Does gestational age influence the predictive accuracy of the cerebroplacental ratio for intrapartum fetal compromise?

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BACKGROUND: The accuracy of the cerebroplacental ratio (CPR) in predicting cesarean section for intrapartum fetal compromise (CS-IFC) prior to the onset of labor remains controversial.

OBJECTIVES: To determine whether advancing gestational age (GA) in the final weeks of pregnancy enhances the predictive performance of CPR and other sonographic parameters for CS-IFC before labor.

STUDY DESIGN: This multicentre retrospective study analysed 590 singleton pregnancies across four tertiary centres in Spain, Italy, and the UK. All participants underwent Doppler ultrasound assessment between 35+0 and 41+0 weeks of gestation and delivered within 24 hours of examination. CS-IFC was defined by abnormal intrapartum fetal heart rate patterns or fetal scalp pH <7.20 necessitating emergency caesarean delivery. The predictive performance of CPR, middle cerebral artery (MCA) pulsatility index (PI), and umbilical artery (UA) PI—expressed as multiples of the median (MoM)—was evaluated using ROC curve analysis and logistic regression, alone and in combination with estimated fetal weight centile (EFWc), fetal sex, and type of labour onset (TLO), stratified by gestational age.

RESULTS: The highest overall predictive performance between 35 and 40 weeks of gestation was observed with the use of CPR MoM and MCA PI MoM (AUC 0.71, 95% confidence interval [95% CI], 0.64−0.79, *P*<.00001, AIC 343.6; AUC 0.70, 95% CI, 0.63−0.77, *P*<.00001, AIC 346.5, respectively). Predictive accuracy further improved with the inclusion of estimated fetal weight centile (EFWc) (AUC 0.73, CI 0.66−0.80, *P*<.00001, AIC 339.3; AUC 0.74, CI 0.68−0.80, *P*<.00001, AIC 336.4), and was enhanced even more when additional clinical variables, such as fetal sex and type of labor onset were incorporated (AUC 0.77, CI 0.71−0.83, *P*<.00001, AIC 327; AUC 0.78, CI 0.72−0.84, *P*<.00001, AIC 323.9).

Across all models, predictive accuracy improved with advancing GA (*P*<.00001), peaking at 39 to 40 weeks. This trend was evident for cerebral Doppler indices (CPR MoM and MCA PI MoM), but not for UA PI or EFWc. The improvement in performance remained significant even when only fetuses appropriate for gestational age were analyzed.

CONCLUSION: The predictive ability of cerebral Doppler for CS-IFC, in both high- and low-risk pregnancies, increases with advancing gestational age during the last weeks of gestation.

Key words: Cerebroplacental ratio, middle cerebral artery Doppler, fetal Doppler, prediction of labor outcome

Introduction

Cerebral Doppler assessment—particularly the evaluation of the middle cerebral artery (MCA) pulsatility index and its ratio with the umbilical artery, known as the cerebroplacental ratio (CPR)—has emerged as one of the most accurate tools for predicting cesarean section for intrapartum fetal compromise (CS-IFC) in the final weeks of pregnancy.[1−5] However, its clinical utility remains a matter of debate,[6,7] especially regarding its incorporation into routine fetal surveillance during late gestation.

To properly evaluate the predictive value of CPR, it is crucial to account for and control the factors that can affect measurement precision. Failure to do so may introduce methodological bias. Key

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The data that support the findings of this study are available from the corresponding author, JMR, upon reasonable request.

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Why was the study conducted?

We investigated whether the ability of the cerebroplacental ratio (CPR) and other Doppler ultrasound parameters to predict intrapartum fetal compromise —leading to cesarean delivery—changes with advancing gestational age in late-term pregnancies

What are the key findings?

CPR and middle cerebral artery pulsatility index (MCA PI) emerged as the most accurate Doppler predictors of cesarean delivery for intrapartum fetal compromise. Their accuracy improved further when combined with estimated fetal weight centile (EFWc), fetal sex, and the mode of labor onset.

The predictive performance of CPR and MCA PI increased steadily with advancing gestational age, reaching its peak at 39 to 40 weeks. This effect was not observed for umbilical artery PI or estimated fetal weight, and it remained significant when analyses were limited to fetuses appropriate for gestational age (AGA).

What does this study add to what is already known?

This study strengthens the evidence that cerebral Doppler indices—particularly CPR and MCA PI—are the most robust sonographic markers for predicting intrapartum fetal compromise. Importantly, it shows that their predictive value improves with advancing gestation, especially at 39 to 40 weeks. These findings underscore the critical role of timing in Doppler interpretation and support the integration of cerebral Doppler into third-trimester surveillance strategies, even in otherwise low-risk pregnancies.

factors that can compromise measurement accuracy include not only fetal body and breathing movements, but also, as recently described, high altitude,[8] elevated fetal heart rate, particularly rates above 155 beats per minute, or even slightly lower if aiming to minimize variability in the pulsatility index (PI) caused by fetal activity.[9] Therefore, CPR measurements should ideally be obtained in the absence of maternal and fetal motion, during periods of fetal quiescence, and when the fetal heart rate is at its lowest baseline.

In addition to technical considerations, several clinical variables may influence CPR performance. For example, a longer interval between Doppler assessment and labor onset is associated with decreased predictive accuracy.[10] Likewise, combining CPR with other clinical or sonographic variables, such as the estimated fetal weight centile (EFWc), may enhance its predictive value.[10,11] The outcome being assessed also plays a role: CPR is more accurate in predicting CS-IFC due to placental insufficiency but less so for events unrelated to placental dysfunction, such as umbilical cord accidents.[12]

In this study, we aimed to evaluate whether gestational age itself affects the predictive performance of CPR for CS-IFC in the final weeks of pregnancy, both independently and in combination with other sonographic and clinical parameters.

Material and methods

This retrospective observational study was conducted on a selected cohort of 590 singleton pregnancies, examined between 35+0 and 41+0 weeks of gestation, with delivery occurring within one day of examination, either following spontaneous or induced onset of labor. The ultrasound examinations involved estimating fetal weight using Hadlock's formula, along with Doppler assessment of the pulsatility indices (PI) for the umbilical artery (UA) and middle cerebral artery (MCA). Doppler evaluations of the UA and MCA were performed using color and pulsed Doppler techniques, as previously described.[13–14] In summary, the MCA Doppler was obtained by the sphenoid wing close to the Willis circle, the UA Doppler was obtained in a free loop of umbilical cord, and the cerebroplacental ratio (CPR) was calculated as the simple ratio of MCA PI to UA PI.[13,15] Values were the average of at least three measurements that were predominantly performed using General Electric Voluson (E8/E6/730) ultrasound machines equipped with 2 to 8 MHz convex probes, during fetal quiescence and in the absence of fetal tachycardia, ensuring the insonation angle was minimized for each vessel examined.

To adjust for the effects of gestational age (GA) on fetal measurements and to facilitate comparisons, estimated fetal weight (EFW) and birth weight (BW) were converted to centiles (EFWc and BWc), adjusting for fetal gender. For consistency, the same reference was used across the entire study population, irrespective of the country of origin.[16] Additionally, CPR, MCA PI, and UA PI values were expressed as multiples of the median (MoM) by dividing each value by the 50th centile (median) at each GA, as previously outlined. The median values for CPR, MCA PI, and UA PI were calculated using the following equations [14,15]:

1. CPR 50th centile=−3.814786276 +0.36363249*GA (weeks) −0.005646672*GA^2 (weeks)
2. MCA 50th centile=−3.266164164 +0.368135209*GA (weeks) −0.005251488*GA^2 (weeks)
3. UA 50th centile=2.2037 −0.057955*GA (weeks) +0.00053953*GA^2 (weeks)

The study population was characterized by accurate GA assessment, based on first-trimester crown-rump length, and excluded twins and fetuses with malformations or aneuploidies. Pregnancies delivered by scheduled cesarean section were excluded to focus on fetal outcomes directly related to labor progression. To minimize the impact of time between ultrasound and labor onset on the performance of the parameters, we filtered the data to include only pregnancies where delivery

occurred within one day of examination. Although this reduced the study cohort from 5194 to 590 pregnancies, it created a homogeneous group for precise evaluation of GA's effect on ultrasound parameter performance. Moreover, as all ultrasounds were performed prior to the onset of labor, premature rupture of membranes, or any other labor-related factors, the risk of biases related to labor initiation was minimized.

The study population was heterogeneous, typical of a tertiary care setting, and included both appropriate-for-gestational-age (AGA) fetuses assessed for routine clinical reasons and small-for-gestational-age (SGA) fetuses. The most common indications for examination included routine follow-up, as well as growth abnormalities, decreased fetal movements, late-onset hypertensive disorders of pregnancy and maternal conditions such as gestational diabetes, cholestasis. And diabetes.

In this context, we sought to determine whether GA's effect was specific to high-risk SGA pregnancies or if it could also be observed in low-risk AGA pregnancies. To address this question, we performed a supplementary analysis that included only AGA fetuses (N=327), comparing the performance of all studied parameters across different GAs.

Outcome data, including BW, BWc, mode of delivery, Apgar score, and umbilical cord arterial pH, were collected postdelivery. Labor onset occurred for obstetric reasons, and fetuses were managed according to their progression during labor.[17] CS-IFC was defined as the need for urgent cesarean section due to abnormal intrapartum fetal heart rate patterns[18] or fetal scalp pH <7.20[19]

Descriptive statistics were performed for maternal age, prepregnancy weight, height, body mass index (BMI), parity, number of gestations, GA at examination (in weeks), GA at delivery (in weeks), interval between ultrasound and delivery, EFW, EFWc, BW, BWc, UA PI MoM, MCA PI MoM, CPR MoM, fetal gender, type of labor onset (TLO) (induced or spontaneous), and mode of delivery (assisted or spontaneous vaginal delivery, cesarean section due to failure to progress, and CS-IFC). Continuous variables were reported as medians with interquartile ranges (IQR), while categorical variables were presented as absolute and relative frequencies.

The diagnostic performance of CPR MoM, MCA PI MoM, UA PI MoM, and EFWc for detecting CS-IFC—defined by the presence of abnormal intrapartum fetal heart rate patterns or fetal scalp pH <7.20, necessitating an urgent cesarean section—was evaluated across the entire study period (35−40 weeks) (N=590), as well as stratified by GA into three groups: ≤37 weeks (N=115), 38 weeks (N=111), and 39 to 40 weeks (N=364). Additionally, four multivariable predictive models were assessed to evaluate whether performance differences persisted in combined models:

Model 1: CPR MoM+EFWc
Model 2: MCA PI MoM+EFWc
Model 3: CPR MoM+EFWc+labor onset type+fetal sex
Model 4: MCA PI MoM+EFWc+labor onset type+fetal sex

We did not study models that included only the EFW centile, as we observed that their accuracy was consistently lower than that of the models that included cerebral Doppler. Accordingly, all models without CPR MoM or MCA PI MoM were discarded.

For the AGA fetuses (N=327), due to the relatively small sample size, the study population was divided into two groups: ≤40 weeks and 40 weeks. Despite the small sample size, we hypothesized that any observed differences would suggest that parameter performance varies even in the AGA population.

Comparisons of descriptive characteristics were performed using the Mann-Whitney U test for continuous variables and the Chi-square test for categorical variables. Receiver operating characteristic (ROC) curves were employed to assess the performance differences in both univariable and multivariable models, with performance quantified by the area under the curve (AUC), Akaike information criterion (AIC), and detection rate (DR, sensitivity) at fixed false-positive rates (FPR) of 10% and 5%. Both AUC and AIC were used to evaluate differences in model performance, with an AIC difference greater than 2 units within the same study period suggesting a better model. This difference in the AIC was used to select the best model when the 95% confidence interval (95% CI) of the AUC between two models overlapped. All statistical analyses were performed using StatPlus for Mac (version 7) and GraphPad Prism for Mac (version 5), with significance set at $P<.05$.

Results

The characteristics of the study population are outlined in Table 1. In summary, the study included 590 singleton pregnancies, of which 51.2% were male and 44.2% SGA. Most pregnancies had an induced onset of labor (61.8%), reflecting the high-risk nature of the population, with 65.9% achieving spontaneous vaginal delivery. The most common indications for induction were fetal growth abnormalities, post-term pregnancy, and premature rupture of membranes. A total of 0.3% of the neonates had an Apgar score <7 at 5 minutes, and 1.9% exhibited a neonatal umbilical cord pH <7.10. Additionally, 9.3% of fetuses presented abnormal intrapartum fetal heart rate patterns and scalp pH <7.20, necessitating emergency cesarean section (CS-IFC), and 44.2% of fetuses were small for gestational age (SGA).

Table 1 also compares pregnancy characteristics according to the studied outcome (CS-IFC). In the adverse outcome group, umbilical artery pulsatility index multiple of the median (UA PI MoM) was significantly higher ($P=.0002$), while gestational age (GA) at examination ($P<.0001$), GA at delivery ($P<.0001$), maternal height ($P=.0369$), estimated fetal weight (EFWc), corrected estimated fetal weight (EFWc), birth weight (BWc), corrected birth weight (BWc), middle cerebral artery pulsatility index multiple of the median (MCA PI MoM), and

TABLE 1
Description of the study population (N=590)

Parameter	1-All (N=590) Mean (SD); Median (IQR)	2-Normal (N=535) Mean (SD); Median (IQR)	3-CS-IFC (N=55) Mean (SD); Median (IQR)	2 vs 3[a] *P*-value
Maternal age in y	31.9 (5.5); 32 (29, 36)	31.9 (5.5); 32 (29, 36)	32.1 (5.6); 33 (29, 36)	.07602
Parity	0.59 (0.85); 0 (0,1)	0.60 (0.85); 0 (0,1)	0.50 (0.81), 0 (0,1)	.03594
Maternal prepregnancy weight (kgs)	61.8 (12.15); 60 (53, 68)	61.7 (12.1); 60 (53.7, 68)	61 (12.6); 59 (51, 70)	.09382
Maternal height (cm)	161.3 (6.5); 161 (157, 165)	161.5 (6.5); 161 (157,165)	158.9 (6.7); 160 (155,163)	.0369
Maternal Body Mass Index, Kg/m2	23.7 (4.3); 23 (20.6, 25.6)	23.6 (4.2); 23 (20.6, 25.5)	24.5 (5); 23.9 (20.2, 27.3)	.02880
Gestational age at scan (wks)	38.9 (1.2); 39.1 (38, 40)	39 (1.2); 39.3 (38.1, 40)	38.4 (1.1); 38.4 (37.6, 39.3)	<.0001
Gestational age at delivery (wks)	39.0 (1.2); 39.3 (38.1, 40)	39.1 (1.2); 40.1 (38.3, 40.1)	38.5 (1.1); 38.4 (37.7, 39.4)	<.00001
UA PI MoM	1.23 (0.34); 1.15 (0.99, 1.40)	1.2 (0.33); 1.14 (0.98,1.37)	1.41 (0.42); 1.35 (1.09, 1.67)	.00002
MCA PI MoM	0.94 (0.23); 0.92 (0.76, 1.09)	0.96 (0.23); 0.95 (0.79, 1.1)	0.81 (0.19); 0.75 (0.67, 0.92)	<.00001
CPR MoM.	0.90 (0.33); 0.88 (0.66, 1.11)	0.92 (0.32);0.90 (0.69, 1.2)	0.70 (0.32); 0.63 (0.47, 0.88)	<.00001
EFW (Hadlock) (grams)	2884 (585); 2781 (2425, 3311)	2918 (586.9); 2836 (2458, 3365)	2553 (451); 2491 (2263, 2753)	<.00001
EFW centile	28.8 (33.2); 9 (2, 56)	30.45 (33.62); 11 (2, 58)	12.8 (23.9); 2 (1, 8)	<.00001
Birth weight (grams)	2880 (556.3); 2873 (2451, 3258)	2918 (555); 2920 (2505, 3300)	2516 (424); 2460 (2250, 2740)	<.00001
Birth weight centile	27.4 (31.3); 13 (2, 46.7)	29.2 (31.69); 15 (3, 49)	10.71 (21.16); 3 (1, 11)	<.00001
	N (%)	N (%)	N (%)	
Nulliparity	263 (44.5)	234 (43.7)	29 (52.7)	.02040
Male sex	302 (51.2)	359 (67.1)	30 (55.5)	.00010
Type of labor onset				
Induction of labor	365 (61.8)	317 (59.2)	48 (83.3)	<.00001
Spontaneous onset of labor	225 (38.1)	218 (40.7)	7 (12.7)	<.00001
Apgar <7 at 5 mins	2 (0.3)[b]	1 (0.2)[d]	1 (1.8)[f]	.01820
Arterial pH <7.10	9 (1.9)[c]	6 (1.4)[e]	3 (6)[g]	.00138
Small-for-gestational-age	261 (44.2)	221 (41.3)	40 (72.7)	<.00001
Mode of birth				
Cesarean section (failure to progress)	57 (9.7)	57(10.6)	0 (0)	.00063
Cesarean section (abnormal CTG)	55 (9.3)	0 (0)	55 (100)	<.00001
Assisted vaginal delivery	89 (15.1)	89 (16.6)	0 (0)	<.00001
Spontaneous vaginal delivery	389 (65.9)	389 (72.7)	0 (0)	<.00001

Values of Apgar and pH were not taken in 100% of cases.

3rd trim, third trimester; CPR, cerebroplacental ratio; IFC, intrapartum fetal compromise; IQR, interquartile range; MCA PI, middle cerebral artery pulsatility index multiples of the median; SD, standard deviation; UA PI MoM, umbilical artery pulsatility index multiples of the median.

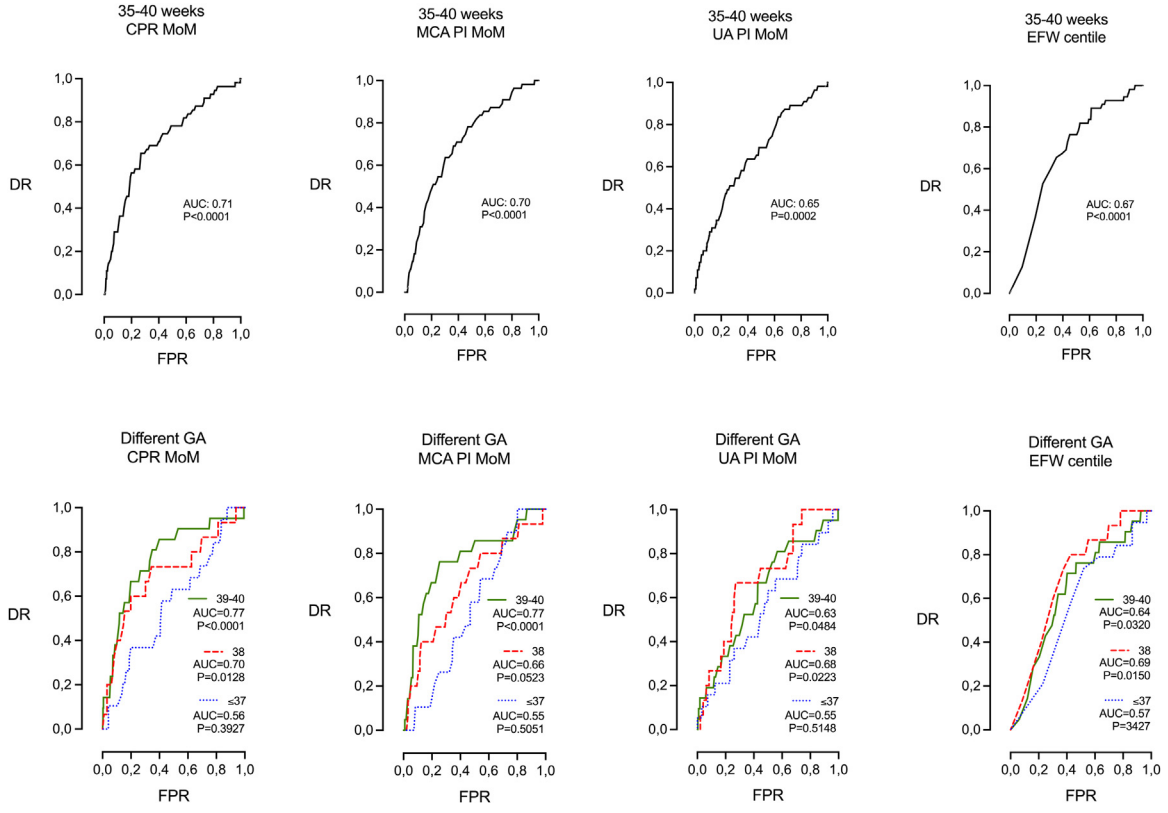
[a] Mann-Whitney U test; [b] In this case N=576; [c] In this case N=479; [d] In this case N=521.; [e] In this case N=429; [f] In this case N=55.; [g] In this case N=50

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cerebroplacental ratio (CPR MoM) (*P*<.0001) were significantly lower. Furthermore, there was a significantly higher proportion of SGA fetuses (*P*<.0001), labor inductions (*P*<.0001), and pH <7.10 (*P*=.0138). No significant differences were observed regarding maternal age, parity, prepregnancy weight, or body mass index (BMI).

Figure 1 and Table 2 illustrate the receiver operating characteristic (ROC) curves representing the overall accuracy of CPR MoM, MCA PI MoM, UA PI MoM, and EFWc for predicting CS-IFC during the same study period (35−40 weeks) (upper line) and at different gestational ages (≤37, 38, and 39−40 weeks) (lower line). The best overall prediction was achieved by CPR MoM (AUC 0.71, 95% CI, 0.64−0.79, *P*<.0001, AIC 343.6) and MCA PI MoM (AUC 0.70, 95% CI, 0.63−0.77, *P*<.0001, AIC 346.5). Moreover, for both CPR MoM and MCA PI MoM, a progressive trend in performance was observed with advancing gestational age, with the best prediction occurring at the highest gestational ages (AUC 0.77, 0.70, 0.56, and 0.77, 0.66, 0.55, respectively, for 39−40, 38, and ≤37 weeks). This trend was not observed with UA PI MoM and EFWc.

FIGURE 1
Receiver operating characteristic (ROC) curves representing the overall accuracy of CPR MoM, MCA PI MoM, UA PI MoM, and EFWc for predicting CS-IFC during the study period (35−40 weeks) (upper line) and at different gestational ages (≤37, 38, and 39−40 weeks) (lower line)



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Figure 2 and Table 3 present the ROC curves representing the overall accuracy of CS-IFC in model 1 (CPR MoM +EFW centile) and model 2 (MCA PI MoM+EFW centile) for predicting CS-IFC during the study period (35−40 weeks) (upper line) and at three different gestational ages (≤37, 38, and 39 −40 weeks) (lower line). The overall predictive accuracy was similar in both models, although slightly higher for the model incorporating MCA PI MoM (AUC 0.73, CI 0.66−0.80, and 0.74, CI 0.68−0.80, *P*<.0001). Additionally, both models showed a progressive increase in performance with advancing gestational age, with the best prediction achieved at the highest gestational age (AUC 0.76, 0.74, 0.56, and 0.78, 0.75, 0.56, respectively, for 39−40, 38, and ≤37 weeks).

Figure 3 and Table 4 display the ROC curves representing the overall accuracy of model 3 (CPR MoM+EFW centile +labor induction+fetal sex) and model 4 (MCA PI MoM+EFW centile+labor induction+fetal sex) for predicting CS-IFC during the study period (35−40 weeks) (upper line) and at three different gestational ages (≤37, 38, and 39 −40 weeks) (lower line). The overall prediction accuracy was very similar in both models, with a slightly higher accuracy for the model including MCA PI MoM (AUC 0.77, CI 0.71−0.83 and 0.78, CI 0.72−0.84, *P*<.0001). In both models, there was a progressive increase in performance with advancing gestational age, with the best prediction observed at the highest gestational age (AUC 0.80, 0.73, 0.74, and 0.82, 0.74, 0.73, respectively, for 39−40, 38, and ≤37 weeks).

Finally, to assess whether the gestational age effect was also present in the appropriate-for-gestational-age (AGA) population, Figure 4 and Table 5 show the accuracy of CPR MoM, MCA PI MoM, UA PI MoM, and EFWc for predicting CS-IFC at two different gestational ages 40 and ≤39 weeks). For CPR MoM and MCA PI MoM, an increase in performance with advancing gestational age was observed, with the best prediction achieved at the highest gestational age (AUC 0.81, 95% CI, 0.69 −0.93, *P*=.0091, 0.66, 95% CI, 0.50 −0.83, *P*=.0555, and 0.82 95% CI, 0.63 −1.00, *P*=.0615, 0.64, 95% CI, 0.46 −0.82, *P*=0.64, respectively, for 40 and ≤39 weeks). This effect was less pronounced for UA PI MoM and EFWc.

Discussion

Principal findings

In this prospective cohort study, cerebral Doppler parameters—specifically, the (CPR) multiple of the median (CPR MoM) and middle cerebral artery

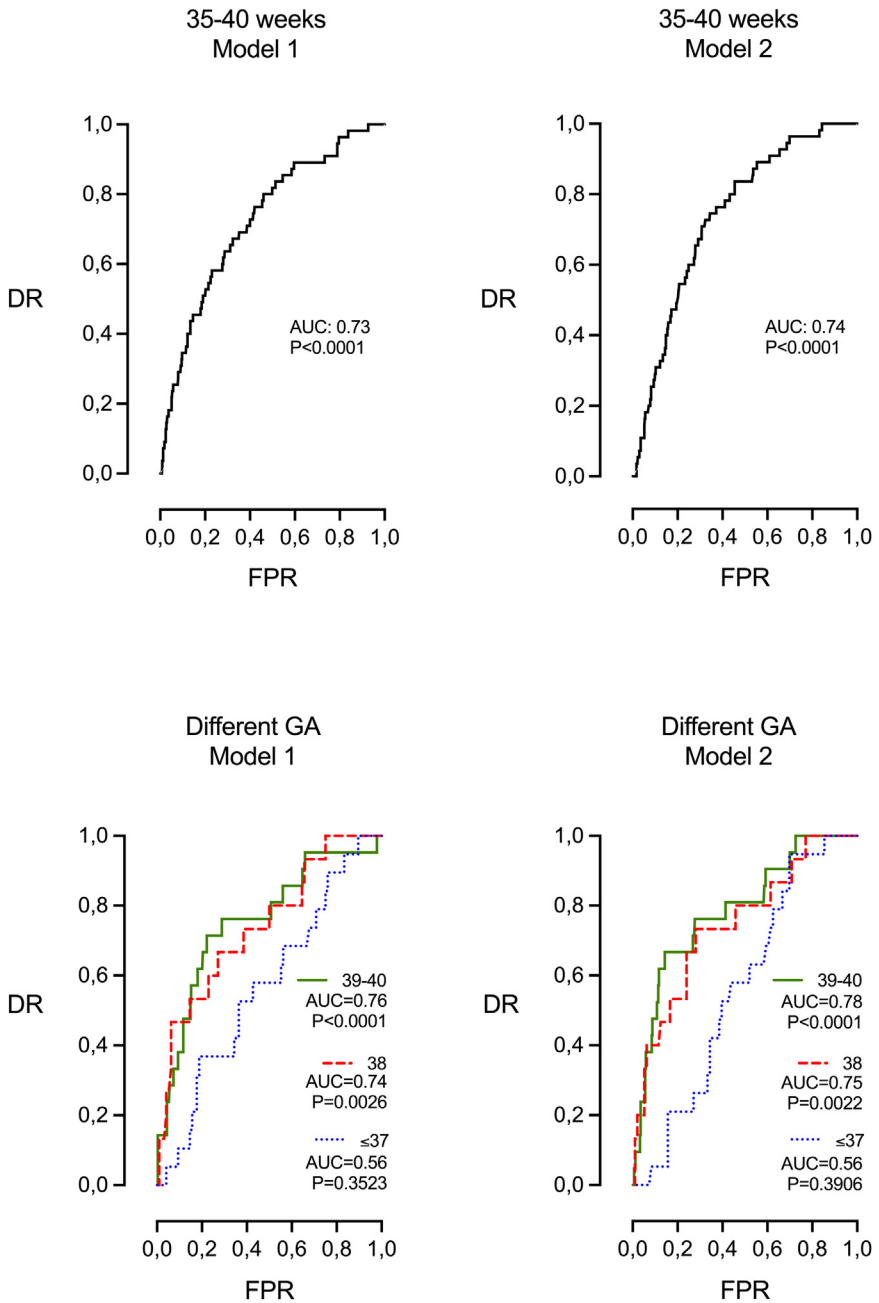
TABLE 2
Univariable logistic regression analysis for the prediction of CS-IFC 1 day prior to labor according to different GAs (35–40, ≤37, 38, and 39–40 weeks)

Parameter	Intercept	Estimate	SE	OR	OR-L95%CI	OR-U95%CI	*P*-value
35–40 wks (N=590)							
CPR MoM	−0.2061	−2.5859	0,5546	0,07533	0,02540	0,22338	<.00001
Model: AUC=0.71, 96% CI=0.64–0.79, *P*<0.0001, AIC=343.6, DR=29% for a FPR of 10% and 16% for a FPR of 5%							
MCA PI MoM	0.6796	−3.3717	0.7618	0.0343	0.0077	0.1528	<.00001
Model: AUC=0.70, 95% CI=0.63–0.77, *P*<.00001, AIC=346.5, DR=27% for a FPR of 10% and 13% for a FPR of 5%							
UA PI MoM	−4.1348	1.4270	0.3549	4.1664	2.0779	8.3541	<.00001
Model: AUC=0.65, 95% CI=0.57–0.073, *P*=.00002, AIC=354.6, DR=24% for a FPR of 10% and 16% for a FPR of 5%							
EFW centile	−1.8100	−0.0229	0.0065	0.9773	0.9648	0.9899	.00005
Model: AUC=0.67, 95% CI=0.61–0.74, *P*<.00001, AIC=352.3, DR=12% for a FPR of 10% and 12% for a FPR of 5%							
≤37 wks (N=115)							
CPR MoM	−0.9839	−0.8676	0.8214	0.4199	0.0839	2.1009	.02909
Model: AUC=0.56, 95% CI=0.42–0.70, *P*=3927, AIC=106.0, DR=10% for a FPR of 10% and 10% for a FPR of 5%							
MCA PI MoM	−1.1095	−1.1095	1.1845	0.3297	0.0323	3.3605	.03489
Model: AUC=0.55, 95% CI 0.42–67, *P*=.05051, AIC=106.3, DR=10% for a FPR of 10% and 0% for a FPR of 5%							
UA PI MoM	−2.3275	0.4961	0.5707	1.6423	0.5367	5.0261	.03846
Model: AUC=0.55, 95% CI=0.40–0.69, *P*=.05148, AIC=106.5, DR=16% for a FPR of 10% and 10% for a FPR of 5%							
EFW centile	−1.5399	−0.0073	0.0122	0.9927	0.9693	1.0166	.05463
Model: AUC=0.57, 95% CI=0.43–0.70, *P*=.03427, AIC=106.5.							
38 wks (N=111)							
CPR MoM	−0.1394	−2.2099	1.0363	0.1097	0.0144	0.8362	.00329
Model: AUC=0.70, 95% CI=0.54–0.86, *P*=.00128, AIC=86.5, DR=40% for a FPR of 10% and 20% for a FPR of 5%							
MCA PI MoM	0.3545	−2.4981	1.4773	0.0822	0.0045	1.4878	.00908
Model: AUC=0.66, 95% CI=0.50–0.81, *P*=.00523, AIC=88.8, DR=27% for a FPR of 10% and 20% for a FPR of 5%							
UA PI MoM	−3.9276	1.4925	0.6795	4.4483	1.1743	16.8502	.00281
Model: AUC=0.68, 95% CI=0.55–0.82, *P*=.00223, AIC=87.2, DR=27% for a FPR of 10% and 13% for a FPR of 5%							
EFW centile	−1.3305	−0,0576	0.0366	0.9440	0,8786	1.0142	.01155
Model: AUC 0.69, 95% CI 0.57–0.82, *P*=.00150, AIC 85.2							
≥39 wks (N=364)							
CPR MoM	0.2118	−3.6169	1.0094	0.0269	0.0037	0.1943	.00003
Model: AUC 0.77, 95% CI 0.66–0.88, *P*<.00001, AIC 148.9, DR 43% for a FPR of 10% and 14% for a FPR of 5%							
MCA PI MoM	1.7889	−5.2497	1,3835	0.0052	0.0003	0.0790	.00001
Model: AUC 0.77, 95% CI 0.65–0.88, *P*<.00001, AIC 145.9, DR 43% for a FPR of 10% and 24% for a FPR of 5%							
UA PI MoM	−4.6618	1.5459	0.6878	4.6924	1.2188	18.0659	.00246
Model: AUC 0.63, 95% CI 0.50–0.75, *P*=.00484, AIC 160.1, DR 19% for a FPR of 10% and 14% for a FPR of 5%							
EFW centile	−2.3002	−0.0168	0.0081	0.9833	0.9678	0.9992	.00393
Model: AUC 0.64, 95% CI 0.52–0.75, *P*=.00320, AIC 159.5, DR 14% for a FPR of 10% and 5% for a FPR of 5%							

AUC, area under the curve; CPR MoM, cerebroplacental ratio multiples of the median; DR, detection rate or sensitivity; EFW centiles, estimated fetal weight centiles; FPR, false positive rate; MCA MoM, middle cerebral artery multiples of the median Mean; OR–L95%CI, odds ratio lower 95% confidence interval; OR-U95%CI, odds ratio upper 95% confidence interval; SE, standard error; UA MoM, Umbilical artery Multiples of the median.

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FIGURE 2
Receiver operating characteristic (ROC) curves representing the overall accuracy of CS-IFC in model 1 (CPR MoM+EFW centile) and model 2 (MCA PI MoM+EFW centile) for predicting CS-IFC during the study period (35−40 weeks) (upper line) and at three different gestational ages (≤37, 38, and 39−40 weeks) (lower line)



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pulsatility index MoM (MCA PI MoM)—demonstrated the highest predictive accuracy for cesarean section due to intrapartum fetal compromise (CS-IFC) between 35 and 40 weeks of gestation. Predictive performance was further enhanced with the addition of estimated fetal weight centile (EFWc) and improved further with the inclusion of clinical variables such as fetal sex and type of labor onset (TLO). Importantly, we observed a gestational age (GA)-dependent increase in predictive accuracy for CPR MoM and MCA PI MoM, a trend not evident for umbilical artery PI MoM or EFWc. This gestational trend persisted in multivariable models and remained evident in a subanalysis restricted to appropriate-for-gestational-age (AGA) fetuses.

TABLE 3

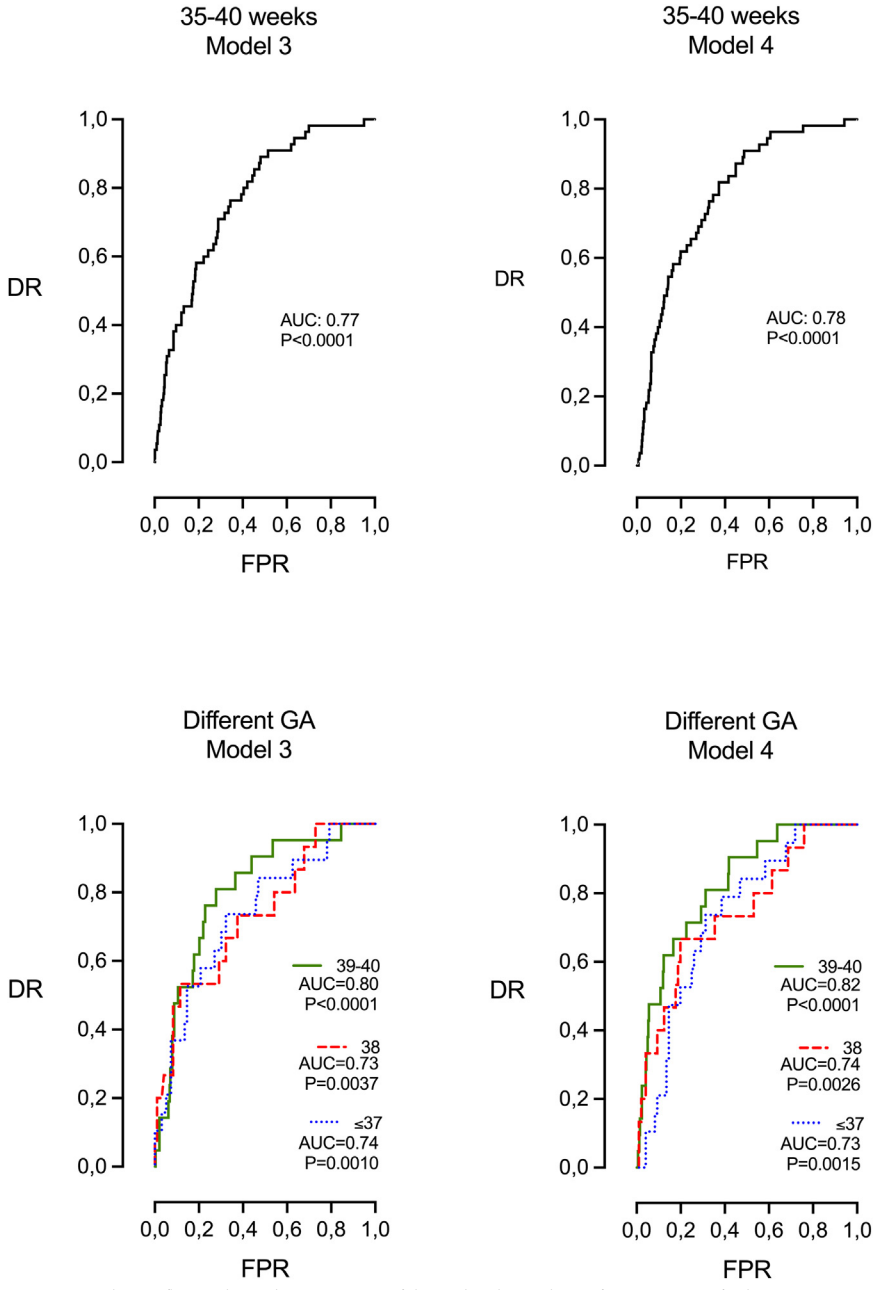
Multivariable logistic regression analysis of model 1 and 2 for the prediction of CS-IFC one day prior to labor, according to different GAs (35−40, ≤37, 38, and 39−40 weeks)

Parameter	Estimate	SE	OR	OR-L95%CI	OR-U95%CI	*P*-value
35−40 wks (N=590)						
Model 1 (CPR MoM+EFW centile)						
CPR MoM	−2.07682	0.5762	0.1253	0.0405	0.3877	.00003
EFW centile	−0.01547	0.0068	0.9846	0.9716	0.9978	.00225
Intercept	−0.30137					
Model: AUC=0.73, 95% CI=0.66−0.80, *P*<.00001, AIC=339.3, DR=34% for a FPR of 10% and 20% for a FPR of 5%						
Model 2 (MCA PI MoM+EFW centile)						
MCA PI MoM	−2.9827	0.7597	0.0507	0.0114	0.2246	<.00001
EFW centile	−0.0200	0.0066	0.9802	0.9675	0.9929	.00025
Intercept	0.7449					
Model: AUC=0.74, 95% CI=0.68−0.80, *P*<.00001, AIC=336.4, DR=29% for a FPR of 10% and 11% for a FPR of 5%						
≤37 wks (N=115)						
Model 1 (CPR MoM+EFW centile)						
CPR MoM	−0.7906	0.8515	0.4536	0.0855	2.4069	.03531
EFW centile	−0.0042	0.0127	0.9958	0.9713	1.0209	.07392
Intercept	−0.9949					
Model: AUC=0.56, 95% CI=0.69−0.50, *P*=.03523, AIC=108, DR=10% for a FPR of 10% and 5% for a FPR of 5%						
Model 2 (MCA PI MoM+EFW centile)						
MCA PI MoM	−1.0606	1.1887	0.3462	0.0337	3.5582	.03723
EFW centile	−0.0066	0.0123	0.9934	0.9697	1.0176	.05907
Intercept	−0.6595					
Model: AUC=0.56, 95% CI=0.44−0.68, *P*=.03906, AIC=108.1, DR=5% for a FPR of 10% and 0% for a FPR of 5%						
38 wks (N=111)						
Model 1 (CPR MoM+EFW centile)						
CPR MoM	−1.6094	1.0545	0.2000	0.0253	1,5801	.01269
EFW centile	−0.0491	0.0363	0.9520	0.8866	1,0223	.01764
Intercept	−0.1689					
Model: AUC=0.74, 95% CI=0.60−0.88, *P*=.00026, AIC=84.6, DR=47% for a FPR of 10% and 26% for a FPR of 5%						
Model 2 (MCA PI MoM+EFW centile)						
MCA PI MoM	−2.3548	1.4800	0.0949	0.0052	1.7265	.01116
EFW centile	−0.0590	0.0379	0.9427	0.8750	1.0155	.01200
Intercept	0.7578					
Model: AUC=0.75, 95% CI=0.61−0.88, *P*=.00022, AIC=84.5, DR=40% for a FPR of 10% and 20% for a FPR of 5%						
≥39 wks (N=364)						
Model 1 (CPR MoM+EFW centile)						
CPR MoM	−3.2972	1.0475	0.0369	0.0047	0.2882	.00016
EFW centile	−0.0084	0.0085	0.9916	0.9752	1.0082	.03192
Intercept	0.1935					
Model: AUC=0.76, 95% CI=0.64−0.87, *P*<.00001, AIC=149.9, DR=38% for a FPR of 10% and 24% for a FPR of 5%						
Model 2 (MCA PI MoM+EFW centile)						
MCA PI MoM	−5.0288	1.3988	0.0065	0.0004	0.1015	.00003
EFW centile	−0.0132	0.0083	0.9862	0.9702	1.0024	.00955
Intercept	2.0033					
Model: AUC=0.78, 95% CI=0.68−0.89, *P*<.00001, AIC=144.7, DR=48% for a FPR of 10% and 24% for a FPR of 5%						

AUC, area under the curve; CPR MoM, cerebroplacental ratio multiples of the median; DR, detection rate or sensitivity; EFW centiles, estimated fetal weight centiles; FPR, false positive rate; MCA MoM, middle cerebral artery multiples of the median Mean; OR−L95%CI, odds ratio lower 95% confidence interval; OR-U95%CI, odds ratio upper 95% confidence interval; SE, standard error; UA MoM, Umbilical artery Multiples of the median.

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FIGURE 3
Receiver operating characteristic (ROC) curves representing the overall accuracy of model 3 (CPR MoM+EFW centile+labor induction+fetal sex) and model 4 (MCA PI MoM+EFW centile+labor induction+fetal sex) for predicting CS-IFC during the study period (35–40 weeks) (upper line) and at three different gestational ages (≤37, 38, and 39–40 weeks) (lower line)



Morales-Roselló. Does gestational age influence the predictive accuracy of the cerebroplacental ratio for intrapartum fetal compromise? AJOG Glob Rep 2025.

Interpretation and comparison with previous studies

Our findings align with prior research identifying cerebral Doppler indices, particularly CPR, as the most accurate sonographic predictors of CS-IFC especially prior to labor.[20,21] The improvement in predictive accuracy with the inclusion of EFWc and clinical variables such as fetal sex and TLO is also supported by earlier reports.[11,22]

Although it is well recognized that cerebral Doppler measurements can be affected by technical factors such as maternal movements, fetal breathing movements, high altitude,[8] and fetal activity and tachycardia,[9] these influences are generally transient and manageable during acquisition. Less well understood are the subtler physiological factors influencing cerebral

TABLE 4
Multivariable logistic regression analysis of model 3 and 4 for the prediction of CS-IFC one day prior to labor, according to different GAs (35−40, ≤37, 38, and 39−40 weeks)

Parameter	Estimate	SE	OR	OR-L95%CI	OR-U95%CI	*P*-value
35−40 wks (N=590)						
Model 3 (CPR MoM+EFW centile+induction on labor+fetal sex)						
CPR MoM	−1.67757	0.58416	0.18683	0.05946	0.58707	.00408
EFW centile	−0.01133	0.00676	0.98873	0.97573	1.00192	.09364
Induction of labor	1.08025	0.43924	2.94540	1.24525	6.96681	.01392
Fetal sex	0.95876	0.32442	2.60847	1.38111	4.92653	.00312
Intercept	−2.10257					
Model: AUC=0.77, 95% CI=0.71−0.83, *P*<.00001, AIC=327, DR=40% for a FPR of 10% and 25% for a FPR of 5%						
Model 4 (MCA PI MoM+EFW centile+induction on labor+fetal sex)						
MCA PI MoM	−2.59304	0.78262	0.07479	0.01613	0.34677	.00092
EFW centile	−0.01520	0.00663	0.98492	0.97221	0.99779	.02182
Induction of labor	1.08176	0.43721	2.94986	1.25210	6.94970	.01335
Fetal sex	0.94772	0.32528	2.57981	1.36365	4.88062	.00357
Intercept	−1.09238					
Model: AUC=0.78, 95% CI=0.72−0.84, *P*<.00001, AIC=323.9, DR=40% for a FPR of 10% and 18% for a FPR of 5%						
≤37 wks (N=115)						
Model 3 (CPR MoM+EFW centile+induction on labor+fetal sex)						
CPR MoM	−0.77482	0.93449	0.46079	0.07380	2.87707	.40703
EFW centile	0.00391	0.01365	1.00392	0.97742	1.03113	.77446
Induction of labor	15.14815	699.933	3.791.029	0.00000	#N/A	.98273
Fetal sex	1.45610	0.57358	4.28921	1.39360	13.20128	.01113
Intercept	−16.93036					
Model: AUC=0.74, 95% CI=0.62−0.86, *P*=.00010, AIC=94, DR=37% for a FPR of 10% and 16% for a FPR of 5%						
Model 4 (MCA PI MoM+EFW centile+induction on labor+fetal sex)						
MCA PI MoM	−0.66484	1.29076	0.51435	0.04098	6.45617	.60650
EFW centile	0.00131	0.01309	1.00131	0.97595	1.02733	.92046
Induction of labor	15.24810	707.721	4.189.529	0.00000	#N/A	.98281
Fetal sex	1.38719	0.57414	4.00356	1.29935	12.33582	.01569
Intercept	−16.96574					
Model: AUC=0.73, 95% CI=0.62−0.84, *P*=.00015, AIC=94.4, DR=21% for a FPR of 10% and 10% for a FPR of 5%						
38 wks (N=111)						
Model 3 (CPR MoM+EFW centile+induction on labor+fetal sex)						
CPR MoM	−1.58502	1.09630	0.20494	0.02390	1.75720	.14823
EFW centile	−0.04984	0.03646	0.95138	0.88577	1.02185	.17161
Induction of labor	−0.14091	0.75054	0.86857	0.19950	3.78159	.85108
Fetal sex	0.10396	0.63944	1.10955	0.31684	3.88556	.87085
Intercept	−0.13517					
Model: AUC=0.73, 95% CI=0.59−0.87, *P*=.00037, AIC=88.9, DR=47% for a FPR of 10% and 27% for a FPR of 5%						

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TABLE 4
Multivariable logistic regression analysis of model 3 and 4 for the prediction of CS-IFC one day prior to labor, according to different GAs (35−40, ≤37, 38, and 39−40 weeks) *(continued)*

Parameter	Estimate	SE	OR	OR-L95%CI	OR-U95%CI	*P*-value
Model 4 (MCA PI MoM+EFW centile+induction on labor+fetal sex)						
MCA PI MoM	−2.27393	1.50568	0.10291	0.00538	1.96837	.13098
EFW centile	−0.05809	0.03790	0.94356	0.87602	1.01632	.12529
Induction of labor	0.02011	0.74040	1.02031	0.23905	4.35483	.97833
Fetal sex	0.18349	0.62748	1.20140	0.35121	4.10966	.76997
Intercept	0.55112					
Model: AUC=0.74, 95% CI=0.60−0.88, *P*=.00026, AIC=88.7, DR=40% for a FPR of 10% and 33% for a FPR of 5%						
≥39 wks (N=364)						
Model 1 (CPR MoM+EFW centile)						
CPR MoM	−2.65635	1.05435	0.07020	0.00889	0.55442	.01175
EFW centile	−0.00567	0.00837	0.99434	0.97816	1.01080	.49813
Induction of labor	1.06584	0.59768	2.90329	0.89978	9.36788	.07453
Fetal sex	0.98816	0.53868	2.68629	0.93459	7.72122	.06659
Intercept	−1.73894					
Model: AUC=0.80, 95% CI=0.71−0.89, *P*<.00001, AIC=146.2, DR=48% for a FPR of 10% and 14% for a FPR of 5%						
Model 2 (MCA PI MoM+EFW centile)						
MCA PI MoM	−4.46497	1.41156	0.01151	0.00072	0.18299	.00156
EFW centile	−0.01091	0.00840	0.98915	0.97299	1.00558	.19416
Induction of labor	0.98850	0.60129	2.68721	0.82694	8.73226	.10018
Fetal sex	1.05341	0.54289	2.86740	0.98939	8.31014	.05234
Intercept	0.10396					
Model: AUC=0.82, 95% CI=0.74−0.91, *P*<.00001, AIC=141, DR=48% for a FPR of 10% and 33% for a FPR of 5%						

AUC, area under the curve; CPR MoM, cerebroplacental ratio multiples of the median; DR, detection rate or sensitivity; EFW centiles, estimated fetal weight centiles; FPR, false positive rate; MCA MoM, middle cerebral artery Multiples of the median Mean; OR−L95%CI, odds ratio lower 95% confidence interval; OR-U95%CI, odds ratio upper 95% confidence interval; SE, standard error; UA MoM, Umbilical artery multiples of the median.

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hemodynamics. Notably, recent work has demonstrated that the interval to labor significantly modifies CPR's predictive accuracy for CS-IFC.[10] Building on this observation, we hypothesized that gestational age per se might affect cerebral Doppler performance, independent of the proximity to labor.

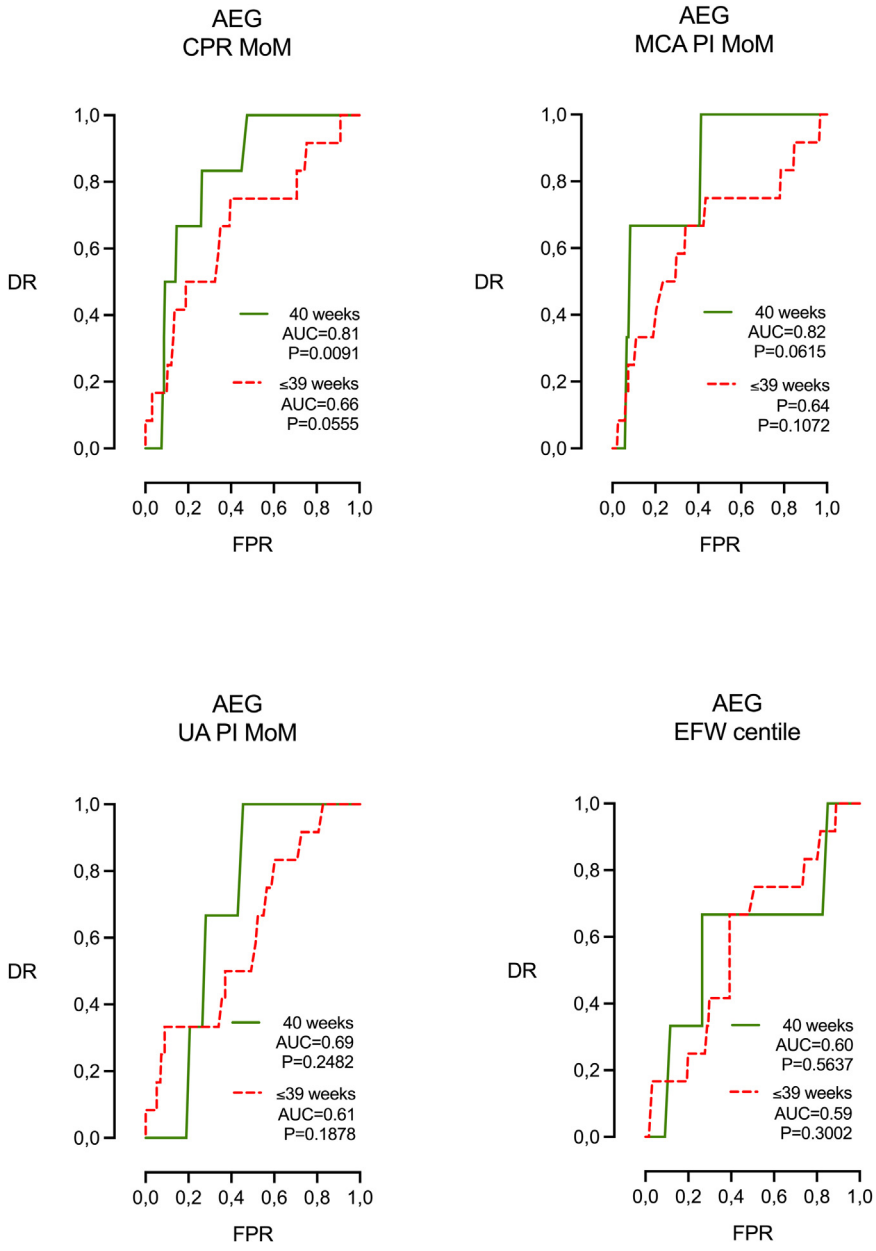
To isolate the effect of GA, we standardized the interval to labor to one day across the cohort, effectively controlling for this potential confounder. Even under this controlled condition, a progressive improvement in predictive performance was observed with advancing GA, particularly beyond 39 weeks. To our knowledge, only one prior study has examined CPR performance stratified by GA,[22] reporting a similar upward trend in area under the curve (AUC) values in both AGA and small-for-gestational-age (SGA) fetuses. However, that study included fetuses delivered up to seven days postassessment and did not account for proximity to labor. Thus, it remains uncertain whether the improved accuracy reflected increasing GA or shorter intervals to delivery. Our findings support the former, highlighting a GA-specific effect on cerebral Doppler predictive performance.

In agreement with earlier studies, labor induction and nulliparity were also identified as significant independent predictors of CS-IFC in our multivariable models.[11,22] Moreover, our AGA-restricted analysis reinforces prior evidence[23−25] that a low CPR is a meaningful predictor of intrapartum compromise even in low-risk populations and regardless of fetal growth, further supporting its potential utility in broader clinical settings.

Clinical and research implications

These results underscore a GA-dependent improvement in the predictive accuracy of CPR MoM and MCA PI MoM, which should be considered when interpreting third-trimester

FIGURE 4
Receiver operating characteristic (ROC) curves representing the accuracy of CPR MoM, MCA PI MoM, UA PI MoM, and EFWc, for predicting CS-IFC at two different gestational ages (≤39 and 40 weeks)



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Doppler findings. Incorporating cerebral Doppler assessment into late third-trimester ultrasound evaluations, particularly at 39 to 40 weeks, may enhance risk stratification prior to labor, informing decisions regarding induction or mode of delivery. Although there is still no consensus on how to manage patients with abnormal CPR and MCA PI, our findings support previous calls for incorporating cerebral Doppler into surveillance protocols at term, especially in the final weeks of gestation when the risk of fetal compromise may be highest and delivery decisions are imminent.

Strengths and limitations

Key strengths of this study include its prospective design, use of standardized Doppler acquisition protocols (including assessment during fetal quiescence and minimized insonation angles), and a homogenous population in which delivery occurred always within 24 hours of ultrasound assessment, thereby minimizing bias from prolonged intervals to labor. Additionally, the dedicated subanalysis of AGA fetuses contributes novel insight into cerebral Doppler utility among low-risk populations.

TABLE 5
Univariable logistic regression analysis for the prediction of CS-IFC 1 day prior to labor in AGA fetuses, according to different GAs (≤39 and 40 weeks)

Parameter	Intercept	Estimate	SE	OR	OR-L95%CI	OR-U95%CI	*P*-value
≤39 wks (N=203)							
CPR MoM	−1.0081	−1.9449	1.0794	0.1429	0.0172	1.1860	.00715
Model: AUC=0.66, 96% CI=0.50−0.83, *P*=.00555, AIC=91.4, DR=25% for a FPR of 10% and 17% for a FPR of 5%							
MCA PI MoM	−1.0766	−1.8477	1.3988	0.1576	0.0102	2.4448	.01865
Model: AUC=0.64, 95% CI=0.46−0.82, *P*=.01072, AIC=93.3, DR=25% for a FPR of 10% and 8% for a FPR of 5%							
UA PI MoM	−4.7415	1.6647	0.8972	5.2841	0.9104	30.6706	.00635
Model: AUC=0.61, 95% CI=0.46−0.77, *P*=.01878, AIC=92, DR=33% for a FPR of 10% and 8% for a FPR of 5%							
EFW centile	−2.3811	−0.0093	0.0091	0.9908	0.9733	1.0085	.03059
Model: AUC=0.59, 95% CI=0.43−0.75, *P*=.03002, AIC=94.1, DR=17% for a FPR of 10% and 17% for a FPR of 5%							
40 wks (N=124)							
CPR MoM	0.2305	−4.5908	2.5822	0.0101	0.0001	1. 6004	.00754
Model: AUC=0.81, 95% CI=0.69−0.93, *P*=.00091, AIC=51.4, DR=50% for a FPR of 10% and 0% for a FPR of 5%							
MCA PI MoM	2.0020	−6.3360	3.7405	0.0018	0.0000	2.7057	.00903
Model: AUC=0.82, 95% CI 0.63−1.00, *P*=.00615, AIC=28.8, DR=67% for a FPR of 10% and 0% for a FPR of 5%							
UA PI MoM	−5.8087	1.8377	2.4779	6.2823	0.0488	807.9887	.04583
Model: AUC=0.69, 95% CI=0.56−0.83, *P*=.02482, AIC=31.8, DR=0% for a FPR of 10% and 0% for a FPR of 5%							
EFW centile	−3.2163	−0.0106	0.0202	0.9894	0.9511	1.0293	.05985
Model: AUC=0.60, 95% CI=0.24−0.96, *P*=.05637, AIC=32.1, DR=33% for a FPR of 10% and 0% for a FPR of 5%							

AEG, appropriate-for-gestational-age; AUC, area under the curve; CPR MoM, cerebroplacental ratio multiples of the median; DR, detection rate or sensitivity; EFW centiles, estimated fetal weight centiles; FPR, false positive rate; MCA MoM, middle cerebral artery multiples of the median Mean; OR-L95%CI, odds ratio lower 95% confidence interval; OR-U95%CI, odds ratio upper 95% confidence interval; SE, standard error; UA MoM, Umbilical artery Multiples of the median.

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Nevertheless, certain limitations warrant consideration. The sample size at earlier gestational ages (≤37 weeks) was relatively small, potentially limiting statistical power within these subgroups. While our design minimized interval bias, residual selection bias may persist, particularly as clinical factors influencing the timing of induction could have affected group composition. The use of a single fetal growth reference across a potentially heterogeneous population may also introduce classification variability. Finally, as this cohort was high-risk and drawn from tertiary hospitals, the external validity to other settings might be limited.

Conclusion

Cerebral Doppler indices, particularly CPR MoM and MCA PI MoM, demonstrate a trend towards a higher predictive accuracy for CS-IFC at term, with performance improving as gestation advances. Their predictive value is further enhanced by the inclusion of fetal biometry and clinical characteristics. These findings support the incorporation of cerebral Doppler into late-pregnancy surveillance protocols, particularly between 39 and 40 weeks of gestation, when delivery decisions are being actively supported especially in the case of an abnormal evaluation. However, their interpretation earlier in the term period should be undertaken with caution, given their more limited predictive utility in that context.

Authors' contributions

José Morales-Roselló designed the study, performed part of the ultrasound examinations, did the statistical analysis, and wrote the manuscript. Silvia Buongiorno, Maia Brik, Manel Mendoza, Carolina Di Fabrizio, Scarinci Elisa, Silvia Salvi, performed part of the ultrasound examinations collected data and suggested valuable inputs to the text. Asma Khalil supervised the final manuscript and made notable contributions to the final text. ■

CRediT authorship contribution statement

José Morales-Roselló: Writing − original draft, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Asma Khalil:** Writing − review & editing, Supervision. **Silvia Buongiorno:** Supervision, Data curation. **Maia Brik:** Supervision, Data curation. **Manel Mendoza:** Writing − review & editing, Supervision, Data curation. **Carolina Di Fabrizio:** Data curation. **Elisa Scarinci:** Data curation. **Silvia Salvi:** Data curation. ■

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.xagr.2025.100585.

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