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# Fetal Doppler to predict cesarean delivery for non-reassuring fetal status in the severe small-for-gestational-age fetuses of late preterm and term

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**Objective**
To evaluate the significance of fetal Doppler parameters in predicting adverse neonatal outcomes and the risk of cesarean delivery due to non-reassuring fetal status, in severe small for gestational age (SGA) fetuses of late preterm and term gestation.

**Methods**
Fetal brain and umbilical artery (UmA) Doppler parameters of cerebroplacental ratio (CPR) and UmA pulsatility index (PI) were evaluated in a cohort of 184 SGA fetuses between 34 and 41 weeks gestational age, who were less than the 5th percentile. The risks of neonatal morbidities and cesarean delivery due to non-reassuring fetal status were analyzed.

**Results**
Univariate analysis revealed that abnormal CPR was significantly associated with cesarean delivery due to non-reassuring fetal status ($P$=0.018), but not with neonatal morbidities. However, abnormal CPR did not increase the risk of cesarean delivery due to non-reassuring fetal status in multivariate logistic regression analysis. Abnormal CPR with abnormal PI of UmA was associated with low Apgar score at 1 minute ($P$=0.048), mechanical ventilation ($P$=0.013) and cesarean delivery due to non-reassuring fetal status ($P$<0.001), in univariate analysis. It increased risk of cesarean delivery for non-reassuring fetal status (adjusted odds ratio, 7.0; 95% confidence interval, 1.2–41.3; $P$=0.033), but did not increase risk of low Apgar score or mechanical ventilation in multivariate logistic regression analysis.

**Conclusion**
Abnormal CPR with abnormal PI of UmA increases the risk of cesarean delivery for non-reassuring fetal status, in severe SGA fetuses of late preterm and term. Monitoring of CPR and PI of UmA can help guide management including maternal hospitalization and fetal monitoring.

**Keywords:** Infant, small for gestational age; Cerebroplacental ratio; Cesarean section

## Introduction

Small for gestational age (SGA) neonates are classified as those whose weights are below the 10th percentile for their gestational age. Such infants are at increased risk for neonatal morbidity and mortality. However, SGA includes growth restricted and constitutionally small fetuses. Since most adverse outcomes increase in SGA infants who are less than the 3rd or 5th percentile, some authors suggested a definition of SGA as the birth weight <3rd or 5th percentile [1].

Fetal Doppler is a valuable tool in the assessment and man-

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agement of high-risk pregnancies. SGA fetuses with less than 5th percentile might have mild placental insufficiency, which is not reflected in the umbilical artery (UmA) Doppler. It has been suggested that prediction of adverse perinatal outcomes in SGA fetuses with late-onset intrauterine growth restriction can be improved by the combination of middle cerebral artery (MCA) and UmA Doppler [2,3]. As a compensatory mechanism to chronic hypoxia, increased placental resistance and brain sparing effect can result in an abnormal cerebroplacental ratio (CPR), which is the ratio between MCA pulsatility index (PI) and UmA PI [2,4]. Abnormal blood flow in the UmA, MCA or both, can still show normal values of PI whereas CPR can show abnormal values [2].

The main aim of this study was to evaluate whether CPR, with or without other Doppler parameters, can predict adverse perinatal outcomes including the risk of cesarean delivery for non-reassuring fetal status, in severe SGA fetuses (less than 5th percentile) of late preterm and term gestation.

## Materials and methods

This was a retrospective study done on pregnant women, with SGA babies between the stages of late preterm to term. All the women gave birth in Seoul St. Mary's Hospital, between January of 2009 and December of 2015. Ethics approval was obtained from the Institutional Review Boards of The Catholic University of Korea (KC17ZESI0171). Late preterm was defined as 34.0–36.6 gestational weeks and term was defined as 37.0–41.6 gestational weeks. SGA in this study was defined as fetuses with estimated body weight below the 5th percentile for the given gestational age, according to the Korean reference curves for the birth weight by gestational age [5]. Exclusion criteria for this study were stillbirth, multiple gestations, SGA fetus with absence or incomplete result of Doppler ultrasonography in any of UmA and MCA, and major congenital anomalies (defined as life-threatening, disabling, or requiring major surgery, including chromosomal trisomies).

The MCA PI was obtained in a transversal view of the fetal head, at the level of its origin from the circle of Willis. UmA Doppler evaluation was performed by sampling of a free-floating loop of umbilical cord and the PI was obtained. CPR was calculated by dividing the MCA PI by the UmA PI. A normal CPR was defined as a value greater than 1.08 [6]. Abnormal PI of UmA Doppler was defined as greater than the 95th percentile for gestational age [7]. Doppler indices with confirmed abnormal values at least 24 hours apart were considered as abnormal. In all cases, only the last examination within 24 hours before the onset of labor induction or cesarean delivery between 34 and 41 weeks' gestation was included in the analysis. Patients were divided into 3 study groups based on the Doppler findings. Group A had normal CPR and was the reference group. Group B had abnormal CPR with normal UmA PI. Group C had abnormal CPR and abnormal UmA PI. Demographic characteristics included maternal age, gestational age, prepregnancy maternal body mass index (BMI), birth weight, parity, fetal gender, complications during pregnancy (diabetes mellitus [DM], gestational hypertension, chorioamnionitis), premature preterm rupture of membrane (PPROM), rate of cesarean section, and oligohydramnios (defined as amniotic fluid index <5). Chorioamnionitis was defined as pathologically proven chorioamnionitis. The following neonatal outcomes were analyzed: Apgar score at 1 and 5 minutes after birth, admission to the neonatal intensive care unit (NICU) within 48 hours after birth, respiratory distress syndrome (RDS), mechanical ventilation within 48 hours after birth, sepsis, seizure, intracranial hemorrhage (ICH), feeding difficulty, neonatal death, metabolic acidosis, and meconium staining.

Indication of cesarean delivery for non-reassuring fetal status was based on abnormal fetal heart rate tracing [8]. Briefly, continuous fetal heart rate monitoring was performed and tracings were classified as normal, suspicious, or abnormal according to the presence, type, and length of decelerations, bradycardia, tachycardia, and the assessment of variability [8]. Sepsis included both suspected infections (with clinical findings suggesting infection) and proven infections (as confirmed in a subgroup of neonates with positive cultures of blood, cerebrospinal fluid, or urine obtained by catheterization or suprapubic aspiration; cardiovascular collapse; or an unequivocal radiograph confirming infection in a neonate with clinical sepsis). Metabolic acidosis was defined as UmA pH <7.15 or base excess >12 mEq/L in the newborn. The listed complications were chosen only when diagnosed by a pediatrician. We constructed a composite morbidity 1 with inclusion of at least one of the following adverse outcomes: NICU admission, RDS, mechanical ventilation, sepsis, seizure, ICH, metabolic acidosis and feeding difficulties, and a composite morbidity 2 with inclusion of at least one of the

following adverse outcomes: NICU admission, RDS, mechanical ventilation, sepsis, seizure, ICH, and metabolic acidosis.

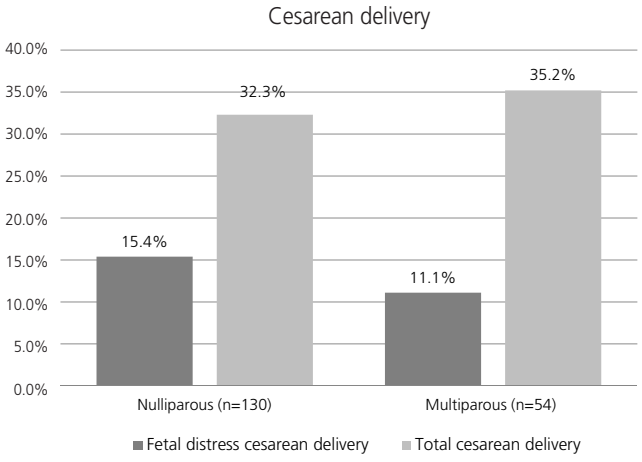


**Fig. 1.** Overall cesarean section rates and cesarean section rates due to non-reassuring fetal status, in multiparous and nulliparous women. Of 184 small-for-gestational-age fetuses, 130 were nulliparous and 54 were multiparous pregnancies. Of the 130 nulliparous women, 42 (32.3%) had cesarean section. Twenty (47.6%) of them received cesarean section due to non-reassuring fetal status. Among the multiparous women (n=54), 19 (35.2%) had cesarean section and 6 (31.6%) of them received cesarean section due to non-reassuring fetal status.

### Statistical analyses

Statistical analyses were performed using SPSS version 18.0 (SPSS, Chicago, IL, USA) and statistical significance was set as a *P*-value <0.05, 2-tailed. All the statistical comparisons were performed with reference group (A: normal CPR). Categorical data are presented as number (%) and compared using $\chi^2$ test or Fisher's exact test. Continuous variables are presented as mean±standard deviation. To assess independent predictors of adverse perinatal outcome, we calculated odds ratios (ORs) and 95% confidence intervals (CIs) using logistic regression models, adjusted by maternal age, prepregnancy maternal BMI, gestational age, birth weight, parity, neonatal sex, DM, gestational hypertension, PPROM, chorioamnionitis, and oligohydramnios.

## Results

### 1. Clinical characteristics

Among 404 singleton pregnancies with SGA fetuses at late preterm and term, a total of 184 pregnancies with complete results of Doppler ultrasonography in UmA and fetal MCA were included for analysis. Of 184 SGA fetuses, 130 were nulliparous and 54 were multiparous pregnancies. Among nulliparous women (n=130), 42 (32.3%) had a cesarean section (Fig. 1).

**Table 1.** Demographic characteristics of mothers and neonates

| Characteristics | Normal CPR (n=140) | Abnormal CPR and normal UmA PI (n=36) | *P*-value | Abnormal CPR and abnormal UmA PI (n=8) | *P*-value |
|---|---|---|---|---|---|
| Maternal age (yr) | 33.1±3.7 | 34.4±4.1 | 0.033 | 35.8±4.6 | 0.033 |
| GA at delivery (wk) | 38.7±1.4 | 38.7±1.6 | 0.125 | 38.6±1.5 | 0.567 |
| Prepregnancy maternal BMI (kg/m$^2$) | 20.4±2.7 | 20.4±2.6 | 0.958 | 20.6±1.6 | 0.839 |
| Weight at delivery (g) | 2,363.6±289.2 | 2,318.1±317.4 | 0.025 | 1,902.4±434.7 | 0.183 |
| Nulliparity | 100 (71.4) | 26 (72.2) | 0.680 | 4 (50) | 0.619 |
| Male | 54 (38.6) | 23 (63.9) | 0.008 | 4 (50) | 0.023 |
| DM | 7 (5) | 3 (8) | 0.130 | 0 | 0.319 |
| Gestational hypertension | 15 (10.7) | 5 (13.9) | 0.354 | 2 (25) | 0.444 |
| Chorioamnionitis | 0 | 0 | 0.239 | 1 (12.5) | 0.000 |
| PPROM | 3 (2.1) | 0 | 0.581 | 0 | 0.619 |
| Cesarean section | 43 (30.7) | 12 (33.3) | 0.210 | 5 (75) | 0.035 |
| Oligohydramnios | 19 (13.6) | 6 (16.7) | 0.451 | 2 (25) | 0.628 |

Data are presented as mean±standard deviation or number (%).
CPR, cerebroplacental ratio; UmA, umbilical artery; PI, pulsatility index; GA, gestational age; BMI, body mass index; DM, diabetes mellitus; PPROM, preterm premature rupture of membrane.

Twenty (47.6%) of them received a cesarean section due to non-reassuring fetal status (Fig. 1). Among the multiparous women (n=54), 19 women (35.2%) had a cesarean section, with 6 women (31.6%) among them due to non-reassuring fetal status. Of the 184 pregnancies, 140 had a normal CPR (group A) and 44 had an abnormal CPR. In pregnancies with abnormal CPR (n=44), 36 pregnancies showed normal UmA PI (group B), and 8 pregnancies showed an abnormal UmA PI (group C). Demographic characteristics of mothers and neonates are shown in Table 1. There were no significant differences in the GA at delivery, prepregnancy maternal BMI, birth weight, parity, incidences of DM, gestational hypertension, PPROM, and oligohydramnios, between groups A and B, and groups A and C. There were significant differences in maternal age, neonatal sex, and incidences of chorioamnionitis and cesarean section, between groups A and C, but not in between groups A and B.

## 2. Perinatal outcomes

### 1) Neonatal adverse outcomes

Abnormal CPR values were not related to neonatal morbidities such as low Apgar score, NICU admission, RDS, mechanical ventilation, sepsis, seizure, ICH, feeding difficulty, neonatal death, metabolic acidosis, and meconium staining. In the univariate analysis, the abnormal CPR values with abnormal UmA PI were associated with low Apgar score (less than 7) at 1 minute after birth ($P$=0.048) and mechanical ventilation ($P$=0.013). However, abnormal CPR values regardless of abnormal UmA PI did not increase the risk of mechanical ventilations within 24 hours after birth, in the multivariate logistic regression analysis.

### 2) Cesarean section due to non-reassuring fetal status

Abnormal CPR was related with cesarean delivery due to non-reassuring fetal status ($P$=0.018 between groups A and B; $P$<0.001

**Table 2.** Adverse perinatal outcomes in small-for-gestational-age pregnancies, according to Doppler finding

| Outcomes | Group A (n=140) | Group B (n=36) | *P*-value | Group C (n=8) | *P*-value |
|---|---|---|---|---|---|
| Apgar score at 1 min | 7.6±1.4 | 7.6±1.1 | 0.288 | 6.3±1.6 | 0.224 |
| Apgar score at 5 min | 8.9±1.0 | 8.8±0.8 | 0.187 | 8.3±0.7 | 0.205 |
| Apgar score at 1 min <7 | 25 (17.9) | 5 (13.9) | 0.804 | 4 (50) | 0.048 |
| Apgar score at 5 min <7 | 5 (3.6) | 0 | 0.585 | 0 | 1.000 |
| NICU admission | 41 (29.3) | 8 (22.2) | 0.974 | 5 (62.5) | 0.077 |
| RDS | 3 (2.1) | 2 (5.6) | 0.393 | 0 | 0.473 |
| Mechanical ventilation | 5 (3.6) | 1 (2.8) | 0.357 | 2 (25.0) | 0.013 |
| Sepsis | 9 (6.4) | 4 (11.1) | 0.548 | 0 | 0.451 |
| Seizure | 4 (2.9) | 2 (5.6) | 0.231 | 1 (12.5) | 0.317 |
| Any ICH | 5 (3.6) | 0 | 0.672 | 1 (12.5) | 0.181 |
| Feeding difficulties | 3 (2.1) | 2 (5.6) | 0.393 | 0 | 0.473 |
| Neonatal death | 0 | 0 | - | 0 | - |
| Metabolic acidosis | 9 (6.4) | 1 (2.8) | 0.289 | 0 | 0.542 |
| Meconium staining | 21 (12.9) | 3 (8.3) | 0.574 | 0 | 0.596 |
| Composite morbidity 1 | 43 (30.7) | 11 (30.6) | 0.484 | 5 (62.5) | 0.169 |
| Composite morbidity 2 | 43 (30.7) | 9 (25.0) | 0.890 | 5 (62.5) | 0.115 |
| Cesarean section due to non-reassuring fetal status | 15 (10.7) | 6 (16.7) | 0.018 | 5 (62.5) | <0.001 |

Data are presented as mean±standard deviation or number (%). Group A: normal CPR; Group B: abnormal CPR with normal UmA PI; Group C: abnormal CPR with abnormal UmA PI. Composite morbidity 1: NICU admission, RDS, mechanical ventilation, sepsis, seizure, ICH, metabolic acidosis, feeding difficulties; Composite morbidity 2: NICU admission, RDS, mechanical ventilation, sepsis, seizure, ICH, metabolic acidosis.
CPR, cerebroplacental ratio; UmA, umbilical artery; PI, pulsatility index; NICU, neonatal intensive care unit; RDS, respiratory distress syndrome; ICH, intracranial hemorrhage.

between groups A and C) in univariate analysis (Table 2). In multivariate logistic regression analysis adjusted by maternal age, gestational age, prepregnancy maternal BMI, birth weight, parity, neonatal sex, maternal DM, gestational hypertension, PPROM, chorioamnionitis, and oligohydramnios, abnormal CPR without abnormal UmA PI did not increase the risk of cesarean delivery for non-reassuring fetal status (adjusted OR [aOR], 1.4; 95% CI, 0.5–4.2; *P*=0.560) (Table 3). However, abnormal CPR with abnormal UmA PI demonstrated an increased risk of cesarean delivery for non-reassuring fetal status (aOR, 7.0; 95% CI, 1.2–41.3; *P*=0.033).

## Discussion

In this study, abnormal CPR with normal UmA PI was significantly associated with cesarean delivery due to non-reassuring fetal status, but not with neonatal morbidities in univariate analysis. However, abnormal CPR with normal UmA PI did not increase risk of cesarean delivery due to non-reassuring fetal status in multivariate logistic regression analysis. Abnormal CPR with abnormal PI of UmA was associated with low Apgar score at 1 minute, mechanical ventilation and cesarean delivery due to non-reassuring fetal status in univariate analysis. Abnormal CPR with abnormal PI of UmA increased risk of cesarean delivery for non-reassuring fetal status (aOR, 7.0; 95% CI, 1.2–41.3; *P*=0.033), but did not increase risk of low Apgar score or mechanical ventilation in multivariate logistic regression analysis.

CPR was initially described in the 1980s to assess both placental function and fetal response by evaluating the UmA and MCA Doppler [9]. The predictive role of CPR has been investigated; the combination of the UmA Doppler, EFW and CPR was reported to be highly predictive of stillbirth and perinatal loss [10]. Others demonstrated that the CPR at term has a strong association with adverse obstetric and perinatal outcomes [11].

Despite advances in the antenatal surveillance tests, the optimal strategy for fetal surveillance and the timing of delivery of pregnancies complicated by SGA or fetal growth restriction (FGR) is contentious [12]. CPR is an emerging parameter that may be an important predictor of adverse pregnancy outcome in fetuses suspected as SGA or FGR. SGA with abnormal CPR has been associated with a higher incidence of the following when compared with fetuses with a normal CPR: lower gestational age at birth, lower birth weight, higher rate of cesarean delivery for fetal distress in labor, higher rate of Apgar scores <7 at 5 minutes, an increased rate of neonatal acidosis, an increased rate of NICU admissions, a higher rate of adverse neonatal outcome, and a greater incidence of perinatal death [13-18]. These findings showed that CPR is an earlier predictor of adverse outcome than the biophysical profile, UmA, or MCA [13,16].

Current American College of Obstetrician and Gynecologists guidelines of fetal arterial Doppler evaluation in fetal growth restriction utilize UmA Doppler exclusively to determine the

**Table 3.** Adjusted odds ratios (aORs) of adverse perinatal outcomes according to Doppler finding, using multivariate logistic regression analyses

| Outcomes | Group A vs. group B | | Group A vs. group C | |
|---|---|---|---|---|
| | aOR (95% CI) | *P*-value | aOR (95% CI) | *P*-value |
| Low Apgar score at 1 min | 0.6 (0.6–1.1) | 0.285 | 1.1 (0.8–1.6) | 0.206 |
| NICU admission | 0.5 (0.2–1.3) | 0.145 | 1.5 (0.3–9.5) | 0.635 |
| Mechanical ventilation | 0.4 (0.1–1.2) | 0.465 | 5.3 (0.5–51.9) | 0.150 |
| Composite morbidity 1 | 0.7 (0.3–1.8) | 0.477 | 1.6 (0.3–9.7) | 0.326 |
| Composite morbidity 2 | 0.5 (0.2–1.4) | 0.200 | 1.6 (0.3–9.7) | 0.335 |
| Cesarean section due to non-reassuring fetal status | 1.4 (0.5–4.2) | 0.56 | 7.0 (1.2–41.3) | 0.033 |

Adjusted by maternal age, gestational age, prepregnancy maternal body mass index, birth weight, parity, neonatal sex, maternal DM, gestational hypertension, PPROM, chorioamnionitis, oligohydramnios. Group A: normal CPR; Group B: abnormal CPR with normal UmA PI; Group C: abnormal CPR with abnormal UmA PI. Composite morbidity 1: NICU admission, RDS, mechanical ventilation, sepsis, seizure, ICH, metabolic acidosis, feeding difficulties; Composite morbidity 2: NICU admission, RDS, mechanical ventilation, sepsis, seizure, ICH, metabolic acidosis.
aORs, adjusted odds ratios; CPR, cerebroplacental ratio; UmA, umbilical artery; PI, pulsatility index; CI, confidence interval; NICU, neonatal intensive care unit; RDS, respiratory distress syndrome; ICH, intracranial hemorrhage.

timing of delivery [19]. A role for CPR in the management of fetuses with late-onset SGA has been suggested where both umbilical Doppler and cardiotocography are not reliable in predicting an adverse perinatal event and may predict an increased chance of perinatal events also in apparently normal-sized fetuses [20,21]. This may suggest a non-adaptive response to subclinical placental insufficiency and reduced tolerance of such a fetus to labor hypoxia or to prolongation of gestation. In this study, abnormal CPR without abnormal UmA PI was not an independent risk factor, but abnormal CPR with abnormal UmA PI was an independent factor for adverse pregnancy outcome or cesarean section due to non-reassuring fetal heart rate in multivariate logistic regression analysis. Because this study included SGA pregnancies less than 5th percentile, fetal growth restriction cases with a poor prognosis among SGA cases might be included. When clinicians encounter a suspected SGA (less than 5th percentile) case with diastolic blood flow of UmA after 34 weeks, the decision for delivery timing and method can be complicated. The present findings indicate that clinicians should pay attention to the risk of non-reassuring fetal heart rate in cases with abnormal CPR with abnormal UmA PI.

The study has several limitations. It is a retrospective study, with the inherent disadvantage of the limited ability to control potential confounding factors like underlying maternal disease and information bias. We performed logistic regression analysis after adjusting variables to overcome this limitation. The second limitation is that the sample size was small, especially in groups B and C. Despite these limitations, this study suggested a CPR as a useful Doppler index when it is combined with UmA Doppler index, in severe SGA pregnancies.

In conclusion, abnormal CPR with abnormal PI of UmA increases the risk of cesarean delivery for non-reassuring fetal status in severe SGA fetuses of late preterm and term. In cases with suspected SGA, the monitoring of CPR and PI of UmA can help guide management decisions, such as maternal hospitalization and aggressive fetal monitoring. Prospective studies with larger sample size will be helpful in confirming the present findings.

## Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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