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Prediction of small-for-gestational-age neonates: screening by uterine artery Doppler and mean arterial pressure at 35–37 weeks

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KEYWORDS: mean arterial pressure; pre-eclampsia; pyramid of antenatal care; small-for-gestational age; third-trimester screening; uterine artery Doppler

ABSTRACT

Objective *To investigate the potential value of uterine artery (UtA) pulsatility index (PI) and mean arterial pressure (MAP) at 35–37 weeks' gestation in the prediction of delivery of small-for-gestational-age (SGA) neonates, in the absence of pre-eclampsia (PE).*

Methods *This was a screening study in singleton pregnancies at 35–37 weeks, including 245 that delivered SGA neonates with birth weight < 5th percentile and 4876 cases unaffected by SGA, PE or gestational hypertension. Multivariable logistic regression analysis was used to determine if UtA-PI and MAP improved the prediction of SGA neonates provided by screening with maternal characteristics and medical history (maternal factors), and estimated fetal weight (EFW) from fetal head circumference, abdominal circumference and femur length.*

Results *Compared to the normal group, the median multiple of the median (MoM) values of UtA-PI and MAP were significantly higher in the SGA < 5th group. Combined screening by maternal factors, EFW Z-score, UtA-PI and MAP at 35–37 weeks predicted, at a 10% false-positive rate, 90%, 86% and 90% of SGA neonates with birth weight < 10th, < 5th and < 3rd percentiles, respectively, delivering < 2 weeks following assessment; the respective values for SGA delivering ≥ 37 weeks were 66%, 74% and 80%. Such performance was not significantly different from screening by maternal factors and EFW Z-score alone.*

Conclusion *Addition of UtA-PI and MAP to combined testing by maternal factors and fetal biometry at 35–37 weeks does not improve the performance of screening for delivery of SGA neonates.* *Copyright © 2015 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

The increased risk of perinatal mortality and morbidity associated with small-for-gestational-age (SGA) neonates can be reduced substantially in cases identified prenatally, as close monitoring and appropriate timing of delivery and prompt neonatal care can be undertaken[1]. The traditional approach of identifying pregnancies with SGA fetuses is maternal abdominal palpation and serial measurements of symphysis–fundal height, but the detection rate (DR) of this approach is less than 30%[2,3]. A higher performance in screening for SGA is achieved by third-trimester assessment which includes ultrasound examination for fetal biometry and the timing of such assessment, at 32 or 36 weeks' gestation, could be defined by the results of assessment at 22 weeks[4,5].

Screening by a combination of maternal characteristics and medical history with estimated fetal weight (EFW), uterine artery (UtA) pulsatility index (PI) and mean arterial pressure (MAP) at 32 weeks' gestation, predicted 83%, 91% and 93% of SGA neonates delivering within 5 weeks of assessment, at a false-positive rate (FPR) of 10%, with respective birth weight < 10th, < 5th and < 3rd percentiles, in the absence of pre-eclampsia (PE)[6]. However, the respective values for delivery ≥ 5 weeks following assessment were only 53%, 58% and 61%.

The objectives of this study, in singleton pregnancies undergoing routine antenatal assessment at 35–37 weeks'

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gestation, were first, to investigate the potential value of UtA-PI and MAP on their own and in combination with maternal characteristics, medical history and EFW in the prediction of delivery of SGA neonates in the absence of PE and second, to develop specific algorithms for the calculation of patient-specific risks for SGA.

METHODS

The data for this study were derived from prospective screening for adverse obstetric outcomes in women attending for their routine hospital visit in the third trimester of pregnancy at King's College Hospital, London, and Medway Maritime Hospital, Kent, between February 2014 and September 2014. This visit, which is held at 35 + 0 to 37 + 6 weeks' gestation, included the recording of maternal characteristics and medical history and estimation of fetal weight (EFW)[7] from transabdominal ultrasound measurement of fetal head circumference, abdominal circumference and femur length[8] and measurement of UtA-PI, MAP and maternal serum metabolites. Gestational age was determined by the measurement of fetal crown–rump length at 11–13 weeks or the fetal head circumference at 19–24 weeks[8,9].

Transabdominal color Doppler ultrasound was used to visualize the left and right UtA at the apparent crossover with the external iliac arteries[10]. Pulsed-wave Doppler was then used to obtain waveforms and, when three similar consecutive waveforms were obtained, the PI was measured and the mean PI of the two vessels was calculated. The scans were carried out by sonographers who had received the Certificate of Competence in Doppler of The Fetal Medicine Foundation (http://www.fetalmedicine.com).

The MAP was measured by validated automated devices (3BTO-A2, Microlife, Taipei, Taiwan), which were calibrated before, and at regular intervals during, the study. Recordings were made by doctors who had received appropriate training on the use of these machines. During measurements, women were in the sitting position with their arms supported at the level of the heart and a small (22 cm), normal (22–32 cm) or large (33–42 cm) adult cuff was used, depending on the mid-arm circumference. After 5 min of rest, two recordings of blood pressure were made in both arms simultaneously. We calculated the final MAP as the average of all four measurements[11].

Written informed consent was obtained from the women agreeing to participate in a study on adverse pregnancy outcome, which was approved by the ethics committee of each participating hospital. This study is part of a research program on the late third-trimester prediction of PE and/or SGA. In this publication, we present the results of combined screening with maternal factors and biophysical markers in the prediction of SGA in the absence of PE. The patients included in the study were all pregnancies resulting in live birth or stillbirth of phenotypically normal babies.

Patient characteristics

Patient characteristics that were recorded included maternal age, racial origin (Caucasian, Afro-Caribbean, South Asian, East Asian and mixed), method of conception (spontaneous/assisted conception requiring the use of ovulation drugs), cigarette smoking during pregnancy (yes/no), medical history of chronic hypertension (yes/no), diabetes mellitus (yes/no), systemic lupus erythematosus (SLE) or antiphospholipid syndrome (APS), and obstetric history including parity (parous/nulliparous if no previous pregnancy $\geq$ 24 weeks' gestation), previous pregnancy with PE (yes/no), previous pregnancy with SGA (yes/no) and the time interval between the last delivery and conception of the current pregnancy in years. Maternal weight and height were also measured.

Outcome measures

Data on pregnancy outcome were collected from the hospital maternity records or the general medical practitioners of the women. The primary outcome of the study was SGA without PE. The newborn was considered to be SGA if the birth weight was < 5th percentile after correction for gestational age at delivery (SGA < 5th)[12]. The definitions of non-proteinuric gestational hypertension (GH) and PE were those of the International Society for the Study of Hypertension in Pregnancy[13]. The obstetric records of all women with pre-existing or pregnancy-associated hypertension were examined to confirm if the condition was chronic hypertension, PE or GH.

Statistical analysis

The observed measurements of EFW were expressed as *Z*-scores, corrected for gestational age[12]. The values of UtA-PI and MAP were $\log_{10}$ transformed to make their distributions Gaussian. Each measured value in the outcome groups was expressed as a multiple of the normal median (MoM) after adjusting for those characteristics found to provide substantial contribution to the $\log_{10}$ transformed value[14,15]. Mann–Whitney *U*-test was used to compare the median MoM values of UtA-PI and MAP between the outcome groups. Regression analysis was used to determine the significance of association between $\log_{10}$MoM of UtA-PI and MAP with the assessment-to-delivery interval and birth-weight *Z*-score.

The *a-priori* risk for SGA < 5th was determined using the algorithm derived from the multivariable logistic regression analysis of maternal characteristics and history, as described previously[16]. Multivariable logistic regression analysis was then used to determine if the maternal factor-derived logit (*a-priori* risk), $\log_{10}$MoM UtA-PI, $\log_{10}$MoM MAP and EFW *Z*-score had a significant contribution in predicting SGA < 5th. The performance of screening was determined by receiver–operating characteristics (ROC) curves. Similarly, the algorithm was used to determine the performance of screening for SGA defined

Table 1 Characteristics of the study population of women with a singleton pregnancy with normal outcome or with a small-for-gestational-age (SGA) neonate, in the absence of pre-eclampsia (PE)

Characteristic	*Normal* (n = *4876)*	*SGA without PE* (n = *245)*	P
Maternal age (years)	31.2 (26.5–35.0)	30.1 (24.6–35.3)	0.061
Maternal weight (kg)	79.0 (70.8–89.8)	73.5 (63.9–84.1)	< 0.0001
Maternal height (cm)	164 (160–168)	162 (158–165)	< 0.0001
GA at screening (weeks)	36.1 (36.0–36.4)	36.3 (36.0–36.4)	0.848
Racial origin			
Caucasian	3495 (71.7)	140 (57.1)	< 0.0001
Afro-Caribbean	941 (19.3)	57 (23.3)	0.137
South Asian	178 (3.7)	30 (12.2)	< 0.0001
East Asian	101 (2.1)	6 (2.4)	0.644
Mixed	161 (3.3)	12 (4.9)	0.200
Obstetric history			
Nulliparous	2352 (48.2)	148 (60.4)	0.0002
Parous with no prior PE and SGA	2318 (47.5)	67 (27.3)	< 0.0001
Parous with prior PE no SGA	77 (1.6)	4 (1.6)	0.795
Parous with prior SGA no PE	121 (2.5)	25 (10.2)	< 0.0001
Parous with prior SGA and PE	8 (0.2)	1 (0.4)	0.357
Interpregnancy interval (years)	3.1 (2.1–5.1)	2.9 (2.1–5.5)	0.965
Cigarette smoker	464 (9.5)	59 (24.1)	< 0.0001
Mode of conception			
Spontaneous	4758 (97.6)	235 (95.9)	0.136
Ovulation drugs	20 (0.4)	2 (0.8)	0.284
In-vitro fertilization	98 (2.0)	8 (3.3)	0.167
Chronic hypertension	64 (1.3)	2 (0.8)	0.770
Pre-existing diabetes mellitus	57 (1.2)	2 (0.8)	> 0.999
Type 1	27 (0.6)	1 (0.4)	> 0.999
Type 2	30 (0.6)	1 (0.4)	> 0.999
SLE or APS	13 (0.3)	0 (0.0)	> 0.999
GA at delivery (weeks)	40.0 (39.1–40.9)	39.4 (38.6–40.4)	< 0.0001
Birth weight (g)	3435 (3140–3745)	2550 (2350–2718)	< 0.0001
Birth-weight percentile	50.6 (26.8–75.6)	2.7 (1.2–3.8)	< 0.0001

Data are given as median (interquartile range) or *n* (%). APS, antiphospholipid syndrome; GA, gestational age; SLE, systemic lupus erythematosus.

by birth weight < 10th percentile (SGA < 10th) and < 3rd percentile (SGA < 3rd).

The statistical software package SPSS 22.0 (SPSS Inc., Chicago, IL, USA) and Medcalc (Medcalc Software, Mariakerke, Belgium) were used for all data analyses.

RESULTS

The characteristics of the study population of 5121 pregnancies, including 245 delivering SGA < 5th neonates in the absence of PE, are presented in Table 1.

Normal pregnancy outcome

In the unaffected pregnancies with birth weight ≥ 5th percentile, the mean ± SD, 90th and 95th percentile of $\log_{10}$MoM UtA-PI were −0.009 ± 0.113, 0.134 and 0.187, respectively. The mean ± SD, 90th and 95th percentile of $\log_{10}$MoM MAP were 0.002 ± 0.033, 0.044 and 0.056, respectively (Table S1).

There was no significant association between $\log_{10}$MoM values of UtA-PI and MAP ($r = -0.004$, $P = 0.893$). There was a significant inverse association between $\log_{10}$MoM UtA-PI and the assessment-to-delivery interval ($r = -0.096$, $P < 0.0001$) and birth-weight *Z*-score ($r = -0.096$, $P < 0.0001$), and between $\log_{10}$MoM MAP and assessment-to-delivery interval ($r = -0.080$, $P < 0.0001$), but not birth-weight *Z*-score ($r = -0.022$, $P = 0.113$).

Small-for-gestational age

In the SGA < 5th group, compared to the normal group, the median MoM values of UtA-PI and MAP at 35–37 weeks were significantly higher (Table S1). There was no significant association between $\log_{10}$MoM values of UtA-PI and MAP ($r = 0.109$, $P = 0.088$). There was a significant inverse association between $\log_{10}$MoM UtA-PI and assessment-to-delivery interval ($r = -0.232$, $P < 0.0001$; Figure S1a) and birth-weight *Z*-score ($r = -0.157$, $P = 0.011$; Figure S1b). There was no significant association between $\log_{10}$MoM MAP and assessment-to-delivery interval ($r = -0.100$, $P = 0.107$; Figure S1c) and birth-weight *Z*-score ($r = -0.057$, $P = 0.354$; Figure S1d).

Multivariable logistic regression analysis demonstrated that, in the prediction of SGA < 5th, there were significant contributions from maternal characteristics, EFW *Z*-score, UtA-PI and MAP (Table S2). Combined screening by maternal characteristics and history with

EFW *Z*-scores, UtA-PI and MAP detected 66.6%, 74.7% and 80.9% of SGA neonates with birth weight < 10th, < 5th and < 3rd percentiles, respectively, at 10% FPR.

The areas under ROC (AUC) curves, detection rates (DRs) at FPRs of 5% and 10% and FPRs for DRs of 100%, 90% and 80% of SGA < 10th, SGA < 5th and SGA < 3rd delivering < 2 weeks following assessment and ≥ 37 weeks' gestation when screening by maternal characteristics, EFW *Z*-score, UtA-PI, MAP and their combination are given in Tables 2, S3 and S4 and Figure 1.

The DRs, at FPR of 10%, of combined screening by maternal characteristics and history with EFW *Z*-scores for the prediction of SGA neonates with birth weight < 10th, < 5th and < 3rd percentiles, delivering < 2 weeks following assessment, were 86.4% (95% CI, 79.6–93.5%; AUC: 0.961 (95% CI, 0.955–0.967)), 86.4% (95% CI, 72.6–94.8%; AUC: 0.969 (95% CI, 0.964–0.974)) and 90.0% (95% CI, 73.5–97.9%; AUC: 0.982 (95% CI, 0.978–0.985)), respectively. The respective values for SGA delivering ≥ 37 weeks, were 66.1% (95% CI, 62.0–70.1%; AUC: 0.887 (95% CI, 0.878–0.896)), 71.4% (95% CI, 65.1–77.1%; AUC: 0.908 (95% CI, 0.900–0.916)) and 79.2% (95% CI, 71.2–85.8%; AUC: 0.929 (95% CI, 0.922–0.936)).

In combined screening by maternal characteristics and history with EFW *Z*-scores, UtA-PI and MAP at 35–37 weeks' gestation, the DRs, at FPR of 10%, of SGA neonates with birth weight < 10th, < 5th and < 3rd percentiles, delivering < 2 weeks following assessment were 90.1% (95% CI, 81.5–95.6%; AUC: 0.963 (95% CI, 0.957–0.968)), 86.4% (95% CI, 72.6–94.8%; AUC: 0.972 (95% CI, 0.967–0.976)) and 90.0% (95% CI, 73.5–97.9%; AUC: 0.985 (95% CI, 0.981–0.988)), respectively. The respective values for SGA delivering ≥ 37 weeks were 66.1% (95% CI, 62.0–70.1%; AUC: 0.888 (95% CI, 0.879–0.897)), 73.9% (95% CI, 67.8–79.4%; AUC: 0.910 (95% CI, 0.902–0.917)) and 80.0% (95% CI, 72.1–86.5%; AUC: 0.929 (95% CI, 0.921–0.936)).

DISCUSSION

Main findings of the study

The findings of the study demonstrate that, in women who deliver SGA neonates in the absence of PE, UtA-PI and MAP at 35–37 weeks' gestation are increased and EFW is reduced, compared to women with a normal pregnancy outcome. The deviation from normal for UtA-PI is inversely related to the severity of the disease, reflected in the gestational age at delivery and the birth-weight *Z*-score.

Combined screening by maternal factors, EFW *Z*-score, UtA-PI and MAP at 35–37 weeks, predicted 90%, 86% and 90% of SGA neonates with birth weight < 10th, < 5th and < 3rd percentiles, at FPR of 10%, delivering < 2 weeks following assessment and the respective values for SGA delivering ≥ 37 weeks were 66%, 74% and 80%. The addition of UtA-PI and MAP at 35–37 weeks does not improve the performance of screening for delivery of SGA neonates achieved by combined testing using maternal factors and fetal biometry alone.

Strengths and limitations of the study

The strengths of this third-trimester screening study for SGA in the absence of PE are, first, examination of a population of pregnant women attending for routine assessment of fetal growth and wellbeing at 35–37 weeks' gestation and, second, use of Bayes' theorem to combine the prior risk from maternal characteristics and medical history with fetal biometry, UtA-PI and MAP to estimate patient-specific risks and the performance of screening for SGA of different severities delivering at selected intervals from the time of assessment.

The main limitation of the study is that the results of fetal biometry at the 35–37-week scan were made available to the obstetricians of the patients who would have taken specific actions of further monitoring of the cases of suspected SGA and, consequently, the performance of screening, particularly those delivering within 2 weeks of assessment, would be positively biased.

Comparison with findings from previous studies

Previous studies examining pregnancies with SGA fetuses in the third trimester reported that the outcome was worse in cases with Doppler evidence of increased, rather than normal, impedance to flow in the UtAs[17,18]. A screening study involving 1848 singleton pregnancies at 30–32 weeks' gestation reported that UtA-PI improved the prediction of SGA neonates provided by fetal biometry alone, with reduction in FPR from 27% to 16%, with the same DR of about 71%[19]. In our screening study of 30 849 singleton pregnancies at 30–34 weeks' gestation, combined screening by maternal factors, fetal biometry, UtA-PI and MAP predicted 91% and 60% of SGA < 5th neonates delivering < 5 and ≥ 5 weeks following assessment, respectively, at FPR of 10%[6].

Implications for clinical practice

In the proposed new pyramid of pregnancy care[20], an integrated clinical assessment at 11–13 weeks' gestation, in which biophysical and biochemical markers are combined with maternal characteristics and medical history, aims to identify pregnancies at high risk of developing PE and/or SGA[21,22] and, through pharmacological intervention, reduce the prevalence of these complications[23,24].

The objective of subsequent visits, at around 22 and 32 or 36 weeks' gestation, are to identify the high-risk group and, through close monitoring of such pregnancies, minimize adverse perinatal events by determining the appropriate time and place for iatrogenic delivery. We have proposed recently that all women should be offered

Table 2 Performance of screening for small-for-gestational-age (SGA) neonates, with birth weight < 10th, < 5th and < 3rd percentile, delivering within 2 weeks of assessment or ≥ 37 weeks' gestation, in the absence of pre-eclampsia, using maternal factors, estimated fetal weight (EFW), uterine artery pulsatility index (UtA-PI) and mean arterial pressure (MAP) at 35–37 weeks' gestation

		DR (%)		*FPR (%)*		
Screening test	*AUC*	*FPR = 5%*	*FPR = 10%*	*DR = 100%*	*DR = 90%*	*DR = 80%*
Delivery within 2 weeks						
SGA < 10th percentile						
Maternal factors	0.744 (0.731–0.756)	25.9 (16.8–36.9)	40.7 (29.9–52.2)	79.8 (78.6–80.9)	64.4 (63.0–65.7)	48.6 (47.2–50.1)
Maternal factors plus EFW	0.961 (0.955–0.967)	77.8 (67.2–86.3)	86.4 (79.6–93.5)	53.4 (51.9–54.8)	11.6 (10.7–12.6)	5.6 (5.0–6.3)
Maternal factors and EFW plus UtA-PI and MAP	0.963 (0.957–0.968)	76.5 (65.8–85.2)	90.1 (81.5–95.6)	51.2 (49.8–52.7)	9.3 (8.4–10.1)	5.7 (5.0–6.4)
SGA < 5th percentile						
Maternal factors	0.800 (0.788–0.811)	34.1 (20.5–49.9)	50.0 (34.6–65.4)	73.5 (72.2–74.7)	57.6 (56.2–59.0)	44.7 (43.3–46.1)
Maternal factors plus EFW	0.969 (0.964–0.974)	84.1 (69.9–93.4)	86.4 (72.6–94.8)	34.0 (32.7–35.4)	13.4 (12.5–14.4)	3.6 (3.1–4.1)
Maternal factors and EFW plus UtA-PI and MAP	0.972 (0.967–0.976)	84.1 (69.9–93.4)	86.4 (72.6–94.8)	34.3 (32.9–35.6)	12.0 (11.1–12.9)	3.0 (2.6–3.6)
SGA < 3rd percentile						
Maternal factors	0.813 (0.802–0.824)	36.7 (19.9–56.1)	50.0 (32.9–67.1)	60.2 (58.8–61.6)	52.8 (51.4–54.2)	38.1 (37.7–39.4)
Maternal factors plus EFW	0.982 (0.978–0.985)	90.0 (73.5–97.9)	90.0 (73.5–97.9)	16.7 (15.6–17.7)	3.6 (3.1–4.1)	0.9 (0.7–1.2)
Maternal factors and EFW plus UtA-PI and MAP	0.985 (0.981–0.988)	90.0 (73.5–97.9)	90.0 (73.5–97.9)	13.1 (12.2–14.1)	2.8 (2.4–3.3)	0.6 (0.4–0.9)
Delivery ≥ 37 weeks						
SGA < 10th percentile						
Maternal factors	0.712 (0.700–0.725)	20.1 (16.8–23.7)	33.2 (29.2–37.3)	98.6 (98.2–98.9)	69.9 (68.5–71.2)	53.5 (52.0–54.9)
Maternal factors plus EFW	0.887 (0.878–0.896)	47.3 (43.1–51.6)	66.1 (62.0–70.1)	82.5 (81.3–83.6)	32.6 (31.3–34.0)	20.2 (19.0–21.4)
Maternal factors and EFW plus UtA-PI and MAP	0.888 (0.879–0.897)	48.6 (44.3–52.9)	66.1 (62.0–70.1)	84.8 (83.7–85.8)	31.4 (30.1–32.8)	19.1 (18.0–20.3)
SGA < 5th percentile						
Maternal factors	0.741 (0.729–0.753)	23.5 (18.2–29.5)	38.0 (31.8–44.6)	98.1 (97.7–98.5)	68.6 (67.3–69.9)	48.8 (47.4–50.2)
Maternal factors plus EFW	0.908 (0.900–0.916)	54.3 (47.7–60.8)	71.4 (65.1–77.1)	83.5 (82.4–84.5)	24.6 (23.4–25.8)	13.4 (12.5–14.4)
Maternal factors and EFW plus UtA-PI and MAP	0.910 (0.902–0.917)	55.6 (48.9–62.0)	73.9 (67.8–79.4)	83.2 (82.1–84.2)	25.2 (24.0–26.5)	14.1 (13.1–15.1)
SGA < 3rd percentile						
Maternal factors	0.775 (0.764–0.787)	26.2 (18.8–34.6)	39.2 (30.8–48.2)	90.8 (90.0–91.6)	53.4 (52.0–54.8)	41.4 (40.0–42.8)
Maternal factors plus EFW	0.929 (0.922–0.936)	64.6 (55.5–71.5)	79.2 (71.2–85.8)	69.1 (67.8–70.4)	17.8 (16.7–18.9)	10.1 (9.3–11.0)
Maternal factors and EFW plus UtA-PI and MAP	0.929 (0.921–0.936)	64.6 (55.8–72.8)	80.0 (72.1–86.5)	70.2 (68.9–71.4)	20.1 (19.0–21.3)	9.9 (9.0–10.7)

Values in parentheses are 95% CIs. AUC, area under receiver–operating characteristics curve; DR, detection rate; FPR, false-positive rate.

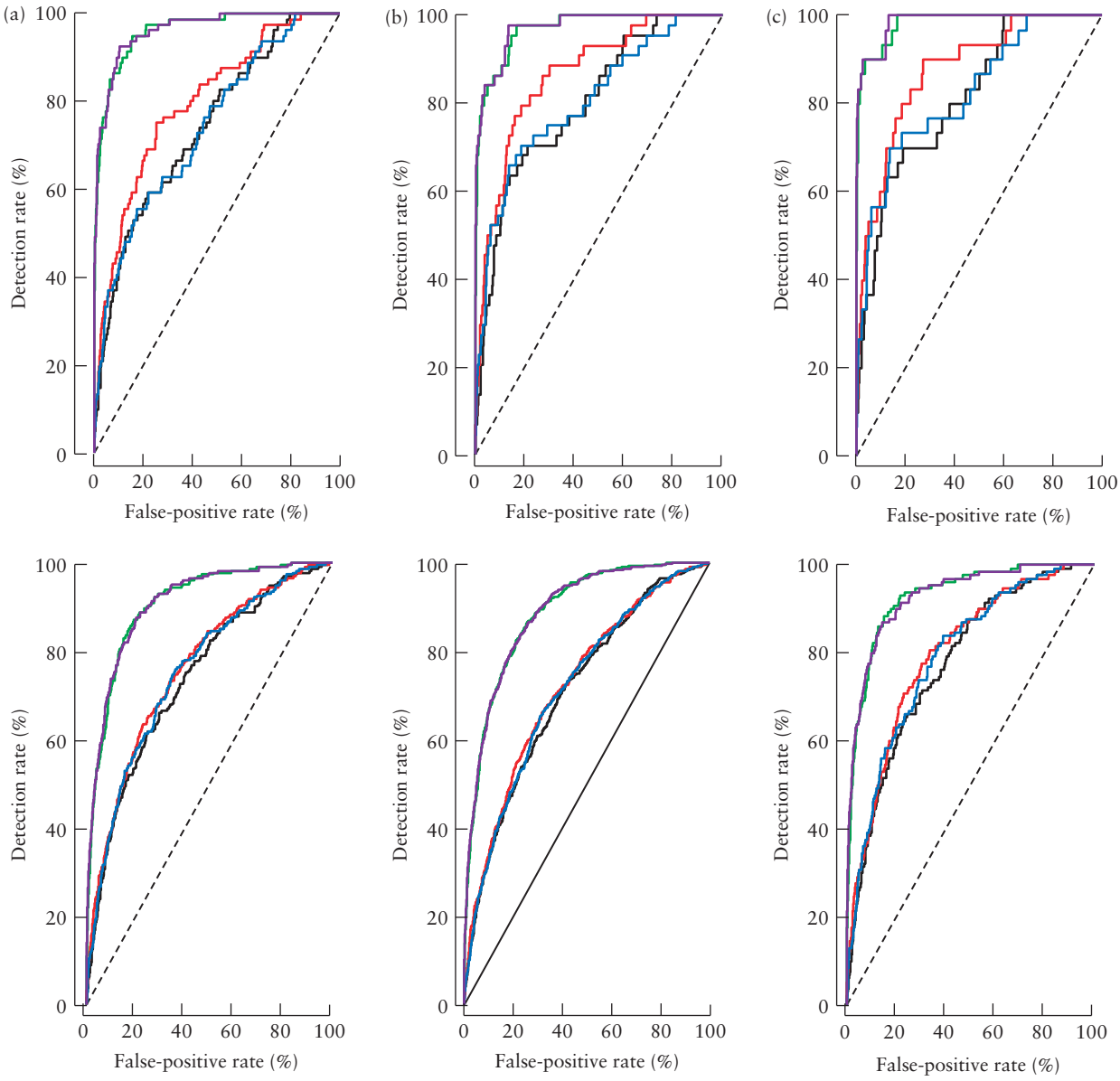

Figure 1 Receiver–operating characteristics curves of maternal factors (——) and maternal factors with uterine artery pulsatility index (——), mean arterial pressure (——), estimated fetal weight *Z*-score (——) and their combination (——), at 35–37 weeks' gestation, in the prediction of small-for-gestational-age neonates with birth weight < 10th (a), < 5th (b) or < 3rd (c) percentile, delivering < 2 weeks following assessment (top) or ≥ 37 weeks' gestation (bottom).

a third-trimester scan for assessment of fetal growth and wellbeing and that the timing of such a scan, at 32 or 36 weeks, should be contingent on the results of the assessment made at around 22 weeks[4,5]. On the basis of the results from this study, screening for SGA at 36 weeks does not benefit from measurement of UtA-PI and MAP.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Figure S1 Log_{10} uterine artery pulsatility index (UtA-PI) (a,b) and log_{10} mean arterial pressure (MAP) (c,d) multiples of median according to assessment-to-delivery interval (a,c) and birth-weight *Z*-score (b,d) in pregnancies delivering small-for-gestational-age neonates with birth weight < 5th percentile, plotted on the 50th (solid line), 90th and 95th (dashed line) percentile of the appropriate normal range.

Table S1 Uterine artery pulsatility index (UtA-PI) and mean arterial pressure (MAP) at 35–37 weeks' gestation in pregnancies that delivered small-for-gestational-age (SGA) neonates with birth weight < 5th percentile, in the absence of pre-eclampsia, and in unaffected pregnancies

Table S2 Fitted regression models with maternal characteristics and history, estimated fetal weight (EFW) *Z*-score, uterine artery pulsatility index (UtA-PI) and mean arterial pressure (MAP) at 35–37 weeks' gestation for the prediction of small-for-gestational-age neonates with birth weight < 5th percentile, in the absence of pre-eclampsia

Table S3 Performance of screening for small-for-gestational-age (SGA) neonates with birth weight < 10th, < 5th and < 3rd percentile, delivering within 2 weeks of assessment, in the absence of pre-eclampsia, using maternal factors, estimated fetal weight (EFW), uterine artery pulsatility index (UtA-PI) and mean arterial pressure (MAP) at 35–37 weeks' gestation

Table S4 Performance of screening for small-for-gestational-age (SGA) neonates with birth weight < 10th, < 5th and < 3rd percentile, delivering ≥ 37 weeks, in the absence of pre-eclampsia, using maternal factors, estimated fetal weight (EFW), uterine artery pulsatility index (UtA-PI) and mean arterial pressure (MAP) at 35–37 weeks' gestation