Amniotic-Umbilical-to-Cerebral Ratio – A Novel Ratio Combining Doppler Parameters and Amniotic Fluid Volume to Predict Adverse Perinatal Outcome in SGA Fetuses At Term

Prädiktion eines adversen perinatalen Outcomes mittels Amniotic-Umbilical-to-Cerebral-Ratio bei SGA-Föten am Termin

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ABSTRACT

Purpose Introduction of a novel ratio – the amniotic-umbilical-to-cerebral ratio (AUCR) – to predict adverse perinatal outcome in SGA fetuses at term and comparison of its predictive accuracy with established parameters.

Materials and Methods This retrospective cohort study included 165 singleton pregnancies with SGA fetuses (birth weight < 10th percentile) at term. Cases with planned vaginal delivery and documented pulsatility indices (PI) of the umbilical artery (UA), middle cerebral artery (MCA), and single deepest pocket (SDP) were included. CPR was calculated as the ratio between MCA PI and UA PI, UCR as the ratio between UA PI and MCA PI. AUCR was defined as follows: SDP/(UA PI/MCA PI). Adverse perinatal outcomes were defined as operative intervention (OI), OI due to fetal distress, admission to the neonatal intensive care unit (NICU), and composite adverse perinatal outcome (CAPO). Associations between Doppler parameters and these outcomes were estimated using regression analyses.

Results OI was statistically significantly associated with UCR, SDP, and AUCR, whereas no association was observed for UA PI, MCA PI, and CPR. Fetuses requiring OI due to fetal distress revealed a significantly higher UA PI and UCR as well as a lower MCA PI, CPR, and AUCR. With regard to NICU admission and CAPO, a significantly higher UA PI and lower CPR were found. Furthermore, a significant association was shown for SDP, UCR, and AUCR. AUCR achieved the best area under the curve for all outcome parameters.

Conclusion AUCR leads to an improvement in the prediction of unfavorable outcome in SGA fetuses at term. Furthermore, results of our study show that UCR might be superior to CPR.

ZUSAMMENFASSUNG

Ziel Beschreibung einer neuen Ratio – der Amniotic-Umbilical-to-Cerebral-Ratio (AUCR) – zur Prädiktion eines ungünstigen Geburtsoutcomes bei SGA-Föten am Geburtstermin und Vergleich mit etablierten Parametern.

Material und Methoden Retrospektive Kohortenstudie mit 165 SGA-Föten (Geburtsgewicht < 10. Perzentile) am Geburtstermin. Fälle mit geplanter Spontangeburt und dokumentierten Pulsatilitätsindizes (PI) der A. umbilicalis (UA), A. cerebri media (MCA) und tiefstem Fruchtwasserdepot (single deepest pocket, SDP) wurden eingeschlossen. Die CPR wurde als Quotient aus MCA und UAPI berechnet, die UCR umgekehrt. Die AUCR wurde wie folgt definiert: AUCR = SDP/(UA PI/MCA PI). Die Assoziationen zwischen Dopplerparametern, operativer Intervention (OI), OI bei pathologischem CTG, Verlegung auf die neonatologische Intensivstation (NICU) und kombiniertem adversem Outcome (CAPO) wurden mittels Regressionsanalyse ausgewertet.

Ergebnisse Eine OI war signifikant mit der UCR, dem SDP und der AUCR assoziiert, wohingegen kein Zusammenhang für UA PI, MCA PI und CPR gefunden wurde. Föten mit OI bei pathologischem CTG hatten signifikant höhere UA PI, niedrigere MCA PI und niedrigere CPR. Weiterhin war die UCR signifikant höher und die AUCR signifikant niedriger. Signifikant höhere UA PI und niedrigere CPR zeigten sich bei NICU und CAPO. Weiterhin bestand ein signifikanter Zusammenhang auch für SDP, UCR und AUCR. Die beste Area under the curve wurde bei allen Outcome-Parametern durch die AUCR erreicht.

Schlussfolgerungen Die AUCR verbessert die Prädiktion eines ungünstigen Outcomes bei SGA-Föten am Termin. Außerdem zeigt unsere Studie, dass die UCR der CPR überlegen zu sein scheint.

Introduction

Impaired fetal growth due to placental insufficiency is usually assessed by combining fetal biometry with maternal (uterine artery) and/or fetal (umbilical artery (UA), middle cerebral artery (MCA)) Doppler parameters [1, 2]. Small-for-gestational-age (SGA) is a statistical value including fetuses that can either be constitutionally or pathologically – referred as fetal growth restriction (FGR) – small. Precise distinction between SGA and FGR still remains an unresolved issue, although consensus definitions of leading experts in this field were recently published [3]. Especially, from 37 weeks of gestation onwards FGR fetuses are at increased risk of being undetected prenatally with the consecutive risk of adverse perinatal outcome [4]. Although sonography is part of the daily obstetrical routine, screening for compromised fetuses at term still remains a major challenge within various collectives of fetuses [5–9].

Studies investigating the ratio of MCA pulsatility index (PI) to UA PI – referred to as the cerebroplacental ratio (CPR) – have shown heterogeneous results regarding the prediction of adverse perinatal outcome [7, 10, 11]. Interestingly, the reversal of this ratio – termed the umbilical-to-cerebral ratio (UCR) – seems to be a more potent discriminator in estimating progressive fetal hypoxia [12, 13].

Another approach for the evaluation of fetal wellbeing is sonographic determination of amniotic fluid volume (AFV). Amniotic liquor generates mainly from the fetal urine and lung liquid. On the one hand, amniotic fluid balance depends on resorption through fetal swallowing and absorption through the amniotic layer into fetal blood vessels of the placenta [14]. On the other hand, AFV relies on the distribution of blood flow within the fetal compartment, especially on kidney perfusion and following fetal urine production [15]. The single deepest pocket technique (SDP) and amniotic fluid index (AFI) are widely used in routine obstetric care to quantify AFV. SDP is superior in reducing unnecessary induction of labor (IOL) and cesarean deliveries (CD) compared to AFI. Oligohydramnios (SDP < 2 cm) is known to be correlated with adverse perinatal outcome [16, 17]. Although a decrease of AFV is associated with an increased risk for an unfavorable perinatal outcome [18], inclusion of AFV into an amniotic-feto-placental ratio has never been the subject of clinical trials. We hypothesized that distribution changes of fetal blood flow mirrored by altered resistance of fetal vasculature are associated with lower AFV, and that integration of the SDP into the UCR might be of higher predictive accuracy. Therefore, we implemented a new amniotic-umbilical-to-cerebral ratio (AUCR) and compared its association to adverse perinatal outcomes with other established parameters, such as CPR and UCR within a population of SGA fetuses at term.

Methods

Study design

This retrospective cohort study, performed in a single tertiary referral center from January 2016 through March 2019, included singleton pregnancies with SGA fetuses (birth weight < 10th percentile) and planned vaginal delivery ≥ 37 weeks of gestation. Cases with measurements of UA PI, MCA PI and SDP assessed within 7 days prior to delivery were included. Women with elective CD, premature rupture of membranes (PROM), or cervical dilatation > 4 cm on the date of the ultrasound scan or scan-to-delivery interval > 7 days were excluded. We also excluded pregnancies complicated by fetal anomaly, intrauterine fetal death, or evidence of intrauterine infection. Cases were identified within our electronic database (ViewPoint 5.6.26.148; ViewPoint Bildverarbeitung GmbH, Weßling, Germany).

The study was approved by our local Ethics committee.

Baseline characteristics

Data on maternal and fetal characteristics were collected from our obstetrical database.

Doppler sonography and evaluation of amniotic fluid volume

All examinations were performed with Voluson machines (GE Medical Systems, Zipf, Austria).

Gestational age was calculated from the last menstrual period and was confirmed by first-trimester crown-rump length measurements.

Doppler ultrasound examinations were conducted routinely in every patient after arriving at our department. MCA Doppler parameters were recorded as described previously [19]. UA Doppler measurements were performed by picking a free-floating loop of the umbilical cord.

CPR was calculated as the ratio between MCA PI and UA PI [20]. UCR was built conversely as the ratio between UA PI and MCA PI. All Doppler indices were adjusted for gestational age (GA).

The SDP technique [21] was used to estimate AFV.

AUCR was calculated as the ratio of SDP to UCR: AUCR = SDP/(UA PI/MCA PI).

Birth weight percentiles were calculated using the Intergrowth 21st standard [22].

▶ **Table 1** Demographic characteristics of the study population.

Parameter	All deliveries	SVD	OI	OI due to fetal distress	NICU	CAPO
Number (%)	165 (100)	114 (69.1)	51 (30.9)	34 (20.6)	54 (32.7)	57 (34.5)
Maternal age: years, median (range)	31 (20–44)	31 (20–44)	31 (20–41)	32 (25–40)	31 (20–41)	31 (20–41)
Gravida: median (range)	1 (1–9)	2 (1–9)	1 (1–5)	1 (1–5)	1 (1–6)	1 (1–6)
Para: median (range)	1 (1–6)	1 (1–6)	1 (1–3)	1 (1–3)	1 (1–3)	1 (1–3)
Maternal BMI: kg/m^2, median (range)	31.0 (20.0–44.0)	27.2 (20.6–43.4)	27.7 (21.6–43.8)	27.8 (21.6–43.8)	27.1 (20.6–43.8)	27.3 (20.6–43.8)
Ethnicity: number (%)						
▪ Europe	84 (50.9)	64 (54.2)	20 (39.2)	14 (41.2)	27 (50.0)	29 (50.9)
▪ others	81 (49.1)	54 (45.8)	31 (60.8)	20 (58.8)	27 (50.0)	28 (49.1)
Gestational diabetes: number (%)	14 (8.5)	10 (8.8)	4 (7.8)	3 (8.8)	3 (5.6)	3 (5.3)
Hypertensive pregnancy disorders: number (%)	9 (5.5)	8 (7.0)	1 (2.0)	0 (0.0)	1 (1.9)	1 (1.8)
Nicotine abuse: number (%)	14 (8.5)	12 (10.5)	2 (3.9)	2 (5.9)	2 (3.7)	3 (5.3)
Pre-existing diseases: number (%)						
Chronic hypertension	19 (11.5)	14 (12.3)	5 (9.8)	5 (14.7)	7 (13.0)	7 (12.3)
Bronchial asthma	4 (2.4)	2 (1.8)	2 (3.9)	1 (2.9)	3 (5.6)	3 (5.3)
Obesity	16 (9.7)	8 (7.0)	8 (15.7)	8 (23.5)	7 (13.0)	8 (14.0)
Thrombophilia	8 (4.8)	6 (5.3)	2 (3.9)	0 (0.0)	4 (7.4)	4 (7.0)
Hypothyroidism	11 (6.7)	8 (7.0)	3 (5.9)	2 (5.9)	3 (5.6)	3 (5.3)

GA: gestational age; SVD: spontaneous vaginal delivery; OI: operative intervention; NICU: neonatal intensive care unit; CAPO: composite adverse perinatal outcome.

Clinical management

Clinical management followed local protocols and guidelines as described in a recent publication [6]. Induction of labor was performed as a sequential approach [23]. First, we used a cervical double-balloon catheter system (Cook Medical, Cervical Ripening Balloon, Cook OB/GYN, Bloomington, Indiana, USA), which was inserted in the evening and was removed after 12 hours. If labor did not start after mechanical ripening, we continued IOL by oral application of misoprostol within 3 hours after removal of the mechanical device. On the first day, dosages were 50 µg with repeated administration after 4 and 8 hours. The following day, IOL was continued with a dosage of 100 µg up to three times per day. In cases of previous CD, we applied prostaglandin E2 instead of misoprostol. Both medications, misoprostol, and prostaglandin E2 after CD, were only used after written informed consent of patients about off-label use.

Outcome definitions

SGA was defined as birth weight < 10th percentile. The following outcome parameters were examined: "Operative intervention (OI)" was defined as secondary CD or operative vaginal delivery (OVD). In analogy, CD and OVD due to fetal distress were summarized to "OI due to fetal distress". Furthermore, we analyzed the 5-min Apgar score, UA birth pH ≤ 7.10, or admission to neonatal intensive care unit (NICU).

UA pH ≤ 7.10 and/or 5-minute Apgar score < 7 and/or NICU admission were defined as "composite adverse perinatal outcome (CAPO)" [24].

The diagnosis of fetal distress was based on CTG abnormalities, the presence of meconium stained liquor and/or abnormal fetal scalp blood samples. Outcome data were collected from our obstetric database.

The small sample size of cases with UA birth pH ≤ 7.10 (n = 2) and a 5-min Apgar score < 7 (n = 6) precluded a formal evaluation of association with adverse perinatal outcome.

Statistical analysis

Sample data are described by median values with interquartile ranges for continuous variables and numbers with percentages for categorical variables. These numbers are reported for both the complete sample and for outcome-specific subgroups.

To compare and assess the discriminatory accuracy of different Doppler sonography values, we used an exploratory analysis approach. First, we computed the mean values for all sonography

▶ **Table 2** Obstetrical and fetal characteristics of the study population.

Parameter	All deliveries	SVD	OI	OI due to fetal distress	NICU	CAPO
Number (%)	165 (100)	114 (69.1)	51 (30.9)	34 (20.6)	54 (32.7)	57 (34.5)
Induction of labor: number (%)	125 (75.8)	88 (77.2)	37 (72.5)	28 (82.4)	45 (83.3)	47 (82.5)
Pathological CTG: number (%)	53 (32.1)	19 (16.7)	34 (66.7)	34 (100.0)	29 (53.7)	29 (50.9)
Oxytocin use for slow progress in labor: number (%)	28 (17.0)	18 (15.8)	10 (19.6)	6 (17.6)	8 (14.8)	8 (14.0)
GA at scan: weeks, median (range)	39.0 (36.4–42.1)	39.9 (36.6–41.4)	39.6 (36.4–42.1)	39.5 (36.7–41.4)	38.0 (36.4–41.4)	38.0 (36.4–41.4)
interval scan to delivery: days, median (range)	1 (0–7)	2 (0–7)	1 (0–5)	1 (0–4)	2 (0–6)	2 (0–6)
GA at delivery: weeks, median (range)	39.4 (37.0–42.4)	39.3 (37.1–41.7)	39.7 (37.0–42.4)	39.8 (37.0–41.7)	38.3 (37.0–41.7)	38.3 (37.0–41.7)
Fetal sex male: number (%)	90 (54.5)	47 (50.0)	33 (64.7)	25 (73.5)	35 (64.8)	36 (63.2)
Birthweight: grams, median (range)	2570 (1570–3140)	2550 (1660–2980)	2610 (1570–3140)	2605 (1620–2930)	2335 (1570–2940)	2370 (1570–2980)

GA: gestational age; SVD: spontaneous vaginal delivery; OI: operative intervention; NICU: neonatal intensive care unit; CAPO: composite adverse perinatal outcome.

indices in all outcome groups and then computed one-by-one logistic regression models with the adverse events as response variables and the corresponding sonography values as predictors. To adjust for potential confounding, we additionally included gestational age as an explanatory variable in each of those models.

For each logistic regression model, we report the resulting adjusted odds ratio (OR) with a 95 % confidence interval and the result of a likelihood ratio test on the null hypothesis OR = 1. The OR quantifies the association between the outcome and the sonography value under consideration. To evaluate discriminatory accuracy, we additionally computed the area under the receiver-operator characteristic curve (AUC) values for each logistic regression model. The AUC reflects the discriminatory accuracy of the sonography values while additionally adjusting for GA.

All statistical analyses were carried out using the R language for statistical computing, version 3.5.1.

Results

We included 165 cases in the analyses. ▶ **Table 1** shows the maternal demographics of the study population while ▶ **Table 2** presents obstetrical and fetal characteristics. The most common indications for IOL were suspected FGR (n = 96; 76.8 %), preeclampsia (n = 6; 4.8 %) and diabetes mellitus (n = 6; 4.8 %) (▶ **Table 3**).

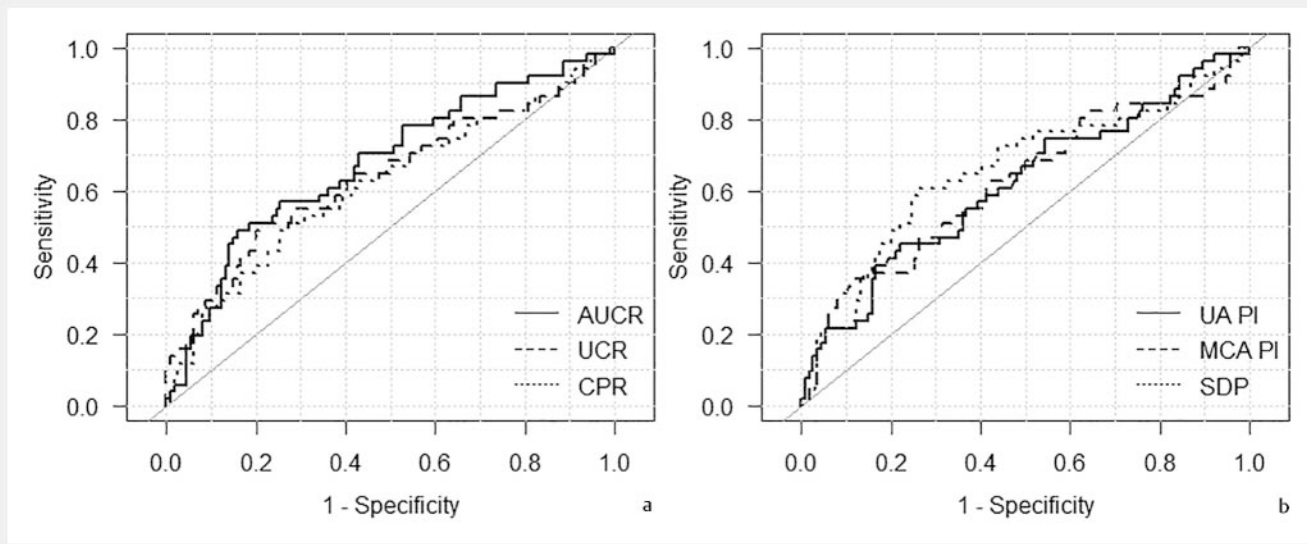
The mean gestational age at ultrasound examination was 39.0 + – 1.3 (36.4 to 42.1) weeks. The mean gestational age at delivery was 39.3 + – 1.3 (37.0 to 42.4) weeks.

▶ **Table 3** Induction of labor – indications.

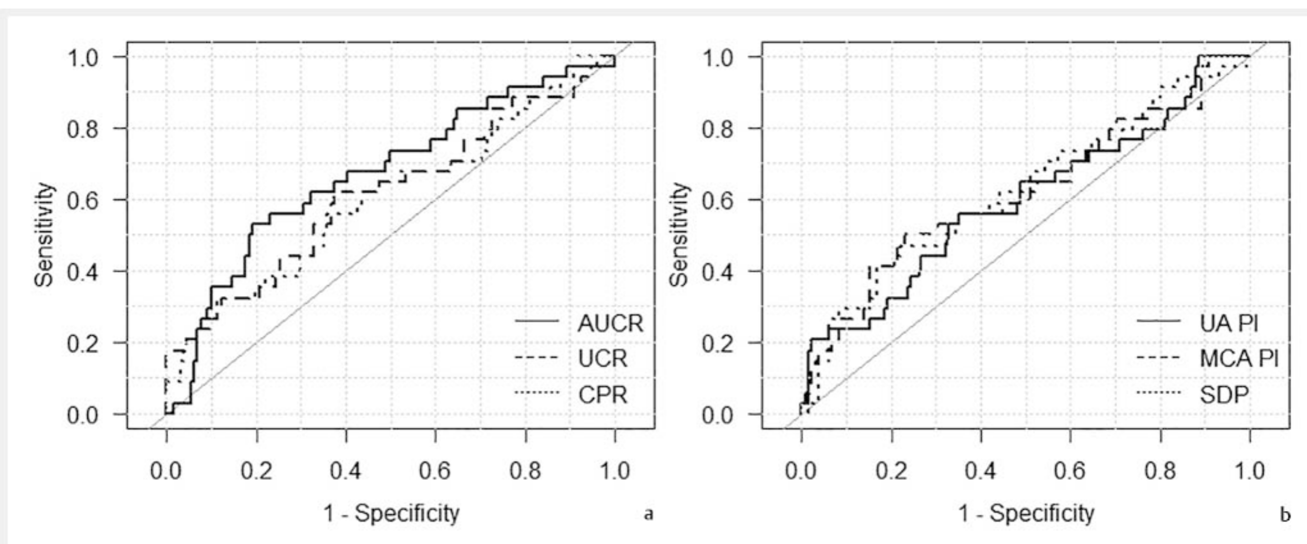
Indication	Number	Percentage
Suspected fetal growth restriction	96	76.8
Preeclampsia	6	4.8
Diabetes mellitus	6	4.8
Oligohydramnios	6	4.8
Suspicious cardiotocography	6	4.8
Other reasons	5	4.0

OI (30.9 %) was not associated with UA PI, MCA PI, and CPR (UA PI: OR 4.06, p = 0.061; MCA PI: OR 0.33; p = 0.082; CPR: OR 0.48; p = 0.083). However, there was a significant correlation with a higher UCR, lower SDP, and lower AUCR (UCR: OR 5.63, p = 0.006; SDP: OR 0.72, p = 0.011; AUCR: OR 0.81; p = 0.003).

In the case of OI due to fetal distress (20.6 %), our data revealed a higher UA PI, lower MCA PI, and lower CPR (UA PI: OR 6.15, p = 0.027; MCA PI: OR 0.20; p = 0.036; CPR: OR 0.35; p = 0.032). Furthermore, we demonstrate a significant association with UCR and AUCR (UCR: OR 8.34, p = 0.002; AUCR: OR 0.81; p = 0.012). Regarding AFV, the SDP tended to be lower in fetuses requiring OI due to fetal distress (OR 0.76; p = 0.065).



▶ **Fig. 1 a, b** Receiver operating characteristics (ROC) curve for the prediction of OI. a AUCR, UCR, CPR. b UA PI, MCA PI, SDP.



▶ **Fig. 2 a, b** Receiver operating characteristics (ROC) curve for the prediction of OI due to fetal distress. **a** AUCR, UCR, CPR. **b** UA PI, MCA PI, SDP.

ROC curve analyses revealed the highest AUC values for AUCR, both for OI (▶ **Fig. 1a, b**) and OI due to fetal distress (▶ **Fig. 2a, b**). Overall, discriminatory accuracy was moderate (▶ **Table 4**).

Risk of NICU admission (32.7 %) and CAPO (34.5 %) results were similar: cases with an unfavorable outcome had a higher UA PI as well as a lower CPR (NICU – UA PI: OR 7.02, $p = 0.022$; CPR: OR 0.29; $p = 0.009$; CAPO – UA PI: OR 7.54, $p = 0.014$; CPR: OR 0.27; $p = 0.004$). The mean values of MCA PI (NICU – MCA PI: OR 0.36; $p = 0.113$; CAPO – OR 0.34; $p = 0.084$) did not differ between both groups. The associations between both outcome parameters and SDP, UCR, as well as AUCR were highly significant (NICU – SDP: OR 0.66; $p = 0.004$; UCR: OR 14.14, $p = 0.001$; AUCR: OR 0.70; $p < 0.001$; CAPO – SDP: OR 0.63; $p = 0.001$; UCR: OR 14.46, $p < 0.001$; AUCR: OR 0.68; $p < 0.001$). Again, the highest AUC values for both NICU (▶ **Fig. 3a, b**) and CAPO (▶ **Fig. 4a, b**) were achieved by AUCR (▶ **Table 4**).

Discussion

This study describes a novel ratio – combining Doppler parameters and SDP – to predict adverse perinatal outcome.

Increasing placental insufficiency leads to redistribution of fetal blood volume – according to the pathophysiological mechanisms described above – to the advantage of cerebral blood flow and disadvantage of kidney perfusion [25]. As reduced kidney blood flow leads to impaired fetal urine production and a subsequent decrease of AFV, we assume an impact on the prediction of adverse perinatal outcome mirrored by AUCR.

▶ **Table 4** Univariate logistic regression analyses for the prediction of adverse perinatal outcome.

Outcome parameter	Parameter	Outcome*	No outcome*	AUC§	Univariate analyses: OR (CI)§	p-value§
OI	UA PI	0.97	0.93	0.617	4.06 (0.94 to 18.23)	0.061
	MCA PI	1.22	1.31	0.624	0.33 (0.08 to 1.14)	0.082
	CPR	1.37	1.47	0.618	0.48 (0.20 to 1.10)	0.083
	UCR	0.84	0.74	0.64	5.63 (1.65 to 21.41)	0.006†
	AUCR	4.07	5.30	0.676	0.81 (0.69 to 0.93)	0.003†
	SDP	2.98	3.59	0.657	0.72 (0.55 to 0.93)	0.011†
OI due to fetal distress	UA PI	1.01	0.92	0.596	6.15 (1.24 to 32.45)	0.027†
	MCA PI	1.19	1.31	0.616	0.20 (0.04 to 0.91)	0.036†
	CPR	1.31	1.47	0.604	0.35 (0.12 to 0.92)	0.032†
	UCR	0.90	0.74	0.614	8.34 (2.23 to 35.88)	0.002†
	AUCR	3.98	5.17	0.670	0.81 (0.67 to 0.96)	0.012†
	SDP	3.01	3.50	0.623	0.76 (0.57 to 1.02)	0.065
NICU	UA PI	1.07	0.88	0.779	7.02 (1.31 to 44.85)	0.022†
	MCA PI	1.27	1.29	0.780	0.36 (0.09 to 1.26)	0.113
	CPR	1.28	1.51	0.788	0.29 (0.11 to 0.74)	0.009†
	UCR	0.91	0.70	0.798	14.14 (2.86 to 83.98)	0.001†
	AUCR	3.83	5.45	0.815	0.70 (0.57 to 0.84)	< 0.001†
	SDP	3.07	3.56	0.792	0.66 (0.48 to 0.88)	0.004‡
CAPO	UA PI	1.06	0.88	0.745	7.54 (1.48 to 45.17)	0.014†
	MCA PI	1.26	1.30	0.744	0.34 (0.09 to 1.15)	0.084
	CPR	1.28	1.52	0.755	0.27 (0.10 to 0.66)	0.004†
	UCR	0.90	0.70	0.764	14.46 (3.08 to 81.48)	< 0.001‡
	AUCR	3.78	5.52	0.793	0.68 (0.56 to 0.82)	< 0.001‡
	SDP	3.02	3.60	0.768	0.63 (0.46 to 0.84)	0.001†

OI: operative intervention; NICU: neonatal intensive care unit; CAPO: combined adverse perinatal outcome; UA: umbilical artery; MCA: middle cerebral artery; CPR: cerebroplacental ratio; UCR: umbilicocerebral ratio; AUCR: amniotic-umbilical-to-cerebral ratio; SDP: single deepest pocket; AUC: area under the curve; OR: odds ratio; ‡ $p < 0.001$.

* mean values.

§ adjusted for gestational age.

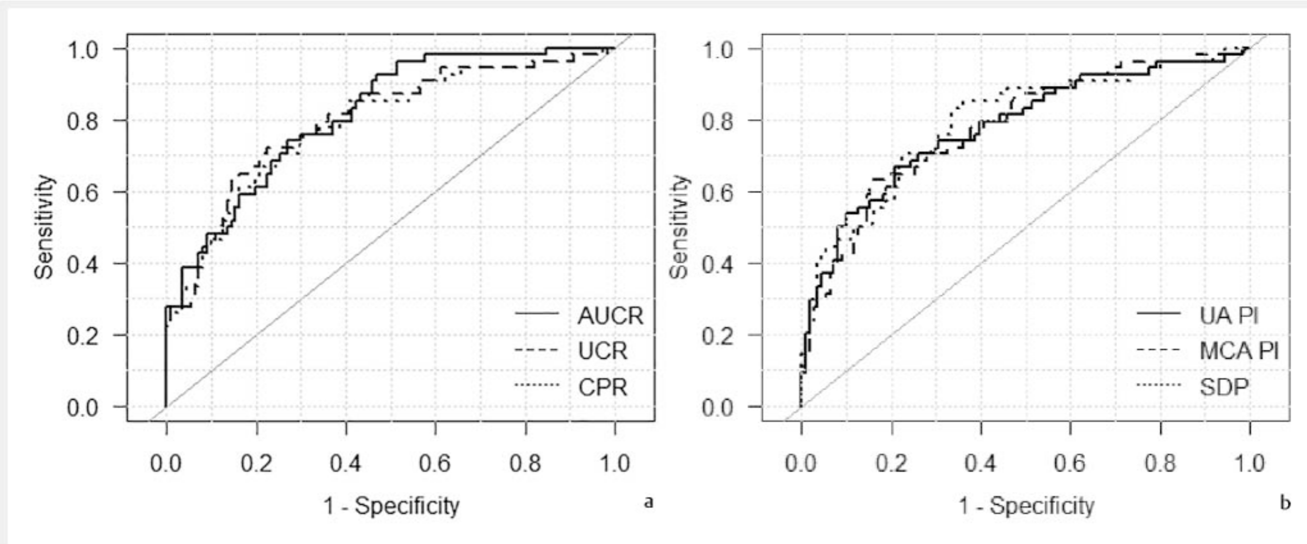
† $p < 0.05$.

Our observations demonstrate that the addition of SDP ameliorates the predictive accuracy of an unfavorable outcome in SGA fetuses at term. Furthermore, our results show that prediction by UCR is superior to CPR.

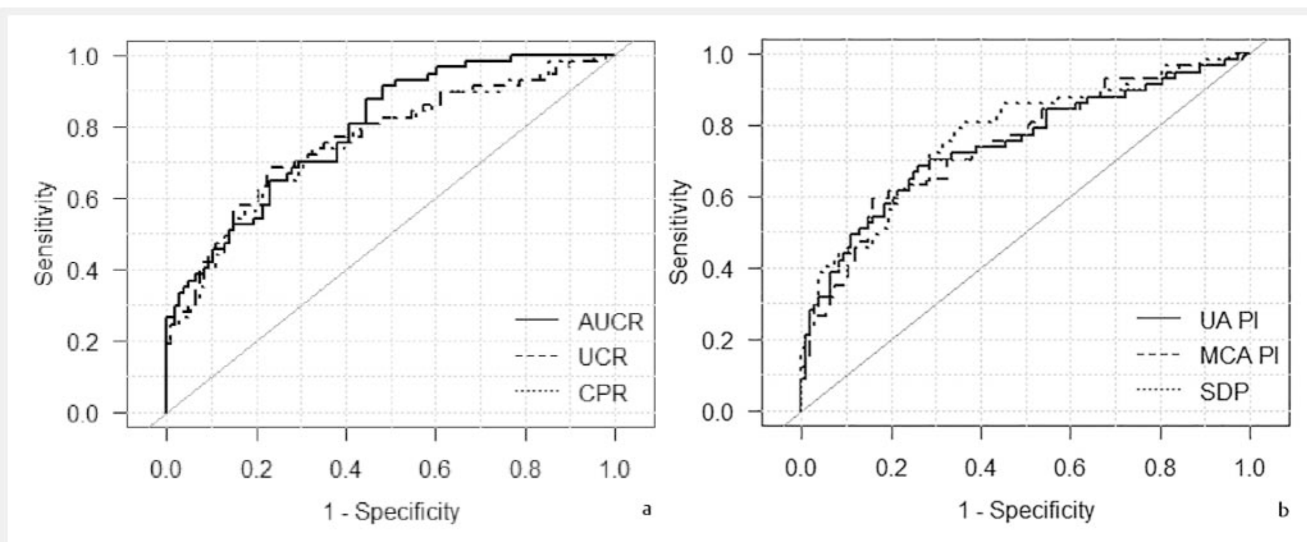
CPR and adverse perinatal outcome

We did not show any significant association between OI and CPR. In contrast, our data reveal a significant correlation with OI due to fetal distress. Recently, a prospective observational study of 1902 women with singleton pregnancies investigated the performance of screening for adverse perinatal outcome by CPR assessment 24 hours before IOL. This study demonstrated that CPR < 10^{th} percentile occurred significantly more often in fetuses requiring CD due to fetal distress compared to those born spontaneously [26]. Another prospective study revealed that late-onset SGA fetuses with a low CPR have a significantly higher risk of emergency CD [27].

Bligh et al. prospectively evaluated the screening performance of CPR < 10^{th} percentile as a predictor of emergency CD and CAPO. They included 483 low-risk pregnancies at term. The predictive value for emergency CD was moderate, while the prediction of CAPO based on a low CPR was poor [24]. Our data showed a significant association between low CPR and CAPO, revealing that SGA fetuses are at higher risk for an unfavorable birth outcome compared to appropriate-for-gestational-age (AGA) babies. Regarding predictive accuracy for adverse perinatal outcome, AUC for CAPO and CD due to fetal distress was better within our study population compared to the Bligh collective, which indi-



► **Fig. 3 a, b** Receiver operating characteristics (ROC) curve for the prediction of NICU admission. **a** AUCR, UCR, CPR. **b** UA PI, MCA PI, SDP.



► **Fig. 4 a, b** Receiver operating characteristics (ROC) curve for the prediction of CAPO. **a** AUCR, UCR, CPR. **b** UA PI, MCA PI, SDP.

cates that CPR might be a superior surrogate marker for impaired placental function in SGA rather than in AGA fetuses.

In our study, NICU admission was significantly associated with low CPR. Another retrospective study analyzed NICU admission rates in 2485 pregnancies, including 25.8 % SGA fetuses and showed that CPR was significantly lower in neonates requiring intensive care compared to infants without NICU admission [8]. Additionally, Gramellini at al. demonstrated a better correlation between CPR and NICU admission, compared to UA and MCA Doppler parameters [28].

UCR and adverse perinatal outcome

Our results suggest that UCR is superior to CPR in the prediction of adverse perinatal outcome in SGA fetuses at term. To date, studies on this ratio are rare. UCR calculation within 14 days prior to delivery showed a sensitivity of 93 % for the detection of SGA infants with adverse perinatal outcome [12].

A secondary analysis of the TRUFFLE study showed a significant association between UCR and 2-year survival without neurodevelopmental impairment in early growth restricted fetuses. Interestingly, there was no association between neurological outcome and CPR [13]. A prospective cohort study evaluated CPR, UCR, and their association to perinatal outcome in 130 patients with gestational diabetes. Doppler measurements of UA and MCA were performed in singleton term pregnancies. MCA PI achieved the best prediction of unfavorable perinatal outcome – including neonatal pH, Apgar score, neonatal weight, and CAPO. While no significant correlations were shown for UA PI and CPR, the results revealed a significant correlation between low birth pH and UCR.

Mathematical considerations might explain the results from studies shown above: UCR is a better discriminator for abnormal values as this ratio has a tendency towards infinity, whereas CPR tends towards zero in fetuses with progressive MCA vasodilatation. Nevertheless, more studies are necessary to confirm these results.

Prognostic accuracy of AUCR for adverse perinatal outcome

Although a decrease of AFV was found to be associated with increasing risk for adverse perinatal outcome [16, 17], an amniotic-feto-placental ratio has never been investigated up to now. Therefore, we implemented a novel ratio – referred to as AUCR.

Decreased AFV (AFI < 5 cm) leads to higher rates of 5-min Apgar scores < 7 [29] and CD due to fetal distress in low-risk pregnancies [30]. In addition, low AFI is an independent predictor of SGA fetuses at birth. Thus, AFV measurement could be useful as a screening method for undetected SGA fetuses at term [30]. As a prospective study demonstrated that the SDP technique – compared to AFI – reduces the frequency of oligohydramnios and consecutively IOL rates, we decided to include SDP as the amniotic fluid parameter in AUCR. Our results highlight that AUCR is significantly correlated with evaluated outcome parameters. Moreover, the predictive value of AUCR is superior to single predictors (UA, MCA, SDP) and other ratios in SGA fetuses. Therefore, we conclude that combining two potent outcome markers could be useful for the prediction of adverse perinatal outcome.

Strengths and limitations

This is the first study that describes a ratio combining fetal Doppler parameters and amniotic fluid volume. However, our study has several limitations, such as the retrospective design and lack of blinding of obstetricians to prenatal examination results. As the presented data were collected during clinical practice by several examiners, there might be some heterogeneity in the data. Furthermore, the number of cases overall is small. Therefore, our results should be evaluated prospectively with a higher number of cases in a future study.

Conclusion

The results of our study suggest that UCR might be superior to CPR with regard to adverse perinatal outcome prediction in SGA infants at term. The combination of SDP and UCR into a ratio leads to a further improvement of predictive value. These findings highlight the importance of fetal monitoring parameters, which are capable of distinguishing between constitutional SGA and its pathological opposite FGR in SGA fetuses at term.

Conflict of Interest

The authors declare that they have no conflict of interest.

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