

ORIGINAL RESEARCH ARTICLE

Management of fetuses with apparent normal growth and abnormal cerebroplacental ratio: A risk-based approach near term

 José Morales-Roselló^{1,2} | Asma Khalil³ | Alicia Martínez-Varea^{1,2}

¹Obstetrics and Gynecology Service, Hospital Universitario y Politécnico La Fe, Valencia, Spain

²Department of Pediatrics, Obstetrics and Gynecology, Universidad de Valencia, Valencia, Spain

³Fetal Medicine Unit, St George's Hospital, St George's University of London, London, UK

Correspondence

José Morales-Roselló, Servicio de Obstetricia, Hospital Universitario y Politécnico La Fe, Avenida Fernando Abril Martorell 106, Valencia 46026, Spain.
Email: jose.morales@uv.es

Abstract

Introduction: Cerebroplacental ratio (CPR) has been shown to be an independent predictor of adverse perinatal outcome at term and a marker of failure to reach the growth potential (FRGP) regardless of fetal size, being abnormal in compromised fetuses with birthweight above the 10th centile. The main aim of this study was to propose a risk-based approach for the management of pregnancies with normal estimated fetal weight (EFW) and abnormal CPR near term.

Material and methods: This was a retrospective study of 943 pregnancies, that underwent an ultrasound evaluation of EFW and CPR at or beyond 34 weeks. CPR values were converted into multiples of the median (MoM) and EFW into centiles according to local references. Pregnancies were then divided into four groups: normal fetuses (defined as EFW \geq 10th centile and CPR \geq 0.6765 MoM), small for gestational age (EFW <10th centile and CPR \geq 0.6765 MoM), fetal growth restriction (EFW <10th centile and CPR <0.6765 MoM), and fetuses with apparent normal growth (EFW \geq 10th centile) and abnormal CPR (<0.6765 MoM), that present FRGP. Intrapartum fetal compromise (IFC) was defined as an abnormal intrapartum cardiotocogram or pH requiring cesarean delivery. Risk comparisons were performed among the four groups, based on the different frequencies of IFC. The risks of IFC were subsequently extrapolated into a gestational age scale, defining the optimal gestation to plan the birth for each of the four groups.

Results: Fetal growth restriction was the group with the highest frequency of IFC followed by FRGP, small for gestational age, and normal groups. The “a priori” risks of the fetal growth restriction and normal groups were used to determine the limits of two scales. One defining the IFC risk and the other defining the appropriate gestational age for delivery. Extrapolation of the risk between both scales placed the optimal gestational age for delivery at 39 weeks of gestation in the case of FRGP and at 40 weeks in the case of small for gestational age.

Abbreviations: CPR, cerebroplacental ratio; EFW, estimated fetal weight; FGR, fetal growth restriction; FRGP, failure to reach the growth potential; IFC, intrapartum fetal compromise; MoM, multiples of the median; SGA, small for gestational age.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial](https://creativecommons.org/licenses/by-nc/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2023 The Authors. *Acta Obstetrica et Gynecologica Scandinavica* published by John Wiley & Sons Ltd on behalf of Nordic Federation of Societies of Obstetrics and Gynecology (NFOG).

Conclusions: Fetuses near term may be evaluated according to the CPR and EFW defining four groups that present a progressive risk of IFC. Fetuses in pregnancies complicated by FRGP are likely to benefit from being delivered at 39 weeks of gestation.

KEYWORDS

adverse perinatal outcome, cerebroplacental ratio, ductus venosus Doppler, failure to reach growth potential, fetal Doppler, fetal growth restriction, middle cerebral artery Doppler, small baby, small for gestational age, umbilical artery doppler

1 | INTRODUCTION

Cerebroplacental ratio (CPR) has emerged as the best individual parameter to predict adverse perinatal outcome and intrapartum fetal compromise (IFC) near term.¹ Nevertheless, its predictive accuracy is moderate.² This can be improved by combination with estimated fetal weight (EFW) and clinical information like maternal body mass index and type of labor onset.³ CPR has been considered as a marker of failure to reach the growth potential (FRGP) at term regardless of EFW⁴ and may be abnormal in compromised fetuses growing over the 10th centile, a frequent feature of stillbirth after 32 weeks of gestation, which contrasts with the observed smallness of stillborn fetuses at earlier gestational weeks.⁵

Current consensus proposes that normal fetuses (normal EFW and normal Doppler) are better managed with induction at 41 weeks of gestation,⁶ that fetuses in pregnancies affected with fetal growth restriction (FGR) should be delivered at 37 weeks,⁷ and that small-for-gestational-age (SGA) fetuses (constitutionally small), are induced at 40 weeks.⁸ However, the controversy persists regarding how to manage fetuses with apparent normal growth (EFW >10th centile) and abnormal CPR, that present with FRGP. From a ponderal perspective, these fetuses remain in an apparent zone of normality, over the 10th centile. However, their risk of acidemia and IFC is notably increased.⁹

The aim of this study was to evaluate the risk of IFC in pregnancies complicated by FRGP and propose a risk-based approach to guide gestation at delivery near term.

2 | MATERIAL AND METHODS

This was a retrospective observational study of 943 women with singleton pregnancies who received antenatal care and gave birth at La Fe hospital between 34 and 41 weeks of gestation, and underwent fetal biometry and Doppler evaluation of the umbilical and middle cerebral artery pulsatility indices (PI). The umbilical and middle cerebral artery waveforms were recorded using color and pulse Doppler according to earlier descriptions¹⁰⁻¹² and the CPR was calculated as the ratio between the middle cerebral artery PI and the umbilical artery PI.¹³ Pregnancies were followed up until the onset of spontaneous labor or until induction of labor was indicated. Gestational age (GA) was determined according to the crown-rump length in the first trimester.

Key message

Extrapolation of intrapartum fetal compromise risk suggests that the optimal gestation for delivery of fetuses with normal estimated fetal weight but abnormal cerebroplacental ratio fetuses might be around 39 weeks.

Pregnancies involving elective cesarean before labor, multiple pregnancies, or those complicated by fetal abnormalities were excluded, and only one (the last) examination per fetus was included in the analysis. EFW and birthweight values were converted into centiles,¹⁴ and CPR values were converted into multiples of the median (MoM) dividing each value by the 50th centile value for each GA as previously described.^{10,11} CPR medians (50th centile) were calculated using this equation to adjust for GA:

$$\text{CPR 50th centile} = -3.814786276 + 0.36363249 \cdot \text{GA} - 0.005646672 \cdot \text{GA}^2.$$

Doppler assessments were performed by the first author, an expert in obstetric ultrasound certified by the Spanish Society of Obstetrics and Gynecology. Examinations were performed using General Electric Voluson® (E8/E6/730) ultrasound machines with 2- to 8-MHz convex probes, during fetal quiescence, in the absence of fetal tachycardia, and keeping the insonation angle with the examined vessels as small as possible.

Demographic and pregnancy characteristics including maternal age, parity, and pre-pregnancy weight and height were collected at the time of the ultrasound assessment. Pregnancy outcomes including birthweight, mode of birth, Apgar scores, cord arterial pH, and admission to the neonatal special care or intensive care units were collected after birth to evaluate the pregnancy outcome.

Concerning the onset of labor, the attending physician was not blinded to the ultrasound findings, and therefore this information was considered to indicate induction or wait for spontaneous onset of labor. In both cases, the attending physician indicated cesarean section exclusively according to the presence of failure to progress or the existence of IFC. This was defined as abnormal intrapartum cardiotocograph (according to the FIGO intrapartum fetal monitoring guidelines),¹⁵ or intrapartum fetal scalp pH <7.20 requiring cesarean delivery. Cases with abnormal intrapartum fetal heart rate at the end of the second stage of labor resulting in vaginal instrumental

delivery were considered of less relevance and were not included. Pregnancies were then divided into four groups: normal fetuses (defined as EFW \geq 10th centile and CPR \geq 0.6765 MoM), SGA (EFW $<$ 10th centile and CPR \geq 0.6765 MoM), FGR (EFW $<$ 10th centile and CPR $<$ 0.6765 MoM), and fetuses with apparent normal growth (EFW \geq 10th centile) and abnormal CPR ($<$ 0.6765 MoM), that represent FRGP.

2.1 | Risk calculation to determine the optimal gestation at birth

Once the groups were established, the frequency of IFC for each group was determined. The IFC risk was then extrapolated using an inverted IFC risk scale (higher values on the left) to determine the optimal GA for delivery. In brief, based on the current consensus,⁶⁻⁸ the limits of the extrapolation scale were established using the highest and lowest risk groups (FGR and normal groups). The risk of IFC in the FGR group, representing the lower limit of the IFC risk scale, was extrapolated at 37 weeks, becoming now the lower limit of the GA scale, while the risk of IFC in normal fetuses, representing the upper limit of the IFC risk scale, was extrapolated at 41 weeks (becoming now the upper limit of the GA scale). Subsequently, by using both scales in parallel, we could determine the optimal gestation at birth in the remaining two groups by simply drawing a vertical line. This will be further explained in the results section.

2.2 | Statistical analyses

Descriptive statistics were performed evaluating maternal age, parity, GA at ultrasound examination in weeks, GA at delivery in weeks, the interval between ultrasound and birth, EFW, EFW centile, birthweight, birthweight centile, CPR MoM, fetal sex, the onset of labor (induction of labor and spontaneous onset of labor), mode of birth (cesarean section for abnormal cardiotocogram, cesarean section for failure to progress, assisted delivery, and unassisted vaginal delivery), Apgar score at 5 minutes, neonatal cord arterial pH, and special or intensive care neonatal admission. Continuous variables were presented as means and standard deviations, whereas categorical variables were presented as absolute numbers and relative frequencies. Significance was evaluated by means of the chi-squared test in the case of simple comparisons, and the chi-squared test for trends (Cochran-Armitage test) and Kruskal-Wallis test in the case of multiple comparisons. Statistical analysis and graphs were produced using Graph Pad Prism®, Mac version 9.0.1, and Stat Plus® Mac Pro version 8.0.1.s. A p -value $<$ 0.05 was considered statistically significant.

2.3 | Ethics statement

Institutional ethics committee approval was obtained for the study (Reference 2014/0063) on April 8, 2014.

3 | RESULTS

Table 1 describes the characteristics of the study population. The mean maternal age was 32.5 years and mean body mass index was 23.5 kg/m². Nearly half of the pregnant women underwent induction of labor (51%), and most had a spontaneous or assisted vaginal birth (81.4%). The mean GA at the time of the last ultrasound examination and at birth were 39.1 and 40 weeks, respectively; 37 (3.9%) neonates were admitted to the neonatal unit.

Figure 1(A) shows the classification of cases into four groups (normal, SGA, FGR, and FRGP) according to the CPR MoM and EFW centile values, whereas **Figure 1(B)** shows the distribution of IFC cases in the study population. Among the total study group there were 64 (6.8%) cases of IFC. Of them, 21 (2.2%) had abnormal EFW and 19 (2%) had abnormal CPR values.

Figure 2 shows the frequency of the four groups in the overall (**Figure 2A**) and IFC (**Figure 2B**) populations. The proportion of FRGP and FGR in pregnancies complicated by IFC was double and triple that in the overall study population (12.5% vs. 6.8% and 17.2% vs. 5.8%), the frequency of normal fetuses diminished in one-third (54.7 vs. 74.3), and the proportion of SGA fetuses was similar in both populations (13.4% vs. 15.6%).

Figure 3(A) and **Table 1** show the frequency of IFC in each of the study groups. FGR, FRGP, SGA, and normal: 20%, 12.5%, 8.1%, and 5%, respectively, representing an increasing risk of IFC ($p <$ 0.001) when the groups were considered in this order. The differences between the normal group and each of the other groups were statistically significant ($p <$ 0.01).

To support our division of cases in four simple study groups according to EFW centile and CPR MoM, with the inclusion of fetuses with EFW below the third centile in the SGA group, we evaluated the risk of IFC in the subgroup of fetuses with normal CPR but EFW below the third centile, and compared it with the overall risk of IFC in SGA fetuses. The proportion was not significantly different: 5.9% (3/51) vs. 8.1% (10/123), ($p =$ NS). This supported the idea that from the risk point of view, all these fetuses belonged to the same category.

Figure 3(B) and **Table 1** show the decreasing acidosis shown by the neonatal arterial pH when the same order of groups is followed (FGR, FRGP, SGA, and normal) ($p <$ 0.01).

Figure 4 needs careful understanding as it supports the rationale of this work. This figure establishes a visual parallelism between the risk of IFC and the optimal GA for pregnancy termination. In red, we observe the inverted "risk scale" of IFC (lower values on the right, higher values on the left), which is depicted in parallel with the "GA scale" in blue, showing the appropriate GA to end the pregnancy. To establish parallelisms between both scales, we first needed to determine at least two reference points where both scales could be anchored. These reference points between both scales (or anchorage points), were obtained using the current consensus regarding termination of pregnancy in fetuses affected with FGR and in fetuses with normal growth.

According to earlier references to avoid further complications, fetuses in pregnancies with FGR should be delivered around

TABLE 1 Descriptive statistics of the four groups studied: normal, failure to reach growth potential (FRGP), small for gestational age (SGA) and fetal growth potential (FGR).

	All (n = 943)	Normal (n = 701)	SGA (n = 123)	FRGP (n = 64)	FGR (n = 55)	p value*
Maternal age (years), mean ± SD	32.5 ± 5.2	32.6 ± 5.2	31.9 ± 5.6	34 ± 4.2	32 ± 4.9	NS
Parity, mean ± SD	0.62 ± 0.82	0.65 ± 0.83	0.6 ± 0.7	0.5 ± 1	0.7 ± 0.7	NS
Maternal pre-pregnancy weight (kg), mean ± SD	62.5 ± 11.8	63 ± 12.1	60 ± 11.2	61 ± 9.5	58 ± 9.9	<0.001
Maternal height (cm), mean ± SD	163 ± 6.2	163 ± 6.1	161 ± 5.6	162 ± 7.6	161 ± 6.2	<0.001
Maternal body mass index (kg/m ²), mean ± SD	23.5 ± 4.2	24 ± 4.3	23 ± 4.1	23.3 ± 3.7	22.4 ± 4	NS
Gestation at ultrasound (weeks), mean ± SD	39.1 ± 1.1	39.3 ± 0.94	38.5 ± 1.3	39.2 ± 0.94	37.8 ± 1.6	<0.0001
EFW hadlock-4 (g), mean ± SD	3166 ± 517	3360 ± 369	2449 ± 318	3159 ± 322	2308 ± 371	<0.0001
EFW hadlock-4 centile, mean ± SD	45.6 ± 32	56.8 ± 27.3	3.8 ± 2.9	39.8 ± 25.3	3.1 ± 3	<0.0001
MCA PI MoM, mean ± SD	0.97 ± 0.23	1.02 ± 0.21	0.99 ± 0.22	0.70 ± 0.14	0.71 ± 0.15	<0.0001
UA PI MoM, mean ± SD	1.09 ± 0.24	1.04 ± 0.19	1.11 ± 0.20	1.36 ± 0.29	1.47 ± 0.29	<0.0001
CPR MoM, mean ± SD	1 ± 0.30	1.08 ± 0.26	1 ± 0.25	0.57 ± 0.09	0.54 ± 0.1	<0.0001
Gestation at birth (weeks), mean ± SD	40 ± 1.1	40.3 ± 0.84	39.2 ± 1.3	39.95 ± 0.97	38.4 ± 1.4	<0.0001
Interval ultrasound-labor (days), mean ± SD	6.1 ± 3.7	6.5 ± 3.6	5 ± 3.8	4.9 ± 3.4	4.3 ± 3.8	<0.0001
Birth weight (g), mean ± SD	3242 ± 500	3414 ± 385	2660 ± 370	3181 ± 342	2419 ± 381	<0.0001
BW centile ^a , mean ± SD	40 ± 30.9	48.8 ± 29	9.4 ± 15	34 ± 25	4 ± 5.1	<0.0001
Apgar at 5 min, mean ± SD	9.8 ± 0.54	9.9 ± 0.5	9.9 ± 0.53	9.8 ± 0.4	9.7 ± 1	NS
Arterial cord pH, mean ± SD	7.26 ± 0.07	7.3 ± 0.07	7.27 ± 0.07	7.24 ± 0.08	7.24 ± 0.08	<0.01
Smoking, n (%)	123 (13)	77 (11)	26 (21.1)	9 (14)	11 (20)	<0.05
Gender male, n (%)	471 (50)	337 (48.1)	67 (54.5)	33 (51.6)	34 (62)	<0.05
Nulliparous, n (%)	504 (53.4)	356 (50.8)	67 (54.5)	40 (62.5)	41 (74.5)	<0.001
Apgar 5 min <7, n (%)	7 (0.74)	5 (0.7)	1 (0.8)	0 (0)	1 (1.8)	NS
Arterial cord pH <7.10, n (%)	18 (1.9)	13 (1.8)	2 (1.6)	1 (1.6)	2 (3.6)	NS
Onset of labor, n (%)						
Spontaneous onset of labor	460 (48.8)	392 (55.9)	36 (29.3)	27 (42.2)	5 (9)	<0.0001
Induction of labor	483 (51.2)	309 (44.1)	87 (70.7)	37 (57.8)	50 (91)	<0.0001
Mode of birth, n (%)						
Spontaneous vaginal birth	547 (58)	430 (61.3)	64 (52)	29 (45)	24 (43.6)	<0.001
Assisted vaginal birth	221 (23.4)	153 (21.8)	34 (27.6)	20 (31.2)	14 (25.4)	NS
Cesarean section abnormal CTG (IFC)	64 (6.8)	35 (5)	10 (8.1)	8 (12.5)	11 (20)	<0.0001
Cesarean section failure to progress	111 (11.8)	83 (11.8)	15 (12.2)	7 (10.9)	6 (10.9)	NS
Neonatal special or intensive care unit	37 (3.9)	11 (1.6)	7 (5.7)	1 (1.6)	18 (32.7)	<0.0001

Abbreviations: BW, birthweight; CPR, cerebroplacental ratio; CTG, cardiotocography; EFW, estimated fetal weight; FGR, fetal growth restriction; GA, gestational age; IFC, intrapartum fetal compromise; MoM, multiples of the median; SD, standard deviation.

^aCentiles according to local population references (Hospital Clínic de Barcelona, Spain population references).

*p value: *Kruskal-Wallis test in case of continuous data and chi-squared test for trends in case of categorical data.

37 weeks (at the onset of term), whereas in normal pregnancies they should be delivered at 41 weeks.⁶⁻⁸ Considering the IFC risk earlier calculated and the above-mentioned information, the two points of anchorage between both scales could be easily observed. The first would be between the IFC risk of FGR (20%) and 37 weeks, while the second would be between the IFC risk of normal fetuses (5%) and 41 weeks of gestation.

Considering that both scales were drawn in parallel, these two anchorage points acting as visual references were used to extrapolate

values of the risk scale into the GA at birth scale, simply by "drawing a vertical line starting at the observed IFC risk". For example, in SGA fetuses the observed IFC risk was 8.1%. As Figure 4 shows, the vertical line passing over 8.1 (SGA fetuses IFC risk) would fall over week 40. Accordingly, the appropriate GA for birth in SGA fetuses would be around 40 weeks, as earlier proposed by other authors.⁸ In FRGP fetuses (IFR risk 12.5%) the vertical line passing over 12.5 would fall over week 39. Accordingly, the appropriate GA for delivery in FRGP fetuses would be around 40 weeks.

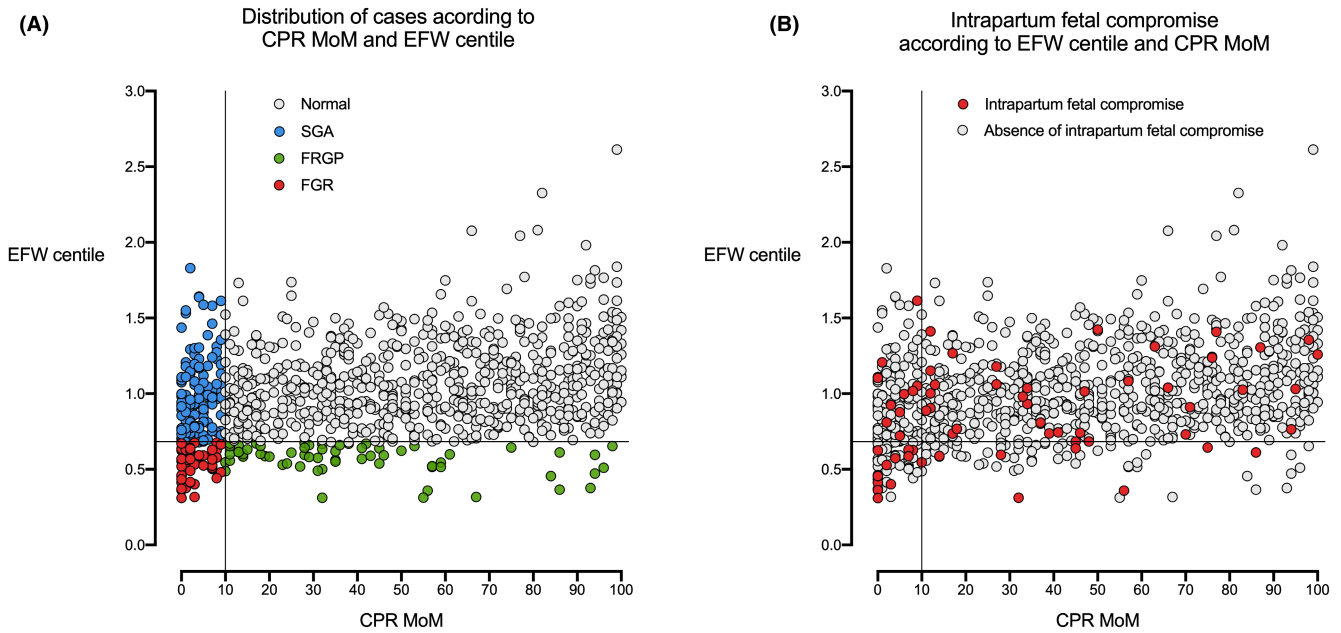


FIGURE 1 (A) Classification of the study population into four groups: normal, failure to reach growth potential (FRGP), small for gestational age (SGA), and fetal growth restriction (FGR) according to the cerebroplacental ratio multiples of the median (CPR MoM) and estimated fetal weight (EFW) centile value. (B) Distribution of intrapartum fetal compromise (IFC) cases in the study population.

FIGURE 2 (A) Classification of the study population ($n = 943$) into four groups. (B) Classification of the pregnancies with intrapartum fetal compromise ($N = 64$) (IFC) into four groups. FGR, fetal growth restriction; FRGP, failure to reach the growth potential; SGA, small for gestational age.

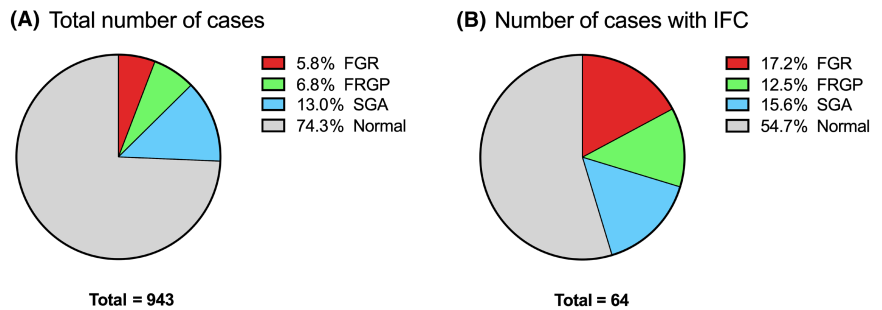
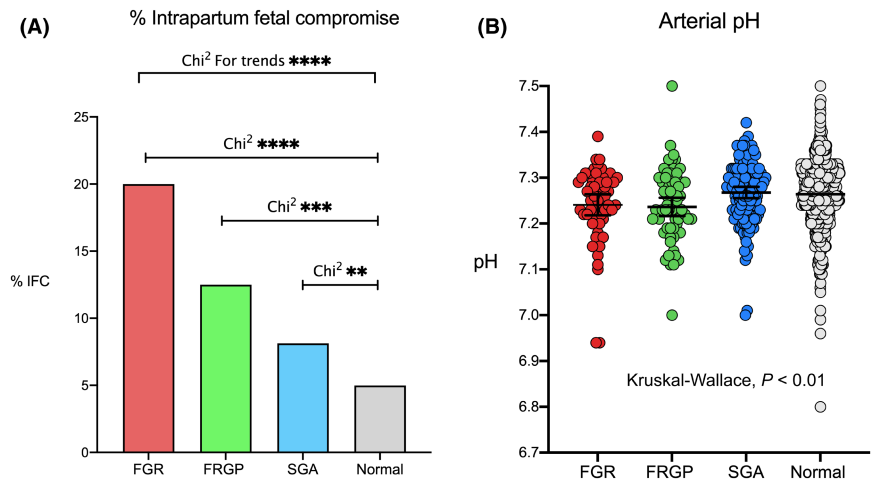


FIGURE 3 (A) Frequency of intrapartum fetal compromise (IFC) in each of the four studied groups. (B) Arterial cord pH. FGR, fetal growth restriction; FRGP, failure to reach growth potential; SGA, small for gestational age.



4 | DISCUSSION

The group with the highest frequency of intrapartum fetal compromise was FGR, followed by FRGP, SGA, and normal groups. The “a priori” risks of the FGR and normal groups were used to determine the limits of the two scales. One defining the IFC risk and the other

defining the appropriate GA for pregnancy termination. Extrapolation of risk between both scales placed the optimal GA for delivery at 39 weeks in the case of FRGP and at 40 weeks in the case of SGA.

The aim of this study was to calculate the optimal time for delivery in FRGP fetuses, based on the risk of IFC. To achieve this goal, we first needed to determine the risk of IFC in the study groups and

establish some reference (or anchorage) points to extrapolate the risk of IFC into an optimal GA at delivery. Fortunately, robust consensus existed regarding the optimal time of delivery in fetuses with normal growth and in fetuses affected with FGR. In normal fetuses, induction of labor at 41 weeks of gestation is considered an effective

way of reducing perinatal morbidity and mortality,^{6,18-20} whereas in FGR fetuses, induction of labor at 37 weeks is considered protective against adverse outcomes, especially stillbirth, and most guidelines recommended delivery at this gestation or even earlier in case of more severe hemodynamic compromise.^{7,8,21-23}

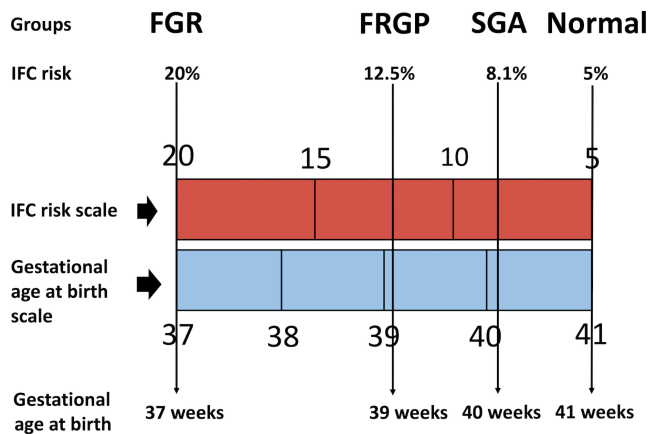


FIGURE 4 Parallellism between the risk of intrapartum fetal compromise (IFC) and the optimal gestational age at birth based on previous consensus (limits of the scale). In red color we observe the “IFC risk scale”, which is inverted (higher values are on the left) and depicted in parallel along with the “gestational age at birth scale” in blue color, depicting the week at which birth should be planned. When the individual risk for the any of four groups is extrapolated into the “gestational age at birth scale”, a specific week for delivery may be automatically established.

Accordingly, we used these references to extrapolate the IFC risks into the optimal GA for delivery scale. Interestingly, we found that extrapolation in SGA fetuses suggested delivery at 40 weeks of gestation. This is consistent with earlier recommendations, suggesting that these fetuses, considered to be constitutionally small, had an increased risk of IFC.^{8,22,23} In addition, we calculated that the optimal gestation for delivery of FRGP fetuses was 39 weeks. Again, this finding was in line with earlier reports, most originating from our research, that FRGP fetuses have a lower risk of IFC than FGR fetuses, but higher than SGA fetuses.^{9,24}

Figure 5 represents our structured proposal for pregnancy management near term (Valencia Protocol). Routine third-trimester ultrasound scan is scheduled, most frequently at 36–37 weeks, as recently proposed.^{16,17} At this stage, two parameters should be evaluated: CPR and EFW, yielding four possible combinations: when both parameters are normal (in green), the fetus is probably normal with a normal placental functional reserve, needing no more than a second surveillance at 40 weeks before induction at 41 weeks. At the other extreme, when both parameters are abnormal (on the left, in red), the fetus is growth restricted (FGR) and probably presents a severely affected placental functional reserve, needing delivery at 37 or 38 weeks. The two other intermediate groups: SGA and FRGP, probably represent different expressions

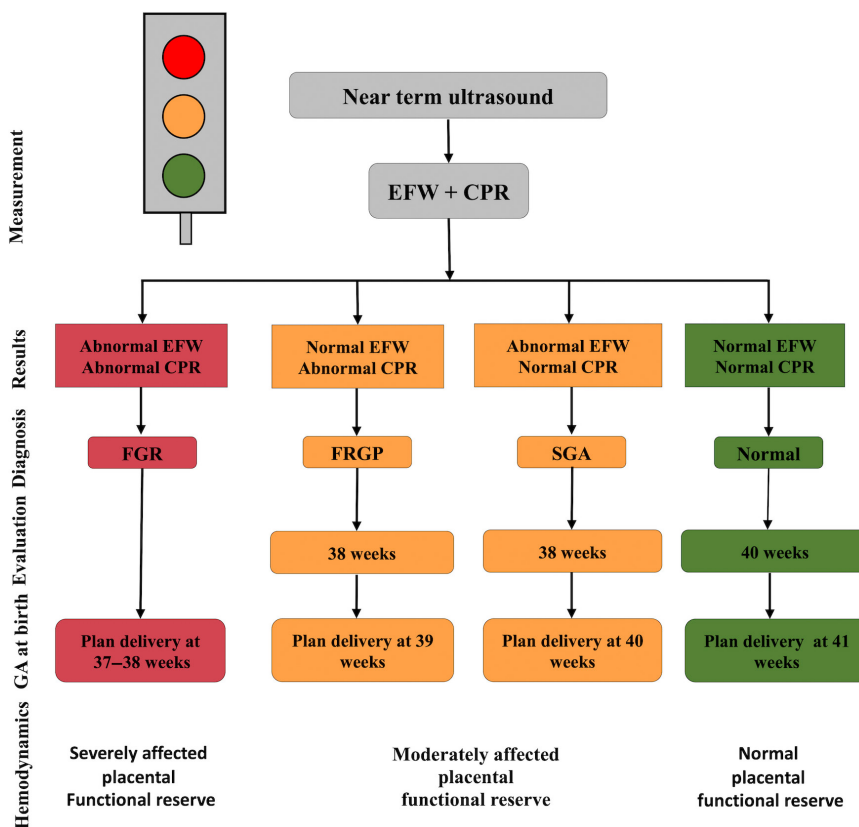


FIGURE 5 Risk-based approach for timing of birth near term based on the cerebroplacental ratio and estimated fetal weight (Valencia Protocol). CPR, cerebroplacental ratio; EFW, estimated fetal weight; FGR, fetal growth restriction; FRGP, failure to reach growth potential; SGA, small for gestational age, normal EFW = EFW \geq 10th centile, normal CPR = CPR \geq 0.6765 MoM or \geq 5th centile.

of a moderately affected placental functional reserve. As earlier suggested, extrapolation of IFC risk indicated that their optimal gestation at birth might be around 39 and 40 weeks, respectively.

The fact that FRGP fetuses have a higher risk of IFC than SGA fetuses strongly reinforces the value of fetal CPR assessment at the end of pregnancy. This is critically important to avoid fetuses with apparently normal growth (because their size is above the 10th centile) being misclassified as “appropriately” grown (AGA). Evaluation of the CPR is the only way to appropriately diagnose these fetuses, that otherwise would be misclassified as low risk despite being clearly at increased risk of compromise.⁴

Our work proves the existence of a variation in the risk of IFC, which is maximal in the FGR group, but still high in FRGP and SGA fetuses. In accordance with this, we have described a simple surveillance protocol that uses CPR evaluation to avoid missing fetuses whose growth is compromised, despite an estimated weight above the 10th centile. This presents two advantages. First, the ability to detect fetuses with hidden compromise by measuring both CPR and EFW (FRGP); second, it establishes a rationale for fetal management and delivery based on the accurate individualized characterization of the risk of IFC.

In summary, our approach classifies fetuses into four discrete categories, facilitating a simple and straightforward management protocol (Valencia Protocol), based on the individualized risk of IFC, which is designed to avoid adverse consequences at term. The greater the risk of IFC, the earlier delivery is advised. Finally, the protocol does not consider data from the cardiotocogram, as the presence of cardiotocogram¹⁵ abnormality close to term would usually mandate delivery regardless of the ultrasound findings.

The strengths of this study include measurement of the cerebral Doppler, evaluation of FRGP fetuses, and the simplicity of the protocol. Limitations include the absence of long-term follow up, the small number of cases, which made some of the comparisons among groups non-significant, the existence of earlier works that deny or minimize the ability of CPR to predict IFC,²⁵⁻²⁸ the inaccuracy of EFW, and the possibility of intervention bias. In addition, the study has not the consistency and soundness of a randomized control trial comparing for each of the groups the different possible managements and different gestational ages for induction. Our message is simple: according to the observed risk of IFC, FRGP fetuses tend to present worse outcomes than SGA fetuses but better outcome than FGR fetuses. Accordingly, if we consider that 37 and 40 weeks are appropriate weeks for induction in FGR and SGA fetuses, FRGP fetuses should be delivered somewhere in between the above-mentioned groups. This should not be taken in absolute terms but only as a proposal. In this regard, future randomized control trials are needed to clarify and define the best management in either of the four study groups.

5 | CONCLUSION

Near term fetuses may be evaluated with CPR and EFW, defining four groups that present different risks of IFC. Based on earlier

consensus, extrapolation of risk suggests that the optimal gestation for delivery of FRGP fetuses might be around 39 weeks.

AUTHOR CONTRIBUTIONS

JM-R designed the study, performed the ultrasound examinations, did the statistical analysis, and wrote the manuscript. AM-V made notable contributions to the final text. AK supervised the final manuscript and made notable contributions to the final text.

CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interests.

REFERENCES

- Morales-Roselló J, Cañada Martínez AJ, Scarinci E, Perales MA. Comparison of cerebroplacental ratio, intergrowth-21st standards, customized growth, and local population references for the prediction of fetal compromise: which is the best approach? *Fetal Diagn Ther.* 2019;46:341-352.
- Morales-Roselló J, Loscalzo G, Gallego A, Jakaitė V, Perales-Marín A. Which is the best ultrasound parameter for the prediction of adverse perinatal outcome within 1 day of delivery? *J Matern Fetal Neonatal Med.* 2022;35:8571-8579.
- Morales-Roselló J, Khalil A, Loscalzo G, et al. Cerebroplacental ratio prediction of intrapartum fetal compromise according to the interval to delivery. *Fetal Diagn Ther.* 2022;49:196-205.
- Morales-Roselló J, Khalil A. Fetal cerebral redistribution: a marker of compromise regardless of fetal size. *Ultrasound Obstet Gynecol.* 2015;46:385-388.
- Poon LC, Tan MY, Yerlikaya G, Syngelaki A, Nicolaides KH. Birth weight in live births and stillbirths. *Ultrasound Obstet Gynecol.* 2016;48:602-606.
- Alkmark M, Wennerholm UB, Saltvedt S, et al. Induction of labour at 41 weeks of gestation versus expectant management and induction of labour at 42 weeks of gestation: a cost-effectiveness analysis. *BJOG.* 2022;129:2157-2165.
- Lausman A, Kingdom J. How and when to recommend delivery of a growth-restricted fetus: a review. *Best Pract Res Clin Obstet Gynaecol.* 2021;77:119-128.
- Figueras F, Gratacós E. Update on the diagnosis and classification of fetal growth restriction and proposal of a stage-based management protocol. *Fetal Diagn Ther.* 2014;36:86-98.
- Khalil AA, 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.e1-54.e10.
- Morales-Roselló J, Khalil A, Alberola-Rubio J, et al. Neonatal Acid-Base status in term fetuses: mathematical models investigating cerebroplacental ratio and birth weight. *Fetal Diagn Ther.* 2015;38:55-60.
- Morales-Roselló J, Khalil A, Morlando M, Hervás-Marín D, Perales-Marín A. Doppler reference values of the fetal vertebral and middle cerebral arteries, at 19-41 weeks gestation. *J Matern Fetal Neonatal Med.* 2015;28:338-343.
- Acharya G, Wilsgaard T, Berntsen GK, et al. Reference ranges for serial measurements of umbilical artery Doppler indices in the second half of pregnancy. *Am J Obstet Gynecol.* 2005;192:937-944.
- Baschat AA, Gembruch U. The cerebroplacental Doppler ratio revisited. *Ultrasound Obstet Gynecol.* 2003;21:124-127.
- Figueras F, Meler E, Iraola A, et al. Customized birthweight standards for a Spanish population. *Eur J Obstet Gynecol Reprod Biol.* 2008;136:20-24.
- Ayres-de-Campos D, Spong CY, Chandraran E, FIGO Intrapartum Fetal Monitoring Expert Consensus Panel. FIGO consensus

- guidelines on intrapartum fetal monitoring: cardiotocography. *Int J Gynaecol Obstet*. 2015;131:13-24.
16. Wanyonyi SZ, Orwa J, Ozelle H, et al. Routine third-trimester ultrasound for the detection of small-for-gestational age in low-risk pregnancies (ROTTUS study): randomized controlled trial. *Ultrasound Obstet Gynecol*. 2021;57:910-916.
 17. Roma E, Arnau A, Berdala R, Bergos C, Montesinos J, Figueras F. Ultrasound screening for fetal growth restriction at 36 vs 32 weeks' gestation: a randomized trial (ROUTE). *Ultrasound Obstet Gynecol*. 2015;46:391-397.
 18. Keulen JK, Bruinsma A, Kortekaas JC, et al. Induction of labour at 41 weeks versus expectant management until 42 weeks (INDEX): multicentre, randomised non-inferiority trial. *BMJ*. 2019;364:1344.
 19. Hussain AA, Yakoob MY, Imdad A, Bhutta ZA. Elective induction for pregnancies at or beyond 41 weeks of gestation and its impact on stillbirths: a systematic review with meta-analysis. *BMC Public Health*. 2011;11(Suppl 3):S5.
 20. Kaimal AJ, Little SE, Odibo AO, et al. Cost-effectiveness of elective induction of labor at 41 weeks in nulliparous women. *Am J Obstet Gynecol*. 2011;204(137):e1-e9.
 21. Rabinovich A, Tsemach T, Novack L, et al. Late preterm and early term: when to induce a growth restricted fetus? A population based study. *J Matern Fetal Neonatal Med*. 2018;31:926-932.
 22. Figueras F, Gratacos E. An integrated approach to fetal growth restriction. *Best Pract Res Clin Obstet Gynaecol*. 2017;38:48-58.
 23. Figueras F, Gratacos E. Stage-based approach to the management of fetal growth restriction. *Prenat Diagn*. 2014;34:655-659.
 24. Khalil AA, Morales-Rosello J, Elsaddig M, et al. The association between fetal Doppler and admission to neonatal unit at term. *Am J Obstet Gynecol*. 2015;213:57.e1-57.e7.
 25. D'Antonio F, Rizzo G, Gustapane S, et al. Diagnostic accuracy of Doppler ultrasound in predicting perinatal outcome in pregnancies at term: a prospective longitudinal study. *Acta Obstet Gynecol Scand*. 2020;99:42-47.
 26. Buca D, Rizzo G, Gustapane S, et al. Diagnostic accuracy of Doppler ultrasound in predicting perinatal outcome in appropriate for gestational age fetuses: a prospective study. *Ultraschall Med*. 2021;42:404-410.
 27. Fiolna M, Kostiv V, Anthoulakis C, Akolekar R, Nicolaides KH. Prediction of adverse perinatal outcome by cerebroplacental ratio in women undergoing induction of labor. *Ultrasound Obstet Gynecol*. 2019;53:473-480.
 28. Semmler J, Abdel-Azim S, Anzoategui S, Zhang H, Nicolaides KH, Charakida M. Influence of birth weight on fetal cardiac indices at 35-37 weeks' gestation. *Ultrasound Obstet Gynecol*. 2021;57:266-272.

How to cite this article: Morales-Roselló J, Khalil A, Martínez-Varea A. Management of fetuses with apparent normal growth and abnormal cerebroplacental ratio: A risk-based approach near term. *Acta Obstet Gynecol Scand*. 2023;00:1-8. doi:[10.1111/aogs.14732](https://doi.org/10.1111/aogs.14732)