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Prediction of small-for-gestational-age neonates at 35–37 weeks' gestation: contribution of maternal factors and growth velocity between 32 and 36 weeks

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KEYWORDS: estimated fetal weight; growth charts; growth velocity; small-for-gestational age; third-trimester screening

ABSTRACT

Objective *To assess the additive value of fetal growth velocity between 32 and 36 weeks' gestation to the performance of ultrasonographic estimated fetal weight (EFW) at 35 + 0 to 36 + 6 weeks' gestation for prediction of delivery of a small-for-gestational-age (SGA) neonate and adverse perinatal outcome.*

Methods *This was a prospective study of 14 497 singleton pregnancies undergoing routine ultrasound examination at 30 + 0 to 34 + 6 and at 35 + 0 to 36 + 6 weeks' gestation. Multivariable logistic regression analysis was used to determine whether addition of growth velocity, defined as the difference in EFW Z-score or abdominal circumference (AC) Z-score between the early and late third-trimester scans divided by the time interval between the scans, improved the performance of EFW Z-score at 35 + 0 to 36 + 6 weeks in the prediction of, first, delivery of a SGA neonate with birth weight < 10th and < 3rd percentiles within 2 weeks and at any stage after assessment and, second, a composite of adverse perinatal outcome, defined as stillbirth, neonatal death or admission to the neonatal unit for ≥ 48 h.*

Results *Multivariable logistic regression analysis demonstrated that significant contributors to the prediction of a SGA neonate were EFW Z-score at 35 + 0 to 36 + 6 weeks' gestation, fetal growth velocity, by either AC Z-score or EFW Z-score, and maternal risk factors. The area under the receiver–operating characteristics curve (AUC) and detection rate (DR), at a 10% screen-positive rate, for prediction of a SGA neonate < 10th percentile born within 2 weeks after assessment achieved by EFW Z-score at 35 + 0 to 36 + 6 weeks (AUC, 0.938 (95% CI, 0.928–0.947); DR, 80.7% (95% CI, 77.6–83.9%)) were not significantly improved by addition of EFW growth velocity and maternal risk factors (AUC, 0.941 (95% CI, 0.932–0.950); P = 0.061; DR, 82.5% (95% CI, 79.4–85.3%)). Similar results were obtained when growth velocity was defined by AC rather than EFW. Similarly, there was no significant improvement in the AUC and DR, at a 10% screen-positive rate, for prediction of a SGA neonate < 10th percentile born at any stage after assessment or a SGA neonate < 3rd percentile born within 2 weeks or at any stage after assessment, achieved by EFW Z-score at 35 + 0 to 36 + 6 weeks by addition of maternal factors and either EFW growth velocity or AC growth velocity. Multivariable logistic regression analysis demonstrated that the only significant contributor to adverse perinatal outcome was maternal risk factors. Multivariable logistic regression analysis in the group with EFW < 10th percentile demonstrated that significant contribution to prediction of delivery of a neonate with birth weight < 10th and < 3rd percentiles and adverse perinatal outcome was provided by EFW Z-score at 35 + 0 to 36 + 6 weeks, but not by AC growth velocity < 1st decile.*

Conclusion *The predictive performance of EFW at 35 + 0 to 36 + 6 weeks' gestation for delivery of a SGA neonate and adverse perinatal outcome is not improved by addition of estimated growth velocity between 32 and 36 weeks' gestation.* Copyright © 2019 ISUOG. *Published by John Wiley & Sons Ltd.*

INTRODUCTION

Several studies have reported on the prenatal diagnosis and management of small-for-gestational-age (SGA)

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fetuses[1–13]. These studies have established that, first, the predictive performance of the traditional method of identifying pregnancies with a SGA fetus, maternal abdominal palpation and serial measurements of symphysis–fundus height, is poor[1,3], second, substantially improved prediction of SGA is achieved by universal sonographic fetal biometry during the third trimester[8–12] and, third, about 85% of SGA neonates are born at ≥ 37 weeks' gestation[14] and the predictive performance of routine ultrasonography at 36 weeks' gestation is superior to that at 32 weeks[8,9,11].

Although the performance of routine ultrasonographic estimated fetal weight (EFW) at 36 weeks' gestation is superior to that of other methods, this requires further improvement. One approach aiming for such improvement in the predictive performance of the 36-week scan is to combine EFW with maternal demographic characteristics and medical history; two studies reported that, with the addition of maternal risk factors, prediction of a SGA neonate born at any stage after assessment was improved from 63% to about 67%, at a screen-positive rate of 10%[9,15]. Further improvement in prediction to about 70% can be achieved with the addition of serum placental growth factor and uterine artery and fetal middle cerebral artery pulsatility indices[14]. Another approach to improving the prediction of a SGA neonate and adverse perinatal outcome provided by fetal biometry is assessment of fetal growth velocity; however, previous studies investigating the potential value of fetal growth velocity reported contradictory results[15–21]. In a study of 44 043 singleton pregnancies undergoing routine ultrasound examination at 19 + 0 to 23 + 6 and at 35 + 0 to 36 + 6 weeks' gestation, we found that the predictive performance of EFW *Z*-score at 35 + 0 to 36 + 6 weeks was not improved by addition of estimated growth velocity between the second and third trimesters of pregnancy[15]. A possible explanation for such failure is the long interval between the two ultrasound examinations that defined growth velocity and the proximity of the second scan to delivery, which would inevitably minimize the contribution of growth velocity to that of EFW at 35 + 0 to 36 + 6 weeks.

The objective of this study was to assess the additive value of fetal growth velocity between 32 and 36 weeks' gestation to the performance of ultrasonographic EFW at 35 + 0 to 36 + 6 weeks' gestation for prediction of a SGA neonate and adverse perinatal outcome.

METHODS

The inclusion criteria for this study were women with a singleton pregnancy undergoing routine ultrasound examination at 35 + 0 to 36 + 6 weeks' gestation, who had a previous scan at least 2 weeks earlier at 30 + 0 to 34 + 6 weeks and delivered a non-malformed liveborn or stillborn neonate. We excluded pregnancies with aneuploidy or major fetal abnormality. The women were examined at King's College Hospital, London or Medway Maritime Hospital, Gillingham, UK between October 2013 and September 2018. We recorded maternal demographic characteristics and medical history and carried out the two ultrasound examinations for fetal anatomy and measurement of fetal head circumference, abdominal circumference (AC) and femur length for calculation of EFW using the Hadlock formula[22], which has been shown to be the most accurate among 70 models reported previously[23]. Gestational age was determined by the measurement of fetal crown–rump length at 11–13 weeks or fetal head circumference at 19–24 weeks[24,25]. The ultrasound examinations were carried out by examiners who had obtained The Fetal Medicine Foundation Certificate of Competence in ultrasound examination for fetal abnormalities. The women gave written informed consent to participate in the study, which was approved by the NHS Research Ethics Committee.

Patient characteristics

Patient characteristics recorded included maternal age and racial origin (white, black, South Asian, East Asian or mixed), method of conception (natural, by *in-vitro* fertilization or use of ovulation induction drugs), cigarette smoking during pregnancy, medical history of chronic hypertension and diabetes mellitus, and obstetric history including parity (parous or nulliparous if no previous pregnancy at ≥ 24 weeks' gestation) and previous pregnancy with SGA. Maternal weight and height were measured.

Outcome measures

Data on pregnancy outcome were collected from the hospital maternity records or the general medical practitioners of the women. The outcome measures of the study were, first, delivery of a SGA neonate with birth weight < 10th and < 3rd percentiles for gestational age[26], within 2 weeks and at any stage after assessment, and, second, a composite of adverse perinatal outcome, defined as stillbirth, neonatal death or admission to the neonatal unit for ≥ 48 h.

Statistical analysis

Data were expressed as median (interquartile range) for continuous variables and *n* (%) for categorical variables. The Mann–Whitney *U*-test and χ^2 test or Fisher's exact test, were used for comparing outcome groups for continuous and categorical data, respectively. Significance was assumed at 5%.

In the dataset of 14 497 singleton pregnancies with paired measurements of fetal biometry at 30 + 0 to 34 + 6 and 35 + 0 to 36 + 6 weeks' gestation, the observed measurements of AC and EFW were expressed as *Z*-scores for gestational age[25,26]. Fetal growth velocity was defined as the difference in AC *Z*-score or EFW *Z*-score between the two ultrasound scans divided by the time interval in days between the scans. Univariable and multivariable regression analyses were carried out to determine whether the addition of AC and EFW growth

velocity and maternal factors to EFW *Z*-score at 35 + 0 to 36 + 6 weeks' gestation improved the performance of screening for, first, a SGA neonate $< 10^{th}$ and $< 3^{rd}$ percentiles delivered within 2 weeks and at any stage after assessment, and, second, adverse perinatal outcome. In the prediction of adverse perinatal outcome, we assumed the relationship between the dependent and independent variables to be linear as growth velocity was evaluated within a narrow gestational-age window (between 30 + 0 to 34 + 6 and 35 + 0 to 36 + 6 weeks' gestation). The *a-priori* risk for SGA based on maternal factors was derived from a dataset of 124 443 singleton pregnancies at 11 + 0 to 13 + 6 weeks' gestation using multivariable logistic regression analysis with backward stepwise elimination to determine which of the factors among maternal characteristics and medical and obstetric histories had a significant contribution in predicting SGA $< 10^{th}$ percentile[14]. Regression analysis was also carried out in the group with EFW $< 10^{th}$ percentile to determine whether EFW *Z*-score at 35 + 0 to 36 + 6 weeks' gestation and AC growth velocity $< 1^{st}$ decile had a significant contribution in the prediction of, first, a SGA neonate $< 10^{th}$ and $< 3^{rd}$ percentiles delivered at any stage after assessment, and, second, adverse perinatal outcome. The performance of screening was determined by receiver–operating characteristics (ROC) curve analysis. We estimated detection rates (DR) with 95% CI for a fixed screen-positive rate of 10% and screen-positive rates (95% CI) for fixed DRs of 85%, 90% and 95%.

The statistical software package SPSS Statistics for Windows version 24.0 (IBM Corp., Armonk, NY, USA) and MedCalc (MedCalc Software, Mariakerke, Belgium) were used for data analyses.

RESULTS

Patient characteristics

During the study period, 44 043 singleton pregnancies underwent routine ultrasound examination at 35 + 0 to 36 + 6 weeks' gestation. A search of our fetal database identified 14 497 of these that had undergone an additional ultrasound examination at least 2 weeks earlier at 30 + 0 to 34 + 6 weeks. The indications for the ultrasound scan at 30 + 0 to 34 + 6 weeks included: (1) high risk of pre-eclampsia (PE) and/or SGA because of abnormal screening results in the first or second trimester of pregnancy, such as low serum pregnancy-associated plasma protein-A, high uterine artery pulsatility index or single umbilical artery (27.8%); (2) previous pregnancy complications, such as perinatal death, placental abruption, PE and/or SGA (11.4%); (3) maternal medical disorders, such as chronic hypertension, antiphospholipid syndrome, diabetes mellitus or hypothyroidism (11.7%); (4) pregnancy complications, such as PE, gestational diabetes mellitus or cholestasis (9.1%); (5) small or large symphysis–fundus height (11.9%); (6) increased maternal age or weight (9.0%); (7) reduced fetal movements (7.0%); (8) minor fetal defects, such as mild ventriculomegaly or mild hydronephrosis (5.0%); (9) low-lying placenta and/or antepartum hemorrhage (6.2%); and (10) increased risk of preterm birth due to abdominal pain, reduced cervical length or history of preterm birth (0.9%).

The characteristics of the study population of 14 497 pregnancies are shown in Table 1. In the group with a SGA neonate, compared to those with birth weight $\geq 10^{th}$ percentile, median maternal age, weight and height, EFW *Z*-score at both visits and birth-weight *Z*-score were lower, more women were of non-white racial origin, a smoker, nulliparous or parous with previous pregnancy affected by SGA, and fewer women had diabetes mellitus Type 1 or Type 2. The incidence of adverse perinatal outcome was significantly higher in the SGA than in the non-SGA group (12.7% *vs* 8.6%; $P < 0.001$).

Prediction of SGA neonate

Multivariable logistic regression analysis demonstrated that significant contributors to the prediction of a SGA neonate were EFW *Z*-score at 35 + 0 to 36 + 6 weeks' gestation, fetal growth velocity, by either AC *Z*-score or EFW *Z*-score, and maternal risk factors (Table 2). The area under the ROC curve (AUC) for prediction of a SGA neonate $< 10^{th}$ percentile born within 2 weeks after assessment achieved by EFW *Z*-score at 35 + 0 to 36 + 6 weeks was not significantly improved by addition of EFW growth velocity and maternal risk factors (0.938 (95% CI, 0.928–0.947 *vs* 0.941 (95% CI, 0.932–0.950); $P = 0.061$) (Table 3 and Figure 1). Similarly, there were no statistically significant differences in DR, at a 10% screen-positive rate, in screening with compared to screening without the addition of EFW growth velocity and maternal risk factors (Table 3); similar results were obtained when growth velocity was defined by AC *Z*-score. There was no significant improvement in the AUC and DR, at a 10% screen-positive rate, for prediction of a SGA neonate $< 10^{th}$ percentile born at any stage after assessment or a SGA neonate $< 3^{rd}$ percentile born within 2 weeks or at any stage after assessment achieved by EFW *Z*-score at 35 + 0 to 36 + 6 weeks by addition of maternal risk factors and either EFW growth velocity or AC growth velocity.

The screen-positive rates necessary to achieve prediction of 85%, 90% and 95% of SGA neonates born within 2 weeks and at any stage after assessment at 35 + 0 to 36 + 6 weeks' gestation are shown in Table 4. For a desired 90% DR of a SGA neonate $< 10^{th}$ percentile born at any stage after assessment, the necessary screen-positive rate would be 30.7% (95% CI, 29.9–31.5%) in screening by EFW *Z*-score at 35 + 0 to 36 + 6 weeks and 29.8% (95% CI, 29.0–30.6%) in screening by EFW *Z*-score, EFW growth velocity and maternal risk factors.

Prediction of adverse perinatal outcome

The incidence of adverse perinatal outcome in the study population was 9.2% (1336/14 497). The contribution

Table 1 Maternal and pregnancy characteristics in 14 497 singleton pregnancies, according to delivery of small-for-gestational-age (SGA) neonate with birth weight (BW) < 10th percentile

Characteristic	*Non-SGA (n = 12 216)*	*SGA (n = 2281)*	P
Maternal age (years)	32.2 (27.8–36.1)	31.2 (26.5–35.3)	< 0.001
Maternal weight (kg)	81.6 (72.0–94.3)	74.0 (65.6–85.0)	< 0.001
Maternal height (cm)	165 (160–169)	163 (158–167)	< 0.001
Racial origin			
White	8917 (73.0)	1428 (62.6)	< 0.001
Black	2142 (17.5)	515 (22.6)	< 0.001
South Asian	573 (4.7)	214 (9.4)	< 0.001
East Asian	228 (1.9)	51 (2.2)	0.238
Mixed	356 (2.9)	73 (3.2)	0.459
Cigarette smoker	942 (7.7)	337 (14.8)	< 0.001
Conception			
Natural	11 693 (95.7)	2190 (96.0)	
Ovulation drugs	71 (0.6)	14 (0.6)	0.852
In-vitro fertilization	452 (3.7)	77 (3.4)	0.448
Medical condition			
Chronic hypertension	383 (3.1)	71 (3.1)	0.955
Diabetes mellitus Type 1	161 (1.3)	1 (0.04)	< 0.001
Diabetes mellitus Type 2	215 (1.8)	22 (1.0)	0.006
Obstetric history			
Nulliparous	4848 (39.7)	1154 (50.6)	< 0.001
Parous with prior SGA	1218 (10.0)	529 (23.2)	< 0.001
Parous without prior SGA	6150 (50.3)	598 (26.2)	< 0.001
30 + 0 to 34 + 6-week scan			
GA (weeks)	32.3 (31.9–32.6)	32.3 (31.9–32.7)	< 0.001
EFW *Z*-score	0.21 (−0.43 to 0.89)	−1.11 (−1.79 to −0.51)	< 0.001
AC *Z*-score	0.04 (−0.40 to 0.50)	−0.76 (−1.19 to −0.37)	< 0.001
35 + 0 to 36 + 6-week scan			
GA (weeks)	36.1 (35.9–36.4)	36.1 (35.9–36.4)	0.020
EFW *Z*-score	0.17 (−0.47 to 0.82)	−1.44 (−2.14 to −0.78)	< 0.001
AC *Z*-score	−0.06 (−0.56 to 0.47)	−1.18 (−1.67 to −0.70)	0.001
GA at delivery (weeks)	39.6 (38.9–40.6)	39.1 (38.0–40.1)	< 0.001
Birth-weight *Z*-score	0.07 (−0.53 to 0.71)	−1.79 (−2.25 to −1.51)	< 0.001
Birth weight (g)	3422 (3155–3725)	2655 (2440–2820)	< 0.001
Adverse perinatal outcome	1046 (8.6)	290 (12.7)	< 0.001

Data are given as median (interquartile range) or *n* (%). AC, abdominal circumference; EFW, estimated fetal weight; GA, gestational age.

Table 2 Univariable and multivariable logistic regression analysis in prediction of small-for-gestational-age (SGA) neonate < 10th and < 3rd percentiles and adverse perinatal outcome by maternal risk factors, estimated fetal weight (EFW) *Z*-score at 35 + 0 to 36 + 6 weeks' gestation and EFW growth velocity or abdominal circumference (AC) growth velocity

	Univariable		*Multivariable**		*Multivariable†*	
Characteristic	*OR (95% CI)*	P	*OR (95% CI)*	P	*OR (95% CI)*	P
SGA < 10th percentile						
Maternal factors	13.55 (11.49–15.99)	< 0.001	5.77 (4.71–7.07)	< 0.001	5.74 (4.69–7.03)	< 0.001
EFW *Z*-score	0.17 (0.16–0.18)	< 0.001	0.17 (0.16–0.18)	< 0.001	0.17 (0.15–0.18)	< 0.001
EFW growth velocity	$3.01e^{-7}$ ($5.44e^{-8}$–$2.01e^{-6}$)	< 0.001	25.11 (8.79–72.07)	< 0.001	—	—
AC growth velocity	$8.04e^{-12}$ ($9.33e^{-13}$–$6.92e^{-11}$)	< 0.001	—	—	116.50 (21.06–175.13)	< 0.001
SGA < 3rd percentile						
Maternal factors	13.80 (10.94–17.40)	< 0.001	4.46 (3.37–5.92)	< 0.001	4.46 (3.37–5.92)	< 0.001
EFW *Z*-score	0.17 (0.15–0.18)	< 0.001	0.16 (0.15–0.18)	< 0.001	0.16 (0.15–0.18)	< 0.001
EFW growth velocity	$3.43e^{-8}$ ($3.28e^{-9}$–$3.60e^{-7}$)	< 0.001	142.41 (23.35–235.98)	< 0.001	—	—
AC growth velocity	$1.76e^{-13}$ ($9.09e^{-15}$–$3.40e^{-12}$)	< 0.001	—	—	62.27 (4.29–243.40)	< 0.001
Adverse perinatal outcome						
Maternal factors	0.66 (0.50–0.87)	0.004	0.66 (0.50–0.87)	0.004	0.66 (0.50–0.87)	0.004
EFW *Z*-score	0.97 (0.91–1.03)	0.282	—	—	—	—
EFW growth velocity	0.48 (0.02–11.09)	0.645	—	—	—	—
AC growth velocity	15.18 (0.37–626.41)	0.152	—	—	—	—

*Model incorporating EFW growth velocity. †Model incorporating AC growth velocity. OR, odds ratio.

Table 3 Performance of prediction of small-for-gestational-age (SGA) neonate with birth weight < 10th and < 3rd percentiles, delivered within 2 weeks and at any stage after screening at 35 + 0 to 36 + 6 weeks' gestation, by maternal risk factors, estimated fetal weight (EFW) *Z*-score and EFW growth velocity or abdominal circumference (AC) growth velocity

	SGA < 10th percentile		*SGA < 3rd percentile*	
Screening test	*AUC*	*DR at 10% SPR (%)*	*AUC*	*DR at 10% SPR (%)*
SGA within 2 weeks				
EFW *Z*-score	0.938 (0.928–0.947)	80.7 (77.6–83.9)	0.943 (0.934–0.952)	80.5 (77.2–83.7)
Maternal factors	0.696 (0.673–0.718)	29.1 (26.5–32.4)	0.691 (0.663–0.718)	28.1 (25.2–31.6)
EFW growth velocity	0.670 (0.645–0.694)	31.3 (28.4–34.7)	0.694 (0.664–0.725)	35.9 (32.3–38.8)
EFW *Z*-score + EFW growth velocity + maternal factors	0.941 (0.932–0.950)	82.5 (79.4–85.3)	0.944 (0.935–0.953)	79.2 (76.3–82.6)
AC growth velocity	0.722 (0.699–0.745)	35.1 (32.0–38.4)	0.747 (0.719–0.775)	38.0 (35.1–41.3)
EFW *Z*-score + AC growth velocity + maternal factors	0.941 (0.932–0.950)	81.9 (78.3–84.7)	0.944 (0.935–0.954)	80.2 (77.7–83.8)
SGA at any stage				
EFW *Z*-score	0.891 (0.885–0.898)	65.3 (63.0–67.7)	0.920 (0.913–0.928)	73.3 (70.2–76.1)
Maternal factors	0.709 (0.697–0.720)	31.1 (28.6–33.1)	0.712 (0.696–0.729)	32.4 (29.7–35.9)
EFW growth velocity	0.613 (0.600–0.626)	21.2 (18.6–24.4)	0.636 (0.617–0.654)	25.4 (22.6–28.7)
EFW *Z*-score + EFW growth velocity + maternal factors	0.902 (0.896–0.908)	69.3 (66.8–72.4)	0.927 (0.920–0.934)	75.2 (72.4–78.6)
AC growth velocity	0.659 (0.647–0.672)	24.4 (21.3–27.7)	0.689 (0.671–0.706)	30.0 (27.1–33.6)
EFW *Z*-score + AC growth velocity + maternal factors	0.902 (0.896–0.908)	69.2 (66.7–72.3)	0.926 (0.919–0.934)	75.9 (73.0–78.8)

Values in parentheses are 95% CI. AUC, area under the receiver–operating characteristics curve; DR, detection rate; SPR, screen-positive rate.

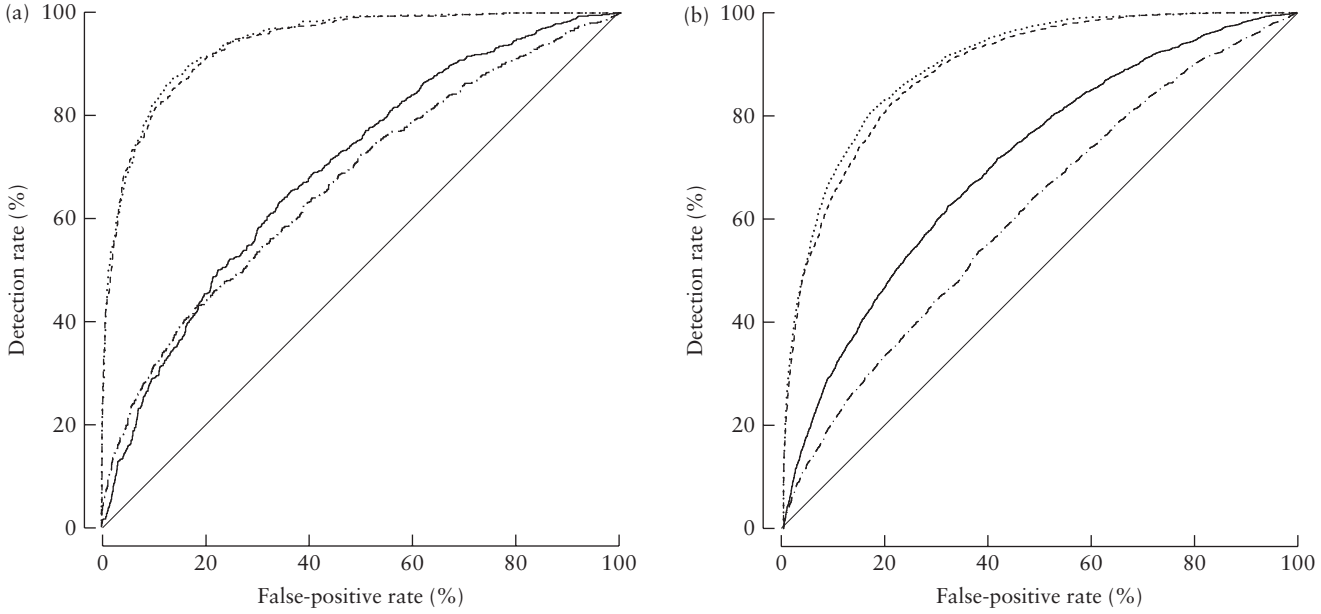

Figure 1 Receiver–operating characteristics curves of maternal risk factors (——), estimated fetal weight *Z*-score at 35 + 0 to 36 + 6 weeks' gestation (- - - -), estimated fetal weight growth velocity (— · —) and combination of the three (·····) in prediction of small-for-gestational-age neonate with birth weight < 10th percentile, delivered within 2 weeks (a) and at any time (b) after assessment.

of SGA neonates with birth weight < 10th percentile to adverse perinatal outcome was 21.7% (290/1336). Multivariable logistic regression analysis in the whole population demonstrated that the only significant contributor to adverse perinatal outcome was maternal risk factors (Table 2).

Prediction in group with EFW < 10th percentile

Multivariable logistic regression analysis in the group with EFW < 10th percentile demonstrated that significant contribution to prediction of delivery of a neonate with birth weight < 10th or < 3rd percentile and adverse perinatal outcome was provided by EFW *Z*-score at 35 + 0 to 36 + 6 weeks, but not by AC growth velocity < 1st decile (Table 5).

DISCUSSION

Main findings

The findings of this study demonstrate that, although significant contributors to the prediction of a SGA neonate

Table 4 Screen-positive rate (SPR) necessary to achieve prediction of 85%, 90% and 95% of small-for-gestational-age (SGA) neonates delivered within 2 weeks and at any stage after assessment at 35 + 0 to 36 + 6 weeks' gestation

Screening test	*SPR for 85% DR (%)*	*SPR for 90% DR (%)*	*SPR for 95% DR (%)*
SGA within 2 weeks			
SGA < 10th percentile			
EFW *Z*-score	16.6 (12.1–15.2)	18.9 (17.2–20.7)	26.4 (24.4–28.4)
EFW *Z*-score + EFW growth velocity + maternal factors	12.0 (10.6–13.6)	17.2 (15.6–19.0)	27.1 (25.1–29.2)
EFW *Z*-score + AC growth velocity + maternal factors	12.6 (11.1–14.2)	17.7 (16.0–19.5)	27.5 (25.5–29.5)
SGA < 3rd percentile			
EFW *Z*-score	13.4 (12.0–14.9)	16.7 (15.1–18.3)	22.0 (20.3–23.8)
EFW *Z*-score + EFW growth velocity + maternal factors	13.1 (11.7–14.6)	16.1 (14.6–17.7)	20.4 (18.7–22.1)
EFW *Z*-score + AC growth velocity + maternal factors	13.1 (11.7–14.6)	15.4 (13.9–16.9)	20.1 (18.5–21.9)
SGA at any stage			
SGA < 10th percentile			
EFW *Z*-score	21.2 (23.4–25.0)	30.7 (29.9–31.5)	43.0 (42.1–43.9)
EFW *Z*-score + EFW growth velocity + maternal factors	22.2 (21.4–22.9)	29.8 (29.0–30.6)	40.0 (39.1–40.8)
EFW *Z*-score + AC growth velocity + maternal factors	22.4 (21.6–23.1)	29.4 (28.5–30.2)	40.2 (39.3–41.2)
SGA < 3rd percentile			
EFW *Z*-score	17.7 (17.1–18.4)	23.1 (22.4–23.9)	32.8 (32.0–33.6)
EFW *Z*-score + EFW growth velocity + maternal factors	16.2 (15.6–16.8)	20.8 (20.1–21.5)	31.0 (30.2–31.8)
EFW *Z*-score + AC growth velocity + maternal factors	16.2 (15.6–16.8)	21.3 (20.6–22.0)	31.0 (30.3–21.8)

Values in parentheses are 95% CI. AC, abdominal circumference; DR, detection rate; EFW, estimated fetal weight.

Table 5 Multivariable logistic regression analysis in prediction of small-for-gestational-age (SGA) neonate < 10th and < 3rd percentiles and adverse perinatal outcome by estimated fetal weight (EFW) *Z*-score and abdominal circumference (AC) growth velocity < 1st decile in pregnancies with EFW < 10th percentile at 35 + 0 to 36 + 6 weeks' gestation

	SGA < 10th percentile		*SGA < 3rd percentile*		*Adverse perinatal outcome*	
Variable	*OR (95% CI)*	P	*OR (95% CI)*	P	*OR (95% CI)*	P
EFW *Z*-score	0.20 (0.16–0.24)	< 0.001	0.23 (0.19–0.28)	< 0.001	0.50 (0.43–0.59)	< 0.001
AC growth velocity < 1st decile	0.84 (0.66–1.05)	0.123	0.98 (0.78–1.24)	0.884	1.15 (0.86–1.55)	0.343

OR, odds ratio.

were EFW *Z*-score at 35 + 0 to 36 + 6 weeks' gestation, fetal growth velocity between 32 and 36 weeks, by either AC *Z*-score or EFW *Z*-score, and maternal risk factors, the predictive performance of EFW *Z*-score was not improved by the addition of growth velocity and maternal risk factors. The incidence of adverse perinatal outcome was higher in SGA than in non-SGA neonates (12.7% *vs* 8.6%), but about 80% of adverse perinatal events occurred in non-SGA neonates. The only significant contributor to adverse perinatal outcome was maternal risk factors. Multivariable logistic regression analysis in the group with EFW < 10th percentile demonstrated that significant contribution to prediction of delivery of a SGA neonate and adverse perinatal outcome was provided by EFW *Z*-score at 35 + 0 to 36 + 6 weeks, but not by AC growth velocity < 1st decile.

Comparison with previous studies

Previous studies have investigated the effect of fetal growth velocity on prediction of, first, delivery of a SGA neonate and, second, adverse perinatal outcome. In relation to prediction of delivery of a SGA neonate, our finding that the performance of EFW is not improved by the addition of growth velocity is consistent with the results of previous studies. Tarca *et al.* examined 3440 pregnancies and reported that serial fetal biometry did not improve the prediction of a SGA neonate provided by the last EFW before delivery alone[16]. Caradeux *et al.* examined 2696 pregnancies at 22 and 32 weeks' gestation and reported that AC growth velocity between 22 and 32 weeks did not improve the prediction of a SGA neonate provided by AC at 32 weeks[17]. Ciobanu *et al.* examined 44 043 singleton pregnancies undergoing routine ultrasound examination at 19 + 0 to 23 + 6 and at 35 + 0 to 36 + 6 weeks' gestation and reported that the predictive performance for a SGA neonate provided by EFW in the third trimester is not improved by addition of growth velocity between the second and third trimesters of pregnancy[15].

In relation to prediction of adverse perinatal outcome, previous studies examined the effect of growth velocity or conditional growth in SGA fetuses rather than in the total population. Sovio *et al.* reported that, in 562 SGA fetuses with EFW < 10th percentile at a third-trimester scan, those with low AC growth velocity < 1st decile between 20 weeks' gestation and the last scan before delivery had a higher prevalence of adverse perinatal outcome, compared to those without such a low degree of AC growth velocity (15.7% *vs* 10.3%; $P = 0.01$); however, the authors did not present evidence that growth velocity improved the performance of screening

for adverse perinatal outcome achieved by EFW percentile alone[12]. Karlsen *et al.* performed serial ultrasound scans in 211 pregnancies with a suspected SGA fetus and reported that growth velocity improved the prediction of adverse perinatal outcome provided by cross-sectional measurements of fetal biometry[18]. In contrast, Cavallaro *et al.* reported that, in 235 SGA fetuses diagnosed at 36–38 weeks' gestation, low AC growth velocity between 19–21 and 36–38 weeks did not improve the prediction of adverse perinatal outcome provided by EFW and cerebroplacental ratio at 36–38 weeks (AUC, 0.741 *vs* 0.669; $P = 0.110$)[19]. Similarly, Hutcheon *et al.* used EFW in 9239 singleton pregnancies undergoing routine ultrasound examination at 32–33 weeks' gestation to predict birth weight and reported that differences between expected and observed birth weights, attributed to varying growth velocity between the scan and delivery, did not improve the prediction of adverse outcome of SGA neonates provided by birth-weight percentile alone[20]. Caradeux *et al.* examined longitudinally 472 SGA fetuses diagnosed at > 32 weeks' gestation and reported that, on subsequent scans, EFW growth velocity did not improve the prediction of adverse perinatal outcome provided by EFW, uterine artery pulsatility index and cerebroplacental ratio recorded at the last scan before delivery[21].

Implications for clinical practice

Several studies have reported, first, how best to monitor and deliver SGA neonates[2,5–7], second, that about 85% of SGA neonates are born at ≥ 37 weeks' gestation and, third, that the best prediction of a SGA neonate is achieved by routine ultrasound examination at 36 weeks' gestation[8,9,11,12,14]. The findings of this study have highlighted the necessity to improve the performance of the 36-week assessment in the prediction of both delivery of a SGA neonate and adverse perinatal outcome, and have demonstrated that these goals cannot be achieved by addition of fetal growth velocity between 32 and 36 weeks' gestation to EFW at 36 weeks.

Strengths and limitations

The strengths of this screening study for SGA neonates are, first, examination of a large population of pregnant women attending for assessment of fetal growth and well-being at both 30 + 0 to 34 + 6 and 35 + 0 to 36 + 6 weeks' gestation, second, assessment of fetal biometry by trained sonographers according to a standardized protocol and use of a widely used model for calculation of EFW[22] which has been shown to be the most accurate among 70 models reported previously[23], third, use of The Fetal Medicine Foundation fetal and neonatal reference ranges which have a common median[26], and, fourth, use of well-accepted indicators for adverse perinatal outcome.

A potential limitation of the study is the selection of patients undergoing the two ultrasound examinations. During the study period, we offered routine ultrasound examinations at 11 + 0 to 13 + 6, 19 + 0 to 23 + 6 and 35 + 0 to 36 + 6 weeks' gestation, whereas a scan at 30 + 0 to 34 + 6 weeks was offered only to women considered to be at increased risk of fetal growth disturbances or adverse outcome based on their demographic characteristics, medical history, results of first- or second-trimester screening for PE, small or large symphysis–fundus height and pregnancy complications. As a consequence of such preselection, the predictive performance of EFW at 35 + 0 to 36 + 6 weeks' gestation for a SGA neonate and adverse perinatal outcome in this study may not be the same as that in an unselected population. However, the objective of the study was to examine the effect of growth velocity on the performance of the EFW at 35 + 0 to 36 + 6 weeks and, in this respect, the results are valid.

Another potential limitation of the study is the assumption of a linear relationship between dependent and independent variables in regression analysis. A linear relationship was assumed as we examined growth velocity in a narrow gestational-age window (between 32 and 36 weeks' gestation).

Conclusions

The predictive performance of EFW at 35 + 0 to 36 + 6 weeks' gestation for delivery of a SGA neonate and adverse perinatal outcome is not improved by addition of estimated growth velocity between 32 and 36 weeks' gestation. The incidence of adverse perinatal outcome is higher in SGA than in non-SGA neonates, but only about one-fifth of adverse perinatal events are found in association with a SGA neonate. Future studies should investigate the potential improvement in prediction of adverse perinatal outcome by biomarkers of impaired placentation at the time of the 36-week assessment.

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