARD guidelines for studies on diagnostic accuracy were followed.[21] Written informed consent was obtained from the women recruited on the study.

3 | RESULTS

In all, 600 consecutive singleton pregnancies from 36 weeks of gestation were included in the study. General characteristics of the included cohort are reported in Table 1. Mean maternal age was 33.1 ± 5.2 years, and mean maternal body mass index 27.6 ± 4.7. All included women were caucasian, and the incidence of smoking either before or during pregnancy and assisted reproductive technology pregnancies was 5.0 and 2.7%, respectively. Of the included

TABLE 1 General characteristics of the study population

Variables	All pregnancies (n = 600)
Antenatal variables	
Mean age in years (SD)	33.1 (5.2)
Mean body mass index (SD)	27.6 (4.7)
Median parity (IQR)	0.0 (0-1.0)
Nulliparity, %	57.5 (345)
Multiparity, %	9.7 (58)
Previous miscarriage, %	24.8 (149)
Caucasian ethnicity, %	100 (600)
Current smoking, %	5.0 (30)
Assisted reproductive technique, %	2.8 (17)
Prenatal ultrasound and Doppler variables	
Mean gestational age at ultrasound in weeks (SD)	37.1 (0.4)
Mean UA PI (SD)	0.85 (0.17)
Mean MCA PI (SD)	1.30 (0.28)
Mean CPR (SD)	1.60 (0.49)
Mean uterine artery PI (SD)	0.78 (0.20)
Median fetal weight centile (IQR)	55.6 (36.5-78.9)
Median abdomen circumference centile (IQR)	49.3 (27.6-71.9)
Intrapartum variables	
Vaginal delivery, %	64.7 (388)
Cesarean section, %	35.3 (212)
Neonatal variables	
Mean gestational age at birth in weeks (SD)	39.3 (1.1)
Male gender, %	53.0 (318)
Mean birthweight in grams (SD)	3342 (393)
Mean length at birth in cm (SD)	50.0 (1.8)
Mean head circumference in cm (SD)	34.5 (1.4)
Apgar at 1 min ≥7, %	96.5 (579)
Apgar at 5 min ≥7, %	99.7 (598)
Arterial mean pH (SD)	7.26 (0.11)
Arterial mean base excess (mEq/L) (SD)	–5.81 (3.10)
Mean glucose levels (mg/dL) (SD)	69.4 (16.5)
Median lactate concentration (mmol/L) (IQR)	3.26 (2.2-4.6)
Median birthweight centile (IQR)	53.5 (27.9-68.8)
Median neonatal length centile (IQR)	61.0 (38.2-85.1)
Median head circumference centile (IQR)	68.0 (28-8-88.1)

Abbreviations: CPR, cerebroplacental ratio; IQR, interquartile range; MCA, middle cerebral artery; PI, pulsatility index; UA, umbilical artery.

TABLE 2 Comparison between the different Doppler parameters in fetuses experiencing compared to those not experiencing composite perinatal morbidity, adverse intrapartum outcome and abnormal acid base status

	Composite adverse outcome (n = 63)	No composite adverse outcome (n = 537)	*P* value
Mean UA PI (SD)	0.84 (0.16)	0.86 (0.18)	0.399
Mean MCA PI (SD)	1.09 (0.19)	1.51 (0.36)	<0.001
Mean CPR (SD)	1.35 (0.39)	1.85 (0.58)	<0.001
Mean uterine artery PI (SD)	0.83 (0.16)	0.73 (0.23)	0.001
Median fetal weight centile (IQR)	52.61 (28.5)	58.62 (33.9)	0.712
Median AC centile (IQR)	45.4 (29.0)	53.2 (38.4)	0.040

Note: Student's *t* test was used for normally distributed continuous variables and Kruskal-Wallis test for non-normally distributed continuous variables.
Abbreviations: CPR, cerebroplacental ratio; IQR, interquartile range; MCA, middle cerebral artery; PI, pulsatility index; UA, umbilical artery.

population, 64.7% had a spontaneous vaginal delivery and 35.3% underwent CS. Mean gestational age at delivery was 39.3 ± 1.1 weeks. The corresponding figures for mean neonatal weight and length centiles were 53.5 and 61.0, respectively. No stillbirth occurred in the present cohort. Adverse intrapartum outcome and abnormal acid base-status occurred in 9.5% (95% confidence interval [CI] 7.3-12.1; 57/600) and 3.2% (95% CI 1.9-4.9; 19/600) of cases. Overall, composite adverse outcome complicated 10.5% (95% CI 8.1-13.2, 63/600) of pregnancies and 13 fetuses experienced both the adverse outcomes explored.

When exploring the differences in the different Doppler parameters, mean MCA PI (1.1 ± 0.2 vs 1.5 ± 0.4, *P* < 0.001) and CPR (1.4 ± 0.4 vs 1.9 ± 0.6, *P* < 0.001) were lower, whereas uterine artery PI (.8 ± 0.2 vs .7 ±0.2, *P* = 0.001) was higher in pregnancies experiencing than those not experiencing composite adverse outcomes (Table 2). Conversely, there was no difference in either UA PI (*P* = 0.399) or estimated fetal weight centile (*P* = 0.712) between the two groups, but AC centile was lower in fetuses experiencing composite adverse outcome (45.4 vs 53.2, *P* = 0.040) (Table 2).

At logistic regression analysis, MCA PI (odds ratio [OR] 0.1, 95% CI 0.01-.2, *P* = 0.001), uterine arteries PI (OR 1.4, 95% CI 1.2-1.6, *P* = 0.001), abdominal circumference centile (OR 1.12, 95% CI 1.1-1.4, *P* = 0.001) and gestational age at birth (OR 1.6, 95% CI 1.2-2.1, *P* = 0.004) were independently associated with composite adverse outcome (Table S1).

Finally, we explored the diagnostic performance of the different Doppler parameters in predicting adverse perinatal outcome. UA PI, MCA PI, CPR and uterine arteries had a low AUC of 0.51 (95% CI 0.44-0.50), 0.57 (95% CI 0.50-0.63), 0.55 (95% CI 0.49-0.61) and 0.57 (95% CI 0.51-0.63) in predicting composite adverse outcome (Table 3, Figure 1).

4 | DISCUSSION

The findings from this study show that mean MCA PI and CPR were lower, and uterine artery PI was higher in singleton pregnancies experiencing a composite adverse outcome at term. MCA and uterine artery PI were independently associated with perinatal outcome irrespective of fetal weight at logistic regression analysis. However, when translating these results into a prediction model, Doppler ultrasound showed a poor diagnostic accuracy for the detection of adverse outcome.

The prospective design, blinded ultrasound assessment and inclusion of consecutive pregnancies represent the main strengths of this study. Furthermore, the study was conducted in a region where third trimester ultrasound was routinely offered to all pregnant women. The relatively small sample size of the study represents the major limitation of the study, although the analysis was powered for the primary outcome. Furthermore, we could not assess the role of Doppler in detecting more relevant but rare outcomes such as fetal death.

Identification of pregnancies at higher risk of perinatal compromise close to or at term is challenging. UA alone is not able fully to discriminate fetuses at higher risk of perinatal compromise at term and is common even in pregnancies complicated by fetal growth restriction in the late third trimester. In pregnancies complicated by late fetal growth restriction, a low PI in the MCA has been shown to carry an additional risk of adverse outcome.[28-33]

More recently, CPR has been suggested to be a reliable predictor of adverse perinatal outcome irrespective of fetal weight, thus questioning its role as a screening test for perinatal compromise. Prior et al[17] reported that fetuses with CPR <0.6765 multiple of the medians (MoM) were significantly more likely to require cesarean delivery because of presumed fetal compromise and were also at increased risk of compromise at any time during labor compared with those with CPR ≥ 0.6765 MoM, and Khalil et al[10] showed that the

TABLE 3 Area under the curve analysis of different Doppler parameters in predicting composite adverse outcome in singleton pregnancies at term

	AUC
Mean UA PI (SD)	0.505 (0.44-0.50)
Mean MCA PI (SD)	0.566 (0.50-0.63)
Mean CPR (SD)	0.549 (0.49-0.61)
Mean uterine artery PI (SD)	0.570 (0.51-0.63)

Abbreviations: CPR, cerebroplacental ratio; MCA, middle cerebral artery; PI, pulsatility index; UA, umbilical artery.

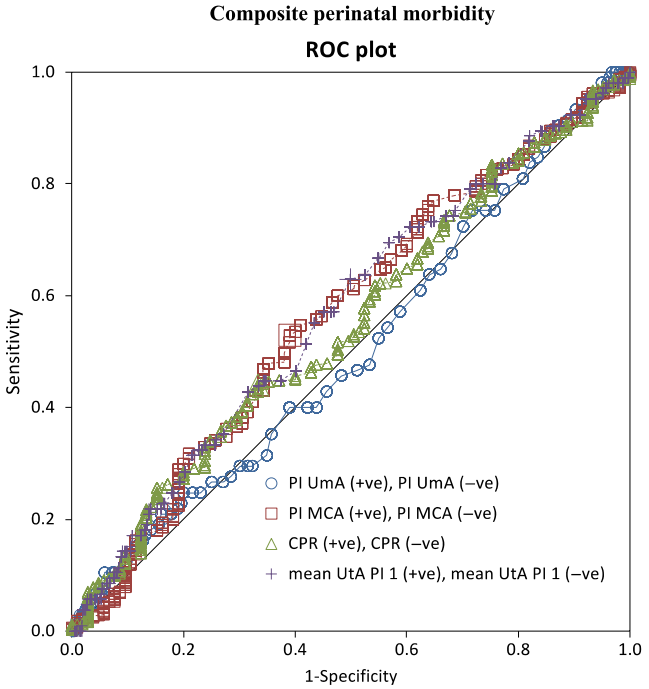

FIGURE 1 Receiver operating characteristics curve showing the diagnostic performance of maternal and fetal Dopplers in detecting composite adverse perinatal outcome. UA, umbilical artery; PI, pulsatility index; UmA, umbilical artery; MCA, middle cerebral artery; CPR, cerebroplacental ratio; UtA, uterine artery [Colour figure can be viewed at wileyonlinelibrary.com]

rates of operative delivery for presumed fetal compromise were significantly higher for appropriate-for-gestational age fetuses with low CPR MoM (22.3%) compared with small-for gestational-age fetuses with normal CPR MoM (17.3%).

Despite this, the actual role of CPR in predicting perinatal outcome remains controversial; the large heterogeneity in inclusion criteria, gestational age at assessment and outcomes observed among the previously published studies do not allow the extrapolation of robust evidence on the prognostic value of CPR, thus suggesting caution in its use in clinical practice.[34]

In the present study, despite being associated, MCA and CPR were not predictive of adverse outcome when applied to pregnancies from 36 weeks of gestation; thus their use as a screening test for adverse pregnancy outcome is not supported, although the study was not powered for the detection of rare outcomes, such as fetal death.

5 | CONCLUSION

A low MCA and CPR are associated with adverse perinatal outcome in singleton pregnancies at term. Despite this, their diagnostic accuracy is poor, and therefore do not support their use as screening tests for perinatal compromise at term, unless a specific indication, such as SGA, is present.

Further large studies are needed to confirm these findings and ascertain whether integrating different maternal, fetal and pregnancy characteristics can improve the diagnostic accuracy of Doppler in predicting perinatal compromise in singleton pregnancies at term.

CONFLICT OF INTEREST

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

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REFERENCES

1. Figueras F, Gardosi J. Intrauterine growth restriction: new concepts in antenatal surveillance, diagnosis, and management. *Am J Obstet Gynecol*. 2011;204:288300.
2. Simonazzi G, Curti A, Cattani L, Rizzo N, Pilu G. Outcome of severe placental insufficiency with abnormal umbilical artery Doppler prior to fetal viability. *BJOG*. 2013;120:754-757.
3. Lees C, Marlow N, Arabin B, et al. 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.
4. Oros D, Figueras F, Cruz-Martinez R, et al. Middle versus anterior cerebral artery Doppler for the prediction of perinatal outcome and neonatal neurobehavior in term small-for-gestational-age fetuses with normal umbilical artery Doppler. *Ultrasound Obstet Gynecol*. 2010;35:456-461.
5. Turan OM, Turan S, Gungor S, et al. Progression of Doppler abnormalities in intrauterine growth restriction. *Ultrasound Obstet Gynecol*. 2008;32:160-167.
6. Ferrazzi E, Bozzo M, Rigano S, et al. Temporal sequence of abnormal Doppler changes in the peripherals and central circulatory systems of the severely growth-restricted fetus. *Ultrasound Obstet Gynecol*. 2002;19:140-146.
7. Baschat AA, Galan HL, Bhide A, et al. Doppler and biophysical assessment in growth restricted fetuses: distribution of test results. *Ultrasound Obstet Gynecol*. 2006;27:41-47.
8. Morris RK, Say R, Robson SC, Kleijnen J, Khan KS. Systematic review and meta-analysis of middle cerebral artery Doppler to predict perinatal wellbeing. *Eur J Obstet Gynecol Reprod Biol*. 2012;165:141-155.
9. Stampalija T, Arabin B, Wolf H, et al. Is middle cerebral artery Doppler related to neonatal and 2-year infant outcome in early fetal growth restriction? *Am J Obstet Gynecol*. 2017;216(521):e1-e13.
10. Khalil A, Morales-Rosello J, Morlando M, et al. Is fetal cerebroplacental ratio an independent predictor of intrapartum fetal compromise and neonatal unit admission? *Am J Obstet Gynecol*. 2015;213(54):e1-e10.
11. Khalil A, Morales-Rosello J, Khan N, et al. Is cerebroplacental ratio a marker of impaired fetal growth velocity and adverse pregnancy outcome? *Am J Obstet Gynecol*. 2017;216(606):e1606-e1610.

12. 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;213:5-15.
13. Sherrell H, Clifton V, Kumar S. Predicting intrapartum fetal compromise at term using the cerebroplacental ratio and placental growth factor levels (PROMISE) study: randomised controlled trial protocol. *BMJ Open*. 2018;8:e022567.
14. Nassr AA, Abdelmagied AM, Shazly SA. Fetal cerebro-placental ratio and adverse perinatal outcome: systematic review and meta-analysis of the association and diagnostic performance. *J Perinat Med*. 2016;44:249-256.
15. Dunn L, Sherrell H, Kumar S. Review: systematic review of the utility of the fetal cerebroplacental ratio measured at term for the prediction of adverse perinatal outcome. *Placenta*. 2017;54: 68-75.
16. Conde-Agudelo A, Villar J, Kennedy SH, Papageorghiou AT. Predictive accuracy of cerebroplacental ratio for adverse perinatal and neurodevelopmental outcomes in suspected fetal growth restriction: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2018;52:430-441.
17. Prior T, Mullins E, Bennett P, Kumar S. Prediction of intrapartum fetal compromise using the cerebroumbelical ratio: a prospective observational study. *Am J Obstet Gynecol*. 2013;208(124): e1-e6.
18. Flood K, Unterscheider J, Daly S, 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(288):e1-e5.
19. Akolekar R, Syngelaki A, Gallo DM, Poon LC, Nicolaides KH. Umbilical and fetal middle cerebral artery Doppler at 35-37 weeks' gestation in the prediction of adverse perinatal outcome. *Ultrasound Obstet Gynecol*. 2015;46:82-92.
20. Bhide A, Acharya G, Bilardo CM, et al. ISUOG practice guidelines: use of Doppler ultrasonography in obstetrics. *Ultrasound Obstet Gynecol*. 2013;41:233-239.
21. Cohen JF, Korevaar DA, Altman DG, et al. STARD 2015 guidelines for reporting diagnostic accuracy studies: explanation and elaboration. *BMJ Open*. 2016;6:e012799.
22. Ayres-de-Campos D, Spong CY, Chandraharan E. FIGO Intrapartum Fetal Monitoring Expert Consensus Panel. *Int J Gynaecol Obstet*. 2015;131:13-24.
23. Nordstrom L, Arulkumaran S. Biochemical monitoring of intrapartum asphyxia. In: Arulkumaran S, Jenkins HML, eds. *Perinatal Asphyxia*. Hyderabad: Orient Longman; 2000:156.
24. Paul P, Pennell ML, Lemeshow S. Standardizing the power of the Hosmer-Lemeshow goodness of fit test in large data sets. *Stat Med*. 2013;32:67-80.
25. Rutter CM, Gatsonis CA. A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. *Stat Med*. 2001;20:2865-2884.
26. Glas AS, Lijmer JG, Prins MH, Bonsel GJ, Bossuyt PM. The diagnostic odds ratio: a single indicator of test performance. *J Clin Epidemiol*. 2003;56:1129-1135.
27. Bligh LN, Alsolai AA, Greer RM, Kumar S. Pre-labour screening for intrapartum fetal compromise in low risk pregnancies at term: cerebroplacental ratio and placental growth factor. *Ultrasound Obstet Gynecol*. 2018;52:750-756.
28. Baschat AA. Neurodevelopment following fetal growth restriction and its relationship with antepartum parameters of placental dysfunction. *Ultrasound Obstet Gynecol*. 2011;37:501-514.
29. Padilla N, Perapoch J, Carrascosa A, Acosta-Rojas R, Botet F, Gratacós E. Twelve-month neurodevelopmental outcome in preterm infants with and without intrauterine growth restriction. *Acta Paediatr*. 2010;99:1498-1503.
30. Murray E, Fernandes M, Fazel M, Kennedy SH, Villar J, Stein A. Differential effect of intrauterine growth restriction on childhood neurodevelopment: a systematic review. *BJOG*. 2015;122:1062-1072.
31. Hernandez-Andrade E, Figueroa-Diesel H, Jansson T, Rangel-Nava H, Gratacos E. Changes in regional fetal cerebral blood flow perfusion in relation to hemodynamic deterioration in severely growth-restricted fetuses. *Ultrasound Obstet Gynecol*. 2008;32:71-76.
32. Scherjon S, Briet J, Oosting H, Kok J. The discrepancy between maturation of visual-evoked potentials and cognitive outcome at five years in very preterm infants with and without hemodynamic signs of fetal brain-sparing. *Pediatrics*. 2000;105:385-391.
33. Garcia-Simon R, Figueras F, Savchev S, Fabre E, Gratacos E, Oros D. 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;46:713-717.
34. Kumar S, Figueras F, Ganzevoort W, Turner J, McCowan L. Using cerebroplacental ratio in non-SGA fetuses to predict adverse perinatal outcome: caution is required. *Ultrasound Obstet Gynecol*. 2018;52:427-429.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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