A critical review of placental function evaluation near term using Doppler ratios

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Introduction

The assessment of placental function at term remains a pivotal aspect of obstetric care given its role in fetal well-being. Doppler ultrasound is a widely used tool to evaluate placental vascular function, with particular focus on the umbilical artery (UA), middle cerebral artery (MCA), and uterine arteries. While individual Doppler indices provide valuable insights, their limitations in detecting mild placental dysfunction have led to the introduction of Doppler ratios such as the cerebroplacental ratio (CPR) and the umbilicocerebral ratio (UCR). This Clinical Opinion critically examines the efficacy of these ratios in evaluating placental function at term and their predictive value for adverse perinatal outcomes. Relevant studies, meta-analyses, and guidelines were identified through PubMed searches and the authors' clinical expertise, with priority given to recent and influential publications.

The evaluation of placental function near term remains a cornerstone of perinatal care, yet subtle dysfunction often escapes detection through conventional Doppler indices of the umbilical artery and middle cerebral artery. In this context, Doppler ratios—particularly the cerebroplacental ratio and the umbilicocerebral ratio—have emerged as promising tools for enhancing sensitivity in identifying early signs of fetal adaptation to hypoxia. This Clinical Opinion critically examines the rationale, clinical relevance, and limitations of cerebroplacental ratio and umbilicocerebral ratio as markers of placental insufficiency in the third trimester.

Cerebroplacental ratio, which combines umbilical artery and middle cerebral artery impedance, has been shown to become abnormal before individual Doppler components, offering earlier recognition of compromised fetuses. Its use is supported in late-onset fetal growth restriction by several guidelines, including those of the International Society of Ultrasound in Obstetrics and Gynecology, although not by others such as the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine, which cite limited evidence of improved outcomes. The role of cerebroplacental ratio in appropriately grown fetuses remains controversial; while associations with adverse perinatal outcomes have been observed, the performance of this ratio in routine screening for adverse perinatal outcomes in the third trimester has been found to be poor, and randomized trials have not demonstrated clinical benefit from delivery based on cerebroplacental ratio alone.

The current evidence is hindered by heterogeneity in cerebroplacental ratio thresholds, lack of standardization in measurement timing, and potential confounding by clinical interventions aimed at reducing adverse outcomes. Furthermore, most studies fail to isolate the predictive value of cerebroplacental ratio independently of abnormal umbilical artery or middle cerebral artery findings.

While cerebroplacental ratio and umbilicocerebral ratio may contribute to risk stratification in late-onset fetal growth restriction, they should not currently be used in isolation to guide delivery timing. An ongoing trial is expected to clarify the role of umbilicocerebral ratio in guiding management decisions in late preterm fetal growth restriction. In the absence of growth restriction, routine assessment of these ratios in low-risk pregnancies may lead to unnecessary interventions without improving outcomes. However, when measured, abnormal ratios may still highlight increased risk and should be interpreted in conjunction with other ultrasound and clinical parameters.

Key words: cerebroplacental ratio, fetal Doppler, fetal growth, fetal growth restriction, umbilicocerebral ratio

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Received June 30, 2025; revised Nov. 14, 2025; accepted Nov. 17, 2025.

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0002-9378

https://doi.org/10.1016/j.ajog.2025.11.032

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Pathophysiology of placental dysfunction and rationale for Doppler ratios

Placental dysfunction predisposes fetuses to nutritional deficiency, hypoxia, and adverse outcomes, with its clinical manifestation depending on the severity and timing of onset. The predominant placental pathology in early-onset placental dysfunction leads to perfusion abnormalities of sufficient magnitude to result in elevated UA blood flow resistance.[1] Elevated resistance to blood flow in the uterine arteries suggests abnormal trophoblastic invasion and an increased risk of preeclampsia.[2,3] The severity of placental vascular dysfunction is clinically assessed in the fetal compartment through Doppler investigation of the UA. When a significant proportion of the villous

vascular tree is abnormal, UA end-diastolic velocities may be absent or even reversed. In contrast, the placental pathology underlying late-onset fetal growth restriction (FGR) produces minimal perfusion abnormalities, but can limit oxygen diffusion sufficiently to trigger brain sparing.[4] This is the primary reason why in late-onset FGR, Doppler findings may be subtle, and standard Doppler indices alone (UA and MCA) may remain within normal ranges despite underlying placental insufficiency. Furthermore, the amniotic fluid may be normal, and fetal size may remain above the 10th percentile because in the early stages of nutrient deficiency, adipose tissue is lost first, followed later by a reduction in the abdominal circumference as liver size decreases due to reduced fetal glycogen storage.[5]

Given the limitations of individual Doppler indices in detecting mild placental insufficiency in the third trimester, ratios from the umbilical and cerebral arteries such as the CPR and UCR have been introduced to enhance diagnostic sensitivity. The CPR is the ratio between the UA and the MCA pulsatility index and the UCR is the inverse.[6–8] By combining the impedance of these 2 vessels, these ratios are sensitive to both perfusion and diffusion abnormalities in the villous circulation,[9,10] and may become abnormal before either component alone, thereby amplifying the detection of early fetal adaptation to placental dysfunction. This provides higher sensitivity for identifying adverse outcomes in the small fetus,[7,11,12] although potentially at the expense of specificity. To minimize interobserver variability, standardized protocols should be followed for Doppler acquisition.[13]

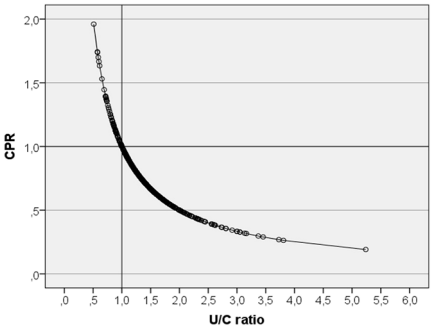
The UCR, being the inverse of the CPR, increases with worsening placental dysfunction. It has been argued that the discrimination of the dynamic development of blood flow redistribution becomes clearer using the UCR rather than the CPR because it becomes more skewed in the abnormal range, with the numerator increasing and the denominator decreasing as Doppler deterioration progresses.[14] The relationship between the UCR and CPR, based on data from 374 cases of early FGR, is illustrated in Figure 1 (reproduced from Stampalija et al,[15] secondary analysis of the TRUFFLE study[16]). However, the clinical utility of the ratios may become redundant once UA and MCA abnormalities are already evident. Moreover, Kalafat and Khalil have shown that inverting CPR into UCR results in a skewed distribution, an increased number of statistical outliers, and complications in statistical modeling using Z-scores, thus questioning whether it adds value over the CPR.[17] In their analysis, this was demonstrated through histograms, quantile plots, and Z-score density plots.

On the other hand, CPR and UCR are mathematically related and can theoretically be interpreted similarly when expressed as percentiles or multiples of the median (MoM). An abnormal value—whether CPR or UCR—corresponds to <10th or > the 90th percentile, or to MoM deviations from the reference median. The CPR may be more informative when placental dysfunction primarily impairs oxygen diffusion, resulting in brain sparing with little or no change in the UA resistance. Conversely, the UCR may be more useful in scenarios where placental disease primarily affects the UA or both vessels. Since placental pathology evolves along the gestational age continuum,[18,19] it remains unclear whether one ratio should be favored over the other at specific gestational stages.

Several studies have suggested that a low CPR or a high UCR is associated with adverse perinatal outcomes not only in small-for-gestational-age (SGA) fetuses[8,11,20–26] but also in appropriately grown fetuses.[8,27–31] This has renewed interest in their potential role in the surveillance of normally grown fetuses.[32–34] However, outcomes assessed in relation to CPR or UCR vary widely, and relatively few studies examined its association with stillbirth or perinatal mortality.[20,24,28] Most evaluated other perinatal outcomes such as cesarean delivery for presumed fetal compromise, surrogate markers of perinatal hypoxia (eg, neonatal acidosis, low 5-minute Apgar score, neonatal intensive care unit [NICU] admission), low birthweight, and neonatal morbidity—either individually or as part of composite adverse outcomes.[11,21,22,26,27,29,30] While informative, these outcomes are less clinically definitive than stillbirth or perinatal death and are not exclusively attributable to placental dysfunction. Therefore, currently, there is insufficient evidence to support a reliable correlation between Doppler ratios and prelabor acidemia and only limited data linking them to stillbirth, primarily due to the rarity of such outcomes. Furthermore, a systematic review reported substantial heterogeneity in CPR thresholds and predictive accuracy,[12] and another focused on fetuses with suspected growth restriction showed moderate to high predictive accuracy for perinatal death but poor performance for other adverse outcomes.[20] Thus, CPR or UCR may help distinguish constitutionally small fetuses from those with true growth restriction,[32,35,36] but their overall predictive value for composite adverse outcomes remains limited.[22,24,37]

It must also be acknowledged that predictive accuracy varies depending on the cutoff used and the gestational age at assessment. For instance, in the prospective study by Akolekar et al,[24] CPR

FIGURE 1
Relationship between UCR and CPR in the TRUFFLE Study (n = 374)



The shaded area defines an abnormal test with a cutoff at 1.0. Reproduced with permission from Stampalija et al[14] Elsevier (2017), secondary analysis of the TRUFFLE study.[15]

CPR, cerebroplacental ratio; *UCR*, umbilicocerebral ratio.

measured between 35+0 and 37+6 weeks demonstrated a low positive likelihood ratio for adverse perinatal outcome, which may have been influenced by the use of the 10th percentile as the threshold for abnormal CPR, whereas the fifth percentile is more clinically relevant.

Similarly, in a secondary analysis of the Prospective Observational Trial to Optimize Pediatric Health in IUGR (PORTO) study[22] evaluating CPR expressed both as an absolute cutoff (<1.08) and via gestational age–specific reference values (<fifth percentile), specificity was limited, likely due to the broad gestational age range (24 weeks to term), as CPR is considered to have little utility in early FGR, where the fetus may exhibit low CPR without clear correlation to adverse outcomes.

Importantly, while these studies report on predictive accuracy, this does not demonstrate whether interventions based on Doppler ratios can actually improve outcomes, highlighting the need for randomized controlled trials such as TRUFFLE 2[38] (See also Table 1 for summary of predictive performance across studies).

Application of cerebroplacental ratio and umbilicocerebral ratio in clinical practice

There is currently no agreement on how calculations of these ratios should be applied in clinical practice and there are 2 distinct scenarios in which their utility is debated.

Small-for-gestational-age fetuses

In early-onset FGR, the CPR is not considered to have clinical utility: while it may provide insight into the pathophysiological process, its use has not been proven beneficial for monitoring or clinical management in this group.[15,39] In contrast, CPR or UCR assessment is considered more clinically relevant in late-onset FGR.[21,25,26,35,36,40,41] In this subgroup, the guidelines of the International Society of Ultrasound in Obstetrics and Gynecology on the diagnosis and management of SGA fetus and FGR recommend the use of the CPR as part of the Doppler surveillance.[42] On the other hand, both the guidelines of both the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine interpret the literature as providing insufficient evidence that CPR improves diagnostic accuracy compared to UA Doppler alone.[43,44] There is also ongoing debate as to whether CPR or UCR should only be used solely to increase surveillance frequency or whether it can guide decisions regarding delivery timing. Given that the predictive performance of the Doppler ratios for adverse perinatal outcomes in late preterm FGR appears to be low, it does not seem appropriate to use it as a delivery trigger, unless within the context of a clinical trial.[25,37] The results of the ongoing TRUFFLE 2 trial will help determine the effectiveness of UCR in guiding clinical management in late-onset FGR.[38] At the time this Clinical Opinion was written, enrollment in the TRUFFLE 2 trial had been completed and data analysis was ongoing, with first results expected in early 2026. The primary outcome is a composite of fetal or neonatal death, poor condition at birth, and neonatal morbidity. Secondary outcomes include health and neurodevelopmental assessments up to 2 years of age.[38]

A proposed flowchart for integrating Doppler ratios into clinical pathways, emphasizing trigger points for intensified surveillance, is shown in Figure 2.

Appropriately grown fetuses (unselected population)

The potential use of CPR and UCR as a safety net to identify late third-trimester/term fetuses requiring surveillance, independently of their size, has also been suggested.[27,32,34,45] This approach is based on the assumption that signs of placental dysfunction are identified by these Doppler ratios, before resulting in measurable growth delay. Accordingly, some appropriately grown fetuses, despite having a weight greater than the 10th centile, may experience placental insufficiency and remain at an increased risk of adverse outcomes. A fetus exposed to hypoxemia from placental insufficiency at term has a short latency to delivery and may therefore be unlikely to manifest SGA as a feature, while still presenting with fetal cerebral blood flow redistribution indicative of fetal hypoxemia.[29,45] Despite the observed association between a low CPR and high UCR with adverse perinatal outcomes in appropriately grown fetuses, there is currently a lack of good evidence supporting the integration of Doppler ultrasound evaluation into routine third-trimester assessment, unless other signs suggesting placental disease are present (eg, a drop in fetal growth of more than 2 quartiles in the third trimester or low amniotic fluid volume). The performance of CPR in routine screening for adverse perinatal outcomes at 30 to 34 or 35 to 37 weeks' gestation was found to be poor in 2 large studies.[46,47]

In a single-site randomized controlled trial including 501 unselected pregnancies, participants were randomized to either routine obstetric care or screening at 37 to 38 weeks' gestation using CPR and placental growth factor, with labor induction offered in cases of positive screening.[48] No difference was found in the rate of composite adverse perinatal outcomes between screened and nonscreened pregnancies. Similarly, a larger recent randomized clinical trial (RATIO 37 trial) showed that adding CPR evaluation to routine third-trimester fetal growth assessment (at 36–37+6 weeks) and planning delivery at term based either on an abnormal CPR or an estimated fetal weight (EFW) below the 10th percentile was not followed by a reduction in perinatal mortality or severe neurological morbidity compared to standard care (delivery based on an EFW below the 10th percentile).[34] Although a statistically significant reduction in severe non-neurological morbidity was reported in the group in which CPR was available for clinical management (P=.014), this mainly consisted in a shorter length of stay in the NICU, with no difference in the overall admission rate, and no details were provided regarding the reasons for prolonged hospitalization in the group where CPR results were concealed. Moreover, the rates of the other 3

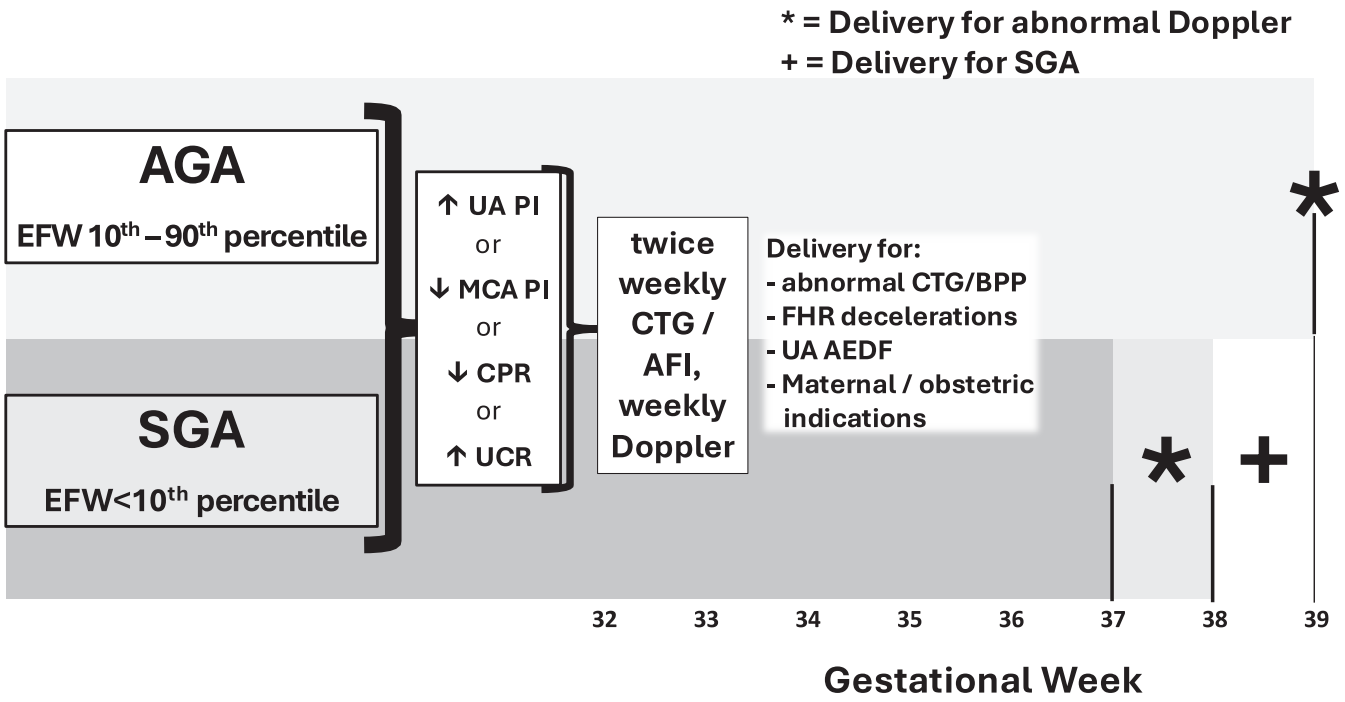
TABLE 1
Summary of CPR and UCR cutoffs and performance from systematic reviews, large prospective studies, and the ongoing RCT

Cutoff (CPR or UCR)	Author/year	Population/GA	Outcome(s)	Key performance metrics	Notes and limitations
CPR <1.0 or <1.1	Vollgraff Heidweiller-Schreurs et al, 2018[12]	Meta-analysis, N=47,748 pregnancies, CPR analyses in 18,731 cases. Mixed risk pregnancies, second −third trimester; 51% of studies on SGA fetuses.	Perinatal death, composite APO, Apgar <7, urgent CS for distress, NICU admission	In 10 studies on SGA/AGA: 93% Sens and 74% Spec for perinatal death; In 4 studies on late SGA, Sens ranged from 8% to 69% and Spec ranged from 56% to 98% for APO	Systematic review; 94% of studies at risk of bias; high heterogeneity; only 9 studies in late SGA.
CPR ≤1.08 or <fifth percentile	Conde-Agudelo et al, 2018[20]	Meta-analysis, N=4301 (suspected FGR, mostly third trimester)	Perinatal death, composite APO, Apgar <7, NICU admission, acidosis	Perinatal death: Sens 93%, Spec 76%, +LR 3.9, −LR 0.09, AUC 0.83; predictive accuracy low for other outcomes (+LR 1.1−2.5; −LR 0.3−0.9)	Substantial between-study heterogeneity
CPR <10th percentile	Akolekar et al, 2019[24]	Large prospective cohort, N=47,211 (general population, 35^{+6}−37^{+6} weeks)	(1) Stillbirth, neonatal death, or HIE 2−3; (2) acidosis, Apgar <7, or NICU admission; (3) CS for fetal compromise; (4) BW <third centile	Detection rate 13%−26% at FPR ∼10%; +LR 1.2−1.8; −LR 0.92−0.98; AUC ∼0.61 (reported for main composite outcome). In SGA: +LR 1.31 −2.26; −LR 0.69−0.92	Mostly AGA fetuses (SGA n=4282); low +LR may reflect use of 10th centile instead of fifth
UCR ≥0.9 or CPR <1.11	Wolf et al, 2021[37]	Prospective multicenter, N=856 (late-preterm FGR, 32−36+6 weeks)	Composite abnormal birth condition & major neonatal morbidity	Sens 70%, Spec 64%; AUC 0.73 (95% CI, 0.67−0.78); aOR, 3.3 (95% CI, 1.7−6.4)	Absolute and percentile thresholds similar; GA adjustment not necessary
CPR <1.0; CPR <1.08; CPR <fifth centile	Flood et al, 2014[22]	Large prospective cohort, N=1100, CPR available in 881 (SGA, GA 24 −36+6 weeks); mean GA at CPR measurement 33 weeks (IQR, 28.7 −35.9)	Composite APO	CPR <1.0: Sens 66%, Spec 85%; CPR <1.08: Sens 73%, Spec 80%; CPR <fifth percentile: Sens 80%−85%, Spec 41%−60%, depending on the reference chart used. Abnormal CPR in 16.6% fetuses; 11-fold ↑ risk of APO	Broad GA range.
UCR >1 at 32+0−33+6 and UCR >0.8 at 34+0 −36+6	Cutoffs used in TRUFFLE 2 protocol (Mylrea Foley et al, 2022),[38] derived from the feasibility study (Stampalija et al, 2020[26])	Multicenter RCT (FGR, 32 −36+6 weeks). Feasibility study: prospective cohort, N=856 pregnancies at risk of FGR	TRUFFLE 2 primary outcome: poor condition at birth and/or fetal or neonatal death and/or major neonatal morbidity. Secondary outcome: 2-year infant general health and neurodevelopmental outcome.	Threshold chosen as delivery trigger. In the feasibility study (Stampalija et al, 2020[26]), were associated with composite APO (RR, 2.0; 95% CI, 1.4−3.0).	Enrollment completed. Data analysis is ongoing, with first results expected in early 2026.

Note: CPR and UCR are inverse ratios (UCR=1/CPR). Thus, CPR <1.0 corresponds to UCR >1.0; CPR<1.1 ≈ UCR>0.9.

+LR/−LR, positive/negative likelihood ratio; *AGA*, appropriate for gestational age; *APO*, adverse perinatal outcome; *AUC*, area under the curve; *BW*, birthweight; *CPR*, cerebroplacental ratio; *CS*, cesarean section; *FGR*, fetal growth restriction; *GA*, gestational age; *HIE*, hypoxic-ischemic encephalopathy; *NICU*, neonatal intensive care unit; *SGA*, small for gestational age; *Sens*, sensitivity; *Spec*, specificity; *UCR*, umbilicocerebral ratio.

FIGURE 2
Proposed flowchart for integrating Doppler ratios into clinical pathways, highlighting trigger points for intensified surveillance



Delivery of an SGA fetus with normal Doppler can be considered from 38 weeks onwards and is recommended by 39 weeks. +=Delivery for SGA. *=Delivery for abnormal Doppler.

AEDF, absent end-diastolic flow; *AFI*, amniotic fluid index; *AGA*, appropriate for gestational age; *BPP*, biophysical profile; *CPR*, cerebroplacental ratio; *CTG*, cardiotocography; *FHR*, fetal heart rate; *MCA*, middle cerebral artery; *SGA*, small for gestational age; *UA*, umbilical artery; *UCR*, umbilicocerebral ratio.

components of the composite outcome of severe non-neurological morbidity (necrotizing enterocolitis, renal failure, and cardiac failure) did not significantly differ between groups. This suggests that the observed difference is more likely of statistical rather than clinical significance. Importantly, none of the outcomes typically associated with low CPR—such as cesarean delivery for nonreassuring fetal status, low Apgar score, and neonatal acidosis—differed between groups, and the median gestational age at delivery (39.5 weeks) was similar. These findings do not support the idea that delivery based solely on low CPR is beneficial in appropriately grown fetuses.

Determining an optimal threshold of Doppler ratios for identifying late-onset fetal growth restriction

Identifying an optimal threshold remains challenging, as varying definitions of abnormal Doppler ratios have been employed across studies (Table 1). These definitions include the use of absolute cutoffs (eg, CPR <1.11, or <1.0, equivalent to UCR ≥0.9 or >1.0, respectively), CPR values below the fifth or the 10th percentile based on published reference charts,[49–51] or a CPR cutoff of 0.6765 MoM, which corresponds to the fifth percentile in a cohort of large-for-gestational-age fetuses (birthweight >90th percentile),[45] a group least likely to exhibit failure to reach growth potential. One study showed that CPR-MoM values are dependent on EFW centiles and that lower birthweight centiles show physiologically a lower CPR-MoM, suggesting that adjusting CPR for EFW may improve the prediction of adverse outcomes.[52]

Furthermore, substantial variability in CPR percentile thresholds across different reference charts has been reported,[37,53] potentially leading to important differences in clinical management. One study reported that using an absolute CPR threshold of <1.11 (or UCR ≥0.9) at 32+0 to 36+6 weeks may provide predictive performance comparable to percentile-based approaches, while offering a simpler and more standardized method for assessing pregnancies at risk of late FGR.[37] However, the definition of "low" CPR continues to vary, with no established consensus on the optimal criteria.

Another important consideration is whether the Doppler ratio should still be taken into account when either the UA or MCA Doppler index is already abnormal. This issue is not clearly addressed in the literature and may contribute to the higher sensitivity reported for Doppler ratios. For example, a small fetus presenting with an elevated UA Doppler index and an abnormal

Doppler ratio can be managed based on the UA findings alone.

Timing for calculation of Doppler ratios

While there is general agreement that both the CPR and UCR are useful markers of placental insufficiency in small fetuses primarily in the context of late-onset disease, the optimal gestational age for their assessment in the third trimester remains unclear. Existing data on the predictive value of CPR during this period are derived from cohorts evaluated at varying gestational ages, with considerable heterogeneity across studies.[20,22–24,28,37]

32 to 36 weeks

Wolf et al found poor predictive performance of low CPR for identifying composite adverse perinatal outcomes in cases of late-preterm FGR (Table 1).[37] In this context, while an abnormal CPR warrants increased surveillance, it is not currently considered a standalone indication for delivery at this gestational age.[42] The forthcoming results of the TRUFFLE 2 study, where the UCR is being evaluated as potential delivery trigger at 32 to 36+6 weeks' gestation, are expected to inform and refine optimal management strategies in such cases.[38]

36 to 38 weeks

Despite evidence of an association between a low CPR and adverse perinatal outcomes, a large prospective study found that the predictive performance of a low CPR (defined as <10th percentile) between 35^{+6} and 37^{+6} weeks was poor (Table 1).[24] An abnormal CPR in this gestational window should prompt increased fetal surveillance rather than immediate delivery.

38 to 40 weeks

There is a paucity of data evaluating the role of Doppler ratios at term in small fetuses, as many clinical protocols recommend delivery of SGA fetuses by 39 weeks. A large retrospective study showed that a low CPR at 38 to 41 weeks' gestation, regardless of the fetal size, was independently associated with the need for operative delivery for presumed fetal compromise and with NICU admission.[29] Nevertheless, randomized controlled trials are still required to assess the clinical utility and guidance of management decisions between 37 and 39 weeks. Beyond 39 weeks, routine Doppler ultrasound assessment is likely unnecessary, as continuing the pregnancy in SGA fetuses beyond this gestational age is generally not recommended.[42]

Limitations in the current evidence on cerebroplacental ratio and umbilicocerebral ratio as predictors of adverse perinatal outcomes

Present studies assessing the predictive performance of low CPR or high UCR for adverse perinatal outcomes face several important limitations. A major confounder is the influence of clinical management, particularly obstetric interventions such as the timing of delivery, which are intended to reduce the risk of adverse outcomes but simultaneously obscure the natural course of the condition. This makes it difficult to isolate the predictive value of these ratios independently. Additionally, most studies lack long-term follow-up data beyond the perinatal period, limiting conclusions about the broader clinical impact. Another key issue is that many studies include fetuses with abnormal UA or MCA Doppler findings, which are already components of the calculation of ratios. This complicates efforts to determine the additive predictive value of these ratios beyond individual vessel assessments.

Conclusion

Doppler ratios are sensitive markers of placental dysfunction regardless of fetal size. However, their accuracy in predicting adverse outcomes varies considerably depending on the population studied, the threshold applied, and the proximity of assessment to delivery.

In normally grown fetuses, current randomized clinical trials have not demonstrated a benefit to delivery solely based on an abnormal CPR. In the absence of FGR or other pathological conditions, the clinical significance of altered cerebral blood flow remains uncertain. Routine Doppler ratios assessment in this population may lead to false-positive findings, unnecessary parental anxiety, and potentially unwarranted interventions.

In cases of late-onset FGR, a low CPR or a high UCR may indicate the need for intensified surveillance. However, these findings should not currently be considered a standalone indication for delivery unless additional abnormalities are present, such as oligohydramnios, abnormal cardiotocography, maternal preeclampsia, or abnormal UA or MCA Doppler findings. Delivery decisions based on UCR alone should await level-1 evidence from randomized controlled trials. ■

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