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An integrated model with classification criteria to predict small-for-gestational-age fetuses at risk of adverse perinatal outcome

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KEYWORDS: Doppler; fetal growth restriction; management; perinatal complications; small-for-gestational age

ABSTRACT

Objective *To develop an integrated model with the best performing criteria for predicting adverse outcome in small-for-gestational-age (SGA) pregnancies.*

Methods *A cohort of 509 pregnancies with a suspected SGA fetus, eligible for trial of labor, was recruited prospectively and data on perinatal outcome were recorded. A predictive model for emergency Cesarean delivery because of non-reassuring fetal status or neonatal acidosis was constructed using a decision tree analysis algorithm, with predictors: maternal age, body mass index, smoking, nulliparity, gestational age at delivery, onset of labor (induced* vs *spontaneous), estimated fetal weight (EFW), umbilical artery pulsatility index (PI), mean uterine artery (UtA) PI, fetal middle cerebral artery PI and cerebroplacental ratio (CPR).*

Results *An adverse outcome occurred in 134 (26.3%) cases. The best performing predictors for defining a high risk for adverse outcome in SGA fetuses was the presence of a CPR < 10^{th} centile, a mean UtA-PI > 95^{th} centile or an EFW < 3^{rd} centile. The algorithm showed a sensitivity, specificity and positive and negative predictive values for adverse outcome of 82.8% (95% CI, 75.1–88.6%), 47.7% (95% CI, 42.6–52.9%), 36.2% (95% CI, 30.8–41.8%) and 88.6% (95% CI, 83.2–92.5%), respectively. Positive and negative likelihood ratios were 1.58 and 0.36.*

Conclusions *Our model could be used as a diagnostic tool for discriminating SGA pregnancies at risk of adverse perinatal outcome.* *Copyright © 2014 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Over the last decade, two different phenotypes of fetal growth restriction (FGR), determined primarily by the gestational age at onset of the disease and the pattern of umbilical artery (UA) Doppler indices, have been characterized[1–4]. In late-onset FGR, cardiovascular abnormalities do not extend beyond the cerebral circulation and normal, or only minimally elevated, UA Doppler indices are usually observed[1,2,4,5].

The distinction between milder cases of late-onset FGR from constitutionally small, but otherwise low-risk, fetuses is a clinical necessity. Since the identification of fetuses with late-onset FGR at an increased risk for adverse perinatal outcome cannot be based on UA Doppler indices, the use of other markers has been proposed. The use of middle cerebral artery (MCA) Doppler indices in this setting is supported by recent studies, which have demonstrated that 15–20% of term small-for-gestational-age (SGA) fetuses with normal UA Doppler have reduced impedance in MCA blood flow, and that this sign is associated with a poorer perinatal outcome[6–8] and neurobehavior, both at birth and at 2 years of age[9,10]. Furthermore, the cerebroplacental ratio (CPR), which combines the pulsatility indices (PI) of the MCA and UA, has been shown to be more sensitive to hypoxia than are its individual components, and it correlates better with adverse outcomes[11–13]. In addition to these Doppler parameters, abnormal uterine artery (UtA) Doppler has been associated with an increased risk of intrapartum fetal distress, emergency Cesarean delivery and admission to the intensive care unit[7,14,15]. Finally, evidence also exists that a very low estimated-fetal-weight (EFW) centile by itself predicts a

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higher risk of adverse perinatal outcome in term SGA fetuses without Doppler signs of brain redistribution and normal UA and UtA Doppler indices[16,17]. A gap in current knowledge is the lack of information about the combined value of these parameters when used in an integrated model.

The objective of this study was to assess the value of combined obstetric, maternal and fetal features and Doppler parameters to define a set of criteria that can predict sonographically pregnancies with SGA fetuses that are at high risk for adverse outcome.

SUBJECTS AND METHODS

Between January 2008 and November 2012, consecutive patients with pregnancies suspected of having an SGA fetus were examined and recorded prospectively at the routine third-trimester scan, performed at the University Hospital Clinic, Barcelona, Spain. All pregnancies were dated according to first-trimester crown–rump length[18]. Inclusion criteria for this study were: (1) singleton pregnancy; (2) normal fetal anatomy; and (3) an EFW < 10th percentile according to local reference values[19] at diagnosis of SGA after 32.0 weeks of gestation. Exclusion criteria were: (1) congenital malformations, including chromosomopathies and infections; (2) maternal consumption of illicit substances; and (3) contraindications for a vaginal delivery before the onset of labor (including the presence at inclusion, or development during follow-up, of absent or reversed UA diastolic flow). Controls ($n = 513$) were defined as singleton appropriate-for-gestational-age (AGA) pregnancies (EFW ≥ 10th centile according to local standards) at routine third-trimester ultrasound examination, and were sampled from our general pregnant population during the same period and matched 1:1 with cases by date of delivery (± 7 days). No Doppler evaluation was performed on controls. The study was approved by the local ethics committee and all women gave their informed consent to participate (IRB/2008/7315). The study design, analysis and reporting adhered to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) recommendations[20].

In all study cases, fetal biometry and prenatal Doppler ultrasound examinations were performed by experienced operators using either a Siemens Sonoline Antares (Siemens Medical Systems, Malvern, PA, USA) or a Voluson E8 (GE Medical Systems, Zipf, Austria) ultrasound machine, equipped with a 6–2-MHz linear curved-array transducer. The EFW was calculated from the biparietal diameter, head and abdominal circumference, and femur length using the Hadlock formula[21]. The UA-PI was calculated from a free-floating portion of the umbilical cord. To minimize variability, the MCA-PI was measured in a transverse view of the fetal head, at the level of its origin from the circle of Willis[22], and CPR was calculated as the ratio MCA-PI/UA-PI[23]. For UtA assessment, the ultrasound probe was placed on the lower quadrant of the abdomen, angled medially, and color Doppler imaging was used to identify the UtA at the apparent crossover with the external iliac artery. Measurements were taken approximately 1 cm distal to the crossover point. Doppler recordings were performed in the absence of fetal movements and voluntary suspended maternal breathing. All pulsed Doppler parameters were recorded automatically from at least three consecutive waveforms, with the angle of insonation as close to 0° as possible, and always below 30°. A high-pass wall filter of 70 Hz was used to record low flow velocities and to avoid artifacts. The last Doppler evaluation, within 1 week of delivery, was considered for analysis.

Follow-up was performed every 2 weeks in cases of normal CPR (≥ 5th centile[23]), weekly in cases of abnormal CPR and twice a week in cases of abnormal MCA (< 5th centile[24]). Induction of labor was recommended at 37 weeks' gestation for cases with abnormal CPR or MCA, otherwise at 40 weeks. Betamethasone was administered for pulmonary maturation in all cases delivering before 34.6 weeks. Cases with pre-eclampsia were delivered at 37 weeks or at diagnosis if identified after that gestational age.

Labor was induced by promoting cervical ripening with the administration of a slow-release prostaglandin E2 vaginal pessary (10 mg). If the onset of labor did not occur within 12 h, oxytocin induction was initiated. All deliveries were attended by a staff obstetrician blinded to the results of the Doppler parameters evaluated in this study. Indication for Cesarean delivery for non-reassuring fetal status was based on abnormal fetal heart-rate monitoring and abnormal fetal-scalp blood pH during intrapartum monitoring. Continuous fetal-heart monitoring was carried out and tracings were classified according to the following three-tiered system[25]: (1) normal: baseline of 110–160 beats per minute (bpm), variability > 5 bpm and absence of decelerations; (2) suspicious, i.e. the presence of one non-reassuring criterion out of: baseline, 100–109 or 161–180 bpm, variability < 5 bpm for less than 90 min, recurrent (> 50% of contractions) typical variable decelerations for more than 90 min and a single prolonged deceleration for up to 3 min; or (3) pathological: more than one non-reassuring criterion or the presence of any abnormal feature, including: baseline of < 100 or > 180 bpm or sinusoidal patterns (for more than 10 min), variability < 5 bpm for more than 90 min, recurrent atypical variable decelerations for more than 30 min, late decelerations for more than 30 min and a single prolonged deceleration for more than 3 min.

In cases with a pathological fetal heart rate or a suspicious pattern not presenting a fetal heart-rate acceleration after digital fetal-scalp stimulation[26], fetal-scalp blood sampling was performed and considered abnormal with pH values of < 7.15 or < 7.20 on two occasions 30 min apart. If cervical conditions did not allow fetal-scalp sampling, indication for Cesarean delivery was considered if an abnormal feature persisted after pessary withdrawal, oxytocin suspension and 10 min of intravenous infusion of ritodrine (200 μg/min). All cases with an adverse outcome were formally assessed to ensure that the management protocol had been followed correctly. Metabolic

acidosis was defined as the presence of a UA pH < 5th centile (7.15) and a base excess greater than −12 mEq/L in the newborn[27].

Statistical analysis

A predictive model for emergency Cesarean delivery because of non-reassuring fetal status or neonatal acidosis was constructed using the Decision Tree Analysis algorithm (SPSS 19.0, IBM, Armonk, NY, USA), which provides clinically comprehensive classification algorithms that allow their use in clinical practice to profile the individual risk for a given patient. The decision tree was developed using Exhaustive Chi-squared Automatic Interaction Detector (CHAID)[28], a recursive partitioning method that builds classification trees for predicting categorical predictor variables by automatically selecting a cut-off for all the parameters, including: maternal age (years); body mass index (kg/m^2); smoking (non-smoker *vs* smoker); nulliparity (no previous births < 22 weeks' gestation); gestational age at delivery (weeks); onset of labor (spontaneous *vs* induction); EFW centile[29]; UA-PI centile[24]; mean UtA-PI centile[30]; MCA-PI centile[24]; and CPR centile[23]. The classification and regression tree was constructed by splitting subsets of the dataset using all predictor variables, to create two child nodes, repeatedly. The best predictor was chosen using a variety of impurity and diversity measures. For a parsimonious model, the number of cases required to be present for a split has to be greater than 15% of the sample. A Bonferroni-adjusted chi-square test giving a P of ≤ 0.05 was used as the indicator of significance. The model was cross-validated by repeating the analysis over 10 random subsamples (leaving out one subsample each time) and constructing the tree from the average accuracy for cross-validated predicted classifications.

RESULTS

A total of 656 women fulfilled the inclusion criteria. Among them, 26 were excluded for breech presentation, 13 for having had more than one previous Cesarean delivery, 103 for absent/reversed end-diastolic velocity in the UA, and five for the presence of a medical contraindication precluding trial of labor, leaving a final population of 509 fetuses. Table 1 summarizes the demographic and perinatal characteristics of the included population of SGA pregnancies.

Of these SGA pregnancies, there were 134 (26.3%) cases of adverse outcome, including, non-exclusively, 106 cases of emergency Cesarean delivery for non-reassuring fetal status (82 of which had abnormal fetal-scalp sampling) and 46 cases of neonatal acidosis. Table 2 shows Doppler parameters before birth and perinatal outcome according to the occurrence of adverse outcome.

The decision tree analysis (Figure 1) showed that cases with a CPR < 10th centile had the highest risk for adverse outcome (37.5% *vs* 19.1%; Bonferroni-adjusted χ^2, $P = 0.049$). Among those with a normal CPR ($\geq$ 10th centile), cases with a mean UtA-PI > 95th centile also had a significantly higher risk of adverse outcome (36.5% *vs* 15.6%; Bonferroni-adjusted χ^2, $P = 0.023$). Finally, among the remaining group with a CPR $\geq$ 10th centile and a mean UtA-PI $\leq$ 95th centile, those with an estimated fetal weight < 3rd centile had a higher risk of adverse outcome (30.9% *vs* 11.4%; Bonferroni-adjusted χ^2, $P = 0.019$).

Cases were considered as low risk for an adverse outcome when they had a CPR $\geq$ 10th centile, a mean UtA-PI $\leq$ 95th centile and an EFW on at least the 3rd percentile. Cases were considered as high risk when any of these parameters was abnormal. The algorithm showed a sensitivity of 82.8% (95% CI, 75.1–88.6%), a specificity of 47.7% (95% CI, 42.6–52.9%), a positive predictive value of 36.2% (95% CI, 30.8–41.8%) and a negative predictive value for adverse outcome of 88.6% (95% CI, 83.2–92.5%). Positive and negative likelihood ratios were 1.58 and 0.36, respectively. Table 3 and Figure 2 display the Doppler parameters before birth and the perinatal outcome according to classification group for risk of adverse outcome, with the control group of AGA fetuses as reference.

DISCUSSION

In this paper we propose criteria for defining high risk for adverse outcome in SGA fetuses, derived from analyzing a large cohort of SGA fetuses delivered near term. The impact of identifying at-risk growth-restricted fetuses from the general population of SGA fetuses cannot be underestimated, considering that SGA affects up to 10% of deliveries in developed countries and represents approximately 400 000 cases per year in Europe alone.

In our study, UA Doppler indices did not differ between SGA fetuses with or without adverse perinatal outcome. This adds to the body of evidence showing that this parameter does not reliably reflect placental insufficiency and does not predict adverse outcome in late-onset intrauterine growth restriction[2,31].

Recent research has demonstrated that up to 20% of term SGA fetuses with normal UA Doppler have abnormal MCA Doppler, probably secondary to fetal hypoxia[8]. While the degree of placental insufficiency leading to such hypoxia is not reflected in the UA, it exposes the fetus to an increased risk of adverse perinatal outcome[7,8,15] and may have consequences on its neurodevelopment[9,10]. These studies support the use of brain Doppler evaluation to distinguish late-onset FGR from constitutionally small fetuses. We have previously shown that induction of labor in SGA cases with isolated MCA Doppler abnormalities is associated with an increased risk of fetal distress and neonatal acidosis[8]. Thus, it was expected that CPR, as a more sensitive marker of hypoxia, would be the first parameter to enter our decision tree[11,12].

Second, in our model, UtA Doppler divided the population with a normal CPR into two groups of significantly different risk for adverse outcome. In a recently reported longitudinal series[32], approximately

Table 1 Demographic and perinatal characteristics of a fetal population suspected of being small-for-gestational age (SGA)

Characteristic	*Overall population (n = 509)*	*Non-adverse outcome (n = 375)*	*Adverse outcome (n = 134)*	P*
Nulliparous	321 (63.1)	223 (59.5)	98 (73.1)	0.005
Non-Caucasian ethnicity	124 (24.4)	96 (25.6)	28 (20.9)	0.29
Maternal age at delivery (years)	33.9 ± 6.1	33.7 ± 6.1	34.5 ± 6.1	0.22
BMI at booking (kg/m^2)	22.3 ± 4.0	22.0 ± 3.7	23.1 ± 4.7	0.024
Low socioeconomic level‡	120 (23.6)	93 (24.8)	27 (20.1)	0.29
Smoker at booking (≥ 1 cigarette/day)	101 (19.8)	80 (21.3)	21 (15.7)	0.17
Alcohol consumption (> 170 g/week)	7 (1.4)	7 (1.9)	—	0.20†

Data are given as mean ± SD or *n* (%). Paired comparisons: **t*-test/Pearson-χ^2 test or †Fisher's exact test. ‡Routine occupation, long-term unemployment or never worked (UK National Statistics Socio-Economic Classification). BMI, body mass index.

Table 2 Doppler parameters before delivery and perinatal outcome in small-for-gestational-age (SGA) fetuses, according to occurrence of adverse outcome

Parameter	*Overall population (n = 509)*	*Non-adverse outcome (n = 375)*	*Adverse outcome (n = 134)*	P*
UA-PI (*Z*-score)	0.47 ± 1.4	0.44 ± 1.5	0.54 ± 0.9	0.669
UtA-PI (*Z*-score)	0.67 ± 1.7	0.46 ± 1.6	1.26 ± 1.7	< 0.001
MCA-PI (*Z*-score)	−0.10 ± 1.2	0.07 ± 1.2	−0.58 ± 1.0	< 0.001
CPR (*Z*-score)	−0.91 ± 1.2	−0.75 ± 1.2	−1.34 ± 1.1	< 0.001
Induction of labor	382 (75.0)	269 (71.7)	113 (84.3)	0.004
GA at delivery (weeks)	38.4 ± 2.3	38.5 ± 2.4	38.1 ± 2.1	0.669
Birth weight (g)	2414 ± 441	2466 ± 429	2270 ± 443	< 0.001
Birth-weight centile	4.5 ± 7.3	5.1 ± 7.7	2.7 ± 6.0	< 0.001
SGA confirmed at birth	457 (89.8)	329 (87.7)	128 (95.5)	0.011
Pre-eclampsia	59 (11.6)	33 (8.8)	26 (19.4)	0.001
Cesarean delivery	146 (28.7)	40 (10.7)	106 (79.1)	< 0.001
Operative vaginal delivery	51 (10.0)	32 (8.5)	19 (14.2)	0.063
Cesarean delivery for NRFS	106 (20.8)	—	106 (79.1)	—
5-min Apgar score < 7	6 (1.2)	5 (1.3)	1 (0.7)	1†
UA pH at delivery	7.23 ± 0.08	7.25 ± 0.05	7.17 ± 0.1	< 0.001
Neonatal acidosis	46 (9.0)	—	46 (34.3)	—
Admission to neonatal unit	36 (7.1)	21 (5.6)	15 (11.2)	0.03

Data are given as mean ± SD or *n* (%). Paired comparisons: **t*-test/Pearson-χ^2 test or †Fisher's exact test. CPR, cerebroplacental ratio; GA, gestational age; MCA, middle cerebral artery; NRFS, non-reassuring fetal status; PI, pulsatility index; UA, umbilical artery; UtA, uterine artery.

one-third of abnormal third-trimester uterine Doppler studies occurred in women with normal scans during the second trimester, suggesting that a proportion of placental disease emerges late in pregnancy. Hence, the potential advantage of a third-trimester Doppler ultrasound scan is the ability to detect placental insufficiency of differing pathways. Our finding that abnormal Doppler indices in the UtA are associated with adverse perinatal outcome, is consistent with a previous report showing that abnormal velocimetry in the UtA and MCA are independently correlated with the occurrence of emergency Cesarean delivery[7].

Third, severe growth restriction, as reflected by an EFW < 3rd centile, further improved the risk stratification in the subgroup in which CPR and UtA Doppler parameters were both normal, allowing us to optimize the diagnostic criteria. We have previously shown that in SGA fetuses with normal CPR and UtA Doppler, an estimated weight < 3rd centile confers a four-fold increased risk of fetal distress and acidosis when compared to SGA fetuses with a percentile above this cut-off value[17].

The finding that SGA fetuses at high risk had a five-fold higher incidence of pre-eclampsia supports the concept that this category corresponds with latent placental insufficiency not reflected in the UA but that confers a lower tolerance to labor. This is in keeping with other series on late-onset SGA with data on placental histology[33].

The clinical relevance of using a combined model over a single predictor is that it provides a significant improvement in prediction without excessive technical sophistication; estimation of fetal weight is an integral part of the third-trimester scan, and Doppler interrogation of the UA, MCA and UtA is easily accomplished in a great majority of cases. This algorithm allows for the profiling of the general population with late SGA in two groups at different risk: while SGA fetuses with moderate growth restriction (≥ 3rd centile) and normal placental function on both the fetal (normal CPR) and maternal (normal uterine Doppler) sides could be considered low risk and managed as constitutionally small babies, those with either severe growth restriction or evidence of placental

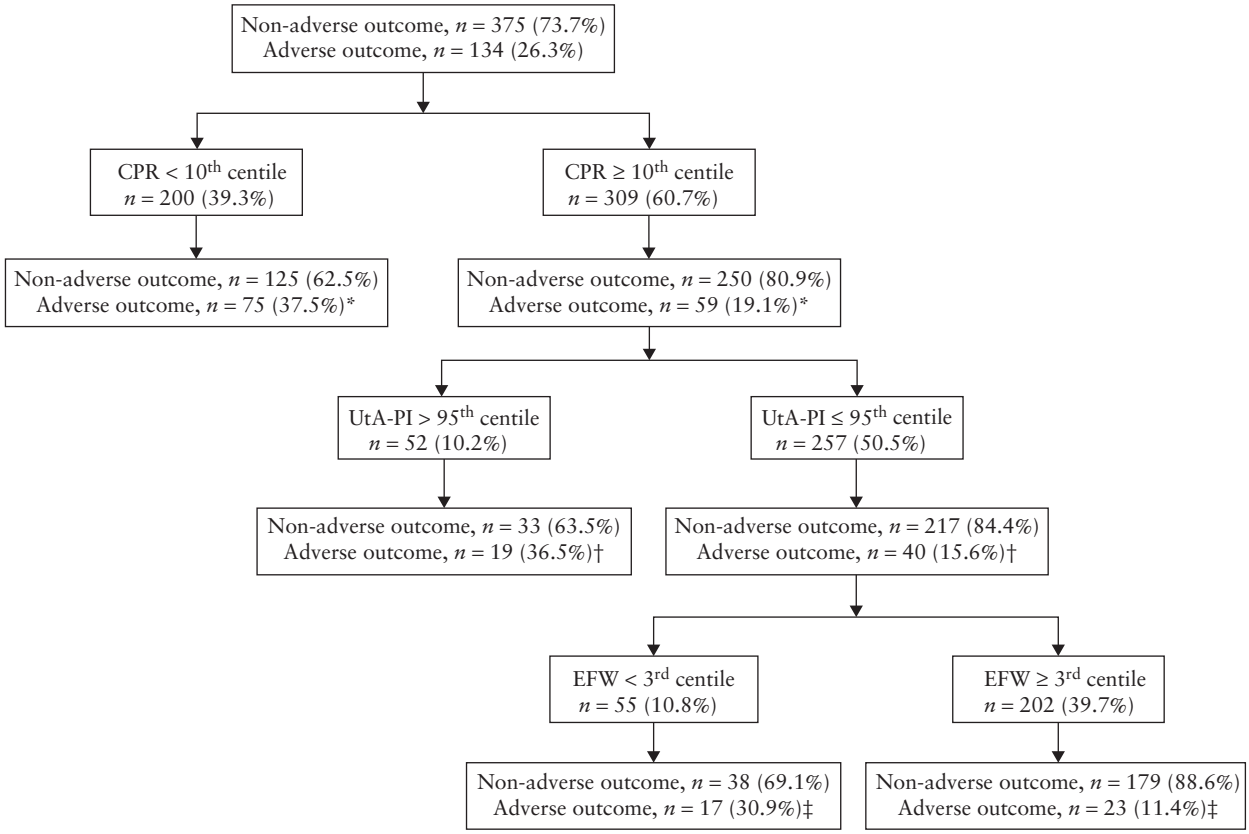

Figure 1 Predictive model for emergency Cesarean delivery because of non-reassuring fetal status or neonatal acidosis with cerebroplacental ratio (CPR), mean uterine artery pulsatility index (UtA-PI) and estimated fetal weight (EFW) as predictors. *$P = 0.049$. †$P = 0.023$. ‡$P = 0.019$.

Table 3 Doppler parameters before delivery and perinatal outcome of appropriate-for-gestational-age (AGA) and small-for-gestational-age (SGA) fetuses according to classification of risk for adverse outcome

Parameter	*AGA* (n = *513*)	*Low-risk SGA* (n = *202*)	*High-risk SGA* (n = *307*)	P*	P‡
UA-PI (*Z*-score)	−0.13 ± 0.52	0.01 ± 0.54	0.77 ± 1.63	0.001	< 0.001
UtA-PI (*Z*-score)	−0.41 ± 1.3	−0.17 ± 1.03	1.22 ± 1.80	0.019	< 0.001
MCA-PI (*Z*-score)	−0.16 ± 0.88	0.55 ± 0.99	−0.53 ± 1.14	< 0.001	< 0.001
CPR (*Z*-score)	−0.29 ± 1.2	−0.17 ± 0.80	−1.38 ± 1.11	0.19	< 0.001
GA at delivery (weeks)	39.7 ± 1.3	39.2 ± 1.1	37.8 ± 2.7	< 0.001	< 0.001
Birth weight (g)	3447 ± 348	2683 ± 226	2236 ± 458	< 0.001	< 0.001
Birth-weight centile	57.6 ± 28.4	7.39 ± 8.35	2.56 ± 5.83	< 0.001	< 0.001
Pre-eclampsia	8 (1.6)	7 (3.5)	52 (16.9)	0.109	< 0.001
Cesarean delivery	78 (15.2)	31 (15.3)	115 (37.5)	1	< 0.001
Operative vaginal delivery	55 (10.7)	16 (7.9)	35 (11.4)	0.26	0.2
Cesarean delivery for NRFS	25 (4.9)	16 (7.9)	90 (29.3)	0.115	< 0.001
5-min Apgar score < 7	3 (0.6)	2 (1.0)	4 (1.3)	0.558†	1†
UA pH at delivery	7.23 ± 0.16	7.24 ± 0.06	7.22 ± 0.08	0.388	0.003
Neonatal acidosis	31 (6.0)	10 (5.0)	36 (11.7)	0.572	0.009
Admission to neonatal unit	20 (3.9)	8 (4.0)	28 (9.1)	0.969	0.026

Data are given as mean ± SD or *n* (%). Paired comparisons: AGA *vs* low-risk SGA compared using **t*-test/Pearson-χ^2 test or †Fisher's exact test; low-risk SGA *vs* high-risk SGA compared using ‡*t*-test/Pearson-χ^2 test or †Fisher's exact test. CPR, cerebroplacental ratio; GA, gestational age; MCA, middle cerebral artery; NRFS, non-reassuring fetal status; PI, pulsatility index; UA, umbilical artery; UtA, uterine artery.

dysfunction should be considered at higher risk. In our series, SGA fetuses at low risk accounted for 40% of the study population, in which only 17% of the adverse outcomes occurred, whereas SGA fetuses at high risk represented the remaining 60% of the study population, in which 83% of the instances of adverse outcome were found.

A large trial carried out in The Netherlands on late-SGA pregnancies, comparing systematic induction at term with expectant management, showed no differences

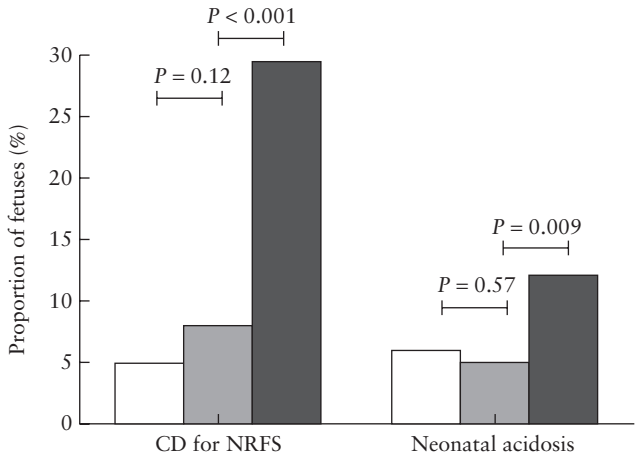

Figure 2 Perinatal outcome of small-for-gestational-age (SGA; low-risk (▩) and high-risk (■)) and appropriate-for-gestational-age (AGA, □) fetuses according to classification of risk for adverse outcome. Groups compared using Pearson-χ^2 test. CD, Cesarean delivery; NRFS, non-reassuring fetal status.

in the perinatal and neonatal outcomes between the strategies[34,35]. This evidence has been translated into guidelines as a general recommendation for the induction of labor at 37–38 weeks' gestation[36–38], with the rationale of avoiding the rare, but devastating, instances of stillbirth. However, with such a strategy, a large fraction of constitutionally and healthy SGA babies are unnecessarily induced, which has the potential to result in lower satisfaction and poorer fulfilment with the birth experience[39]. Despite the low positive predictive value and likelihood ratio, our algorithm showed a good capacity to rule out perinatal adverse outcome, as reflected in the negative predictive value and likelihood ratio, which suggests that it would be suitable for risk stratification to select women for expectant management.

We acknowledge that there are some limitations to our study. It could be argued that the fact that, in most cases, labor was induced may affect the external validity of our results by increasing *per se* the risk of Cesarean delivery. However, results from a large trial on late SGA showed no differences whatsoever in the rate of Cesarean delivery when systematic induction beyond 36 weeks was performed, compared with expectant management[35]. Furthermore, we do not have information on the use of oxytocin for labor augmentation, which may also have played a role as a risk factor for fetal distress.

Another limitation is that Cesarean delivery for non-reassuring fetal status and, to a lesser degree, neonatal acidosis, is a soft proxy for adverse outcome. Other series have failed to find an association between term SGA and short-term neonatal hard outcomes, such as hypoxic-ischemic encephalopathy[40]. The study was underpowered to evaluate these outcomes. It could be argued that the occurrence of an abnormal cardiotocograph prompts an emergency Cesarean delivery that, in turn, prevents overt adverse outcome, so these are competitive risks. This limitation could be overcome by combining these two outcomes into a composite outcome. Furthermore, we believe that non-reassuring fetal status is a finding that has an impact on the delivery management of SGA babies. In addition, some studies have revealed an increased risk of maternal and neonatal consequences following an emergency Cesarean delivery[41,42]. Moreover, despite our attempt to address confounding by entering a set of clinical variables (such as nulliparity or body mass index, which differ between cases with and without adverse outcome) in the multivariate analysis as candidate predictors, we acknowledge that it would have been a more robust design to have matched the groups by these potential confounders. Finally, the analysis automatically selected a non-conventional cut-off centile for CPR (the 10th instead of the 5th centile), which may limit the clinical applicability of our model. This could be overcome easily by using supporting software, such as that available at: http://medicinafetalbarcelona.org/en/research/resources.

In conclusion, the model developed here could be used in the risk stratification of pregnancies suspected prenatally of having late-onset SGA. The model is based on standard fetal biometrics and Doppler parameters that can be obtained readily in most clinical settings.

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