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# Prediction of small-for-gestational-age neonates at 35–37 weeks' gestation: contribution of maternal factors and growth velocity between 20 and 36 weeks

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**KEYWORDS:** estimated fetal weight; growth velocity; pyramid of pregnancy care; small-for-gestational age; third-trimester screening

## ABSTRACT

***Objectives*** *To evaluate the performance of ultrasonographic estimated fetal weight (EFW) at 35 + 0 to 36 + 6 weeks' gestation in the prediction of delivery of a small-for-gestational-age (SGA) neonate and assess the additive value of, first, maternal risk factors and, second, fetal growth velocity between 20 and 36 weeks' gestation in improving such prediction.*

***Methods*** *This was a prospective 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. Multivariable logistic regression analysis was used to determine whether addition of maternal risk factors and growth velocity, the latter defined as the difference in EFW Z-score or fetal abdominal circumference (AC) Z-score between the third- and second-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 delivery of a SGA neonate with birth weight < 10$^{th}$ and < 3$^{rd}$ percentiles within 2 weeks and at any stage after assessment.*

***Results*** *Screening by EFW Z-score at 35 + 0 to 36 + 6 weeks' gestation predicted 63.4% (95% CI, 62.0–64.7%) of neonates with birth weight < 10$^{th}$ percentile and 74.2% (95% CI, 72.2–76.1%) of neonates with birth weight < 3$^{rd}$ percentile born at any stage after assessment, at a screen-positive rate of 10%. The respective values for SGA neonates born within 2 weeks after assessment were 76.8% (95% CI, 74.4–79.0%) and 81.3% (95% CI, 78.2–84.0%). For a desired 90% detection rate of SGA neonate delivered at any stage after assessment, the necessary screen-positive rate would be 33.7% for SGA < 10$^{th}$ percentile and 24.4% for SGA < 3$^{rd}$ percentile. Multivariable logistic regression analysis demonstrated that, in the prediction of a SGA neonate with birth weight < 10$^{th}$ and < 3$^{rd}$ percentiles, there was a significant contribution from EFW Z-score at 35 + 0 to 36 + 6 weeks' gestation, maternal risk factors and AC growth velocity, but not EFW growth velocity. However, the area under the receiver–operating characteristics curve for prediction of delivery of a SGA neonate by screening with maternal risk factors and EFW Z-score was not improved by addition of AC growth velocity.*

***Conclusion*** *Screening for SGA neonates by EFW at 35 + 0 to 36 + 6 weeks' gestation and use of the 10$^{th}$ percentile as the cut-off predicts 63% of affected neonates. Prediction of 90% of SGA neonates necessitates classification of about 35% of the population as being screen positive. The predictive performance of EFW is not improved by addition of estimated growth velocity between the second and third trimesters of pregnancy.* 

## INTRODUCTION

Small-for-gestational-age (SGA) neonates are at increased risk of perinatal mortality and both short- and long-term morbidity, but these risks can be reduced if the condition is identified prenatally because, in such cases, close monitoring, appropriate timing of delivery and prompt neonatal care can be undertaken[1–3]. National guidelines of many developed countries define fetal growth

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restriction on the basis of ultrasonographic estimated fetal weight (EFW) < 10th percentile and severe growth restriction as EFW < 3rd percentile, with recommendations on the timing of delivery varying from 37 to 40 weeks' gestation depending on the severity of SGA and fetal Doppler findings[4]. However, there are several important issues that are often overlooked in such recommendations: first, the method of screening that leads to an ultrasound examination for estimation of fetal weight, second, the accuracy of such ultrasound examination, third, the selection of the reference ranges of EFW and birth weight for the diagnosis of SGA fetuses and SGA neonates, and, fourth, the degree of fetal growth between assessment and delivery.

In this paragraph, we summarize an approach for addressing the above issues. First, the traditional method of identifying pregnancies with a SGA fetus is maternal abdominal palpation and serial measurements of symphysis–fundus height, but the predictive performance of such screening is poor[5,6]. There is some evidence that substantially improved prediction of SGA is achieved by universal sonographic fetal biometry during the third trimester, especially at about 36 weeks' gestation[7–11]; this is because 85% of SGA neonates with birth weight < 10th percentile are born at ≥ 37 weeks' gestation[12]. Second, a systematic review of 45 studies describing a total of 70 models for EFW by various combinations of measurements of fetal head circumference (HC), biparietal diameter, femur length (FL) and abdominal circumference (AC)[13] reported that the most accurate model was provided by the formula of Hadlock *et al.*[14], which incorporates measurements of HC, AC and FL; the EFW measured within 2 days of delivery was within 10% of birth weight in 80% of cases[13]. Third, reference ranges of EFW are representative of the whole population, whereas, in the construction of reference ranges of birth weight, particularly for gestational ages < 37 weeks, there is over-representation of pathological pregnancies; to overcome this problem, we proposed the use of EFW and birth-weight charts with a common median[15]. Fourth, in a previous study of 5515 pregnancies undergoing routine ultrasound examination at 36 weeks' gestation, we found that EFW < 10th percentile predicted 87% of SGA neonates born within 2 weeks following assessment but only 63% of those born ≥ 37 weeks' gestation[8]. The study also reported that, for a desired prediction of 90% of SGA neonates delivered ≥ 37 weeks, the necessary screen-positive rate would be about 35%[8].

On the basis of the observed predictive performance for a SGA neonate of EFW at 36 weeks' gestation, compliance with national guidelines on the diagnosis and management of SGA fetuses would necessitate intensive monitoring and/or early iatrogenic delivery of about 35% of pregnancies and accepting that we would still miss about 10% of SGA neonates[8]. The objectives of this expanded series of 44 043 singleton pregnancies were to evaluate the performance of EFW at 35 + 0 to 36 + 6 weeks' gestation in the prediction of a SGA neonate and assess the additive value of, first, maternal risk factors and, second, fetal growth velocity between 20 and 36 weeks' gestation in improving such prediction.

## METHODS

This was a prospective 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 at King's College Hospital, London or Medway Maritime Hospital, Gillingham, UK between October 2013 and September 2018. At the first visit, we recorded maternal demographic characteristics and medical history and, at both visits, we carried out an ultrasound examination for fetal anatomy and measurement of fetal HC, AC and FL for calculation of EFW[14]. Gestational age was determined by the measurement of fetal crown–rump length at 11–13 weeks or fetal HC at 19–24 weeks[16,17]. The ultrasound examinations were carried out by 256 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. The inclusion criteria for this study were singleton pregnancy examined at both 19 + 0 to 23 + 6 and at 35 + 0 to 36 + 6 weeks' gestation and delivering a non-malformed liveborn or stillborn neonate. We excluded pregnancies with aneuploidy and/or major fetal abnormality.

### Patient characteristics

Patient characteristics recorded included maternal age, racial origin (white, black, South Asian, East Asian or mixed), method of conception (natural, *in-vitro* fertilization or use of ovulation induction drugs), cigarette smoking during pregnancy, medical history of chronic hypertension or 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 birth of a neonate with birth weight < 10th or < 3rd percentile for gestational age at delivery[14].

### Statistical analysis

Data are expressed as median (interquartile range) for continuous variables and *n* (%) for categorical variables. Mann–Whitney *U*-test and $\chi^2$ 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 44 043 singleton pregnancies with paired measurements of fetal biometry examined at 19 + 0 to 23 + 6 and 35 + 0 to 36 + 6 weeks' gestation, the observed measurements of EFW and AC were expressed as *Z*-scores for gestational age[14,17]. 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 history had a significant contribution in predicting SGA < 10$^{th}$ percentile[12]. Fetal growth velocity was defined as the difference in EFW *Z*-score or AC *Z*-score between the third- and second-trimester 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 maternal factors and EFW or AC growth velocity to the EFW *Z*-score at 35 + 0 to 36 + 6 weeks' gestation improved the performance of screening for a SGA neonate < 10$^{th}$ and < 3$^{rd}$ percentiles delivered within 2 weeks and at any stage after assessment. The performance of screening was determined by receiver–operating characteristics (ROC) curve analysis. We estimated detection rates (95% CI) for a fixed screen-positive rate of 10%, and screen-positive rates (95% CI) for fixed detection rates of 85%, 90% and 95%.

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

## RESULTS

### Patient characteristics

The characteristics of the study population are shown in Table 1. In the group with a SGA neonate, compared to the group with birth weight ≥ 10$^{th}$ percentile, the median maternal age, weight and height, EFW *Z*-score and AC *Z*-score at both visits and birth-weight *Z*-score were lower, more women were of non-white racial origin, were a smoker, had chronic hypertension, were nulliparous and were parous with previous pregnancy affected by SGA, and fewer women had diabetes mellitus Type 1.

**Table 1** Maternal and pregnancy characteristics in 44 043 singleton pregnancies, according to delivery of small-for-gestational-age (SGA) neonate with birth weight < 10$^{th}$ percentile

| *Characteristic* | *Non-SGA* (n = *38 994*) | *SGA* (n = *5049*) | P |
|---|---|---|---|
| Maternal age (years) | 31.7 (27.5–35.4) | 30.9 (26.2–35.0) | < 0.001 |
| Maternal weight (kg) | 80.0 (71.5–91.0) | 73.4 (65.5–83.4) | < 0.001 |
| Maternal height (cm) | 165 (161–170) | 163 (158–167) | < 0.001 |
| Racial origin | | | |
| White | 29 825 (76.5) | 3224 (63.9) | < 0.001 |
| Black | 5684 (14.6) | 1055 (20.9) | < 0.001 |
| South Asian | 1594 (4.1) | 467 (9.2) | < 0.001 |
| East Asian | 761 (2.0) | 121 (2.4) | 0.034 |
| Mixed | 1130 (2.9) | 182 (3.6) | 0.005 |
| Cigarette smoker | 2832 (7.3) | 726 (14.4) | < 0.001 |
| Conception | | | |
| Natural | 37 645 (96.5) | 4851 (96.1) | |
| Ovulation drugs | 219 (0.6) | 34 (0.7) | 0.323 |
| *In-vitro* fertilization | 1130 (2.9) | 164 (3.2) | 0.165 |
| Medical condition | | | |
| Chronic hypertension | 459 (1.2) | 88 (1.7) | 0.001 |
| Diabetes mellitus Type 1 | 156 (0.4) | 5 (0.1) | 0.001 |
| Diabetes mellitus Type 2 | 178 (0.5) | 18 (0.4) | 0.315 |
| Obstetric history | | | |
| Nulliparous | 17 114 (43.9) | 2811 (55.7) | < 0.001 |
| Parous with prior SGA | 2989 (7.7) | 920 (18.2) | < 0.001 |
| Parous without prior SGA | 18 891 (48.4) | 1318 (26.1) | < 0.001 |
| 19 + 0 to 23 + 6-week scan | | | |
| GA (weeks) | 21.7 (21.1–22.1) | 21.7 (21.1–22.1) | 0.003 |
| EFW *Z*-score | 0.06 (−0.58 to 0.69) | −0.56 (−1.17 to 0.07) | < 0.001 |
| AC *Z*-score | −0.01 (−0.29 to 0.28) | −0.24 (−0.52 to 0.04) | < 0.001 |
| 35 + 0 to 36 + 6-week scan | | | |
| GA (weeks) | 36.1 (35.9–36.4) | 36.1 (35.9–36.4) | 0.003 |
| EFW *Z*-score | 0.20 (−0.39 to 0.81) | −1.20 (−1.88 to −0.65) | < 0.001 |
| AC *Z*-score | 0.00 (−0.47 to 0.49) | −1.01 (−1.49 to −0.57) | < 0.001 |
| GA at delivery (weeks) | 40.0 (39.0–40.9) | 39.4 (38.2–40.3) | < 0.001 |
| Birth-weight *Z*-score | 0.13 (−0.45 to 0.75) | −1.72 (−2.14 to −1.48) | < 0.001 |
| Birth weight (g) | 3490 (3220–3790) | 2715 (2510–2860) | < 0.001 |

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

### Prediction of SGA neonate by EFW at 35 + 0 to 36 + 6 weeks' gestation

ROC curves for prediction by EFW at 35 + 0 to 36 + 6 weeks' gestation of a SGA neonate $< 10^{th}$ and $< 3^{rd}$ percentiles born within 2 weeks following and at any time after assessment are shown in Figure 1. The group with EFW *Z*-score < −1.2106, which is equivalent to 10% of the population, contained 63.4% (95% CI, 62.0–64.7%) of neonates with birth weight $< 10^{th}$ percentile and 74.2% (95% CI, 72.2–76.1%) of neonates with birth weight $< 3^{rd}$ percentile born at any stage after screening. The respective values for SGA neonates born within 2 weeks following screening were 76.8% (95% CI, 74.4–79.0%) and 81.3% (95% CI, 78.2–84.0%). For a desired 90% detection rate of SGA neonates delivered at any stage after assessment, the necessary screen-positive rate would be 33.7% for SGA $< 10^{th}$ percentile and 24.4% for SGA $< 3^{rd}$ percentile.

### Prediction of SGA neonate: additional contribution of maternal risk factors and growth velocity

Multivariable logistic regression analysis demonstrated that, in the prediction of a SGA neonate with birth weight $< 10^{th}$ or $< 3^{rd}$ percentile, there was a significant contribution from maternal risk factors, EFW *Z*-score at 35 + 0 to 36 + 6 weeks' gestation and AC growth velocity, but not EFW growth velocity (Table 2).

The area under the ROC curve (AUC) for a SGA neonate $< 10^{th}$ percentile born within 2 weeks following assessment in screening by maternal risk factors and EFW *Z*-score (0.936; 95% CI, 0.929–0.943) was marginally higher than that in screening by EFW *Z*-score alone (0.933; 95% CI, 0.926–0.941; $P = 0.040$); the AUC in screening by maternal risk factors and EFW *Z*-score was not improved by addition of AC growth velocity ($P = 0.232$). In prediction of a SGA neonate $< 3^{rd}$ percentile, addition of maternal risk factors did not

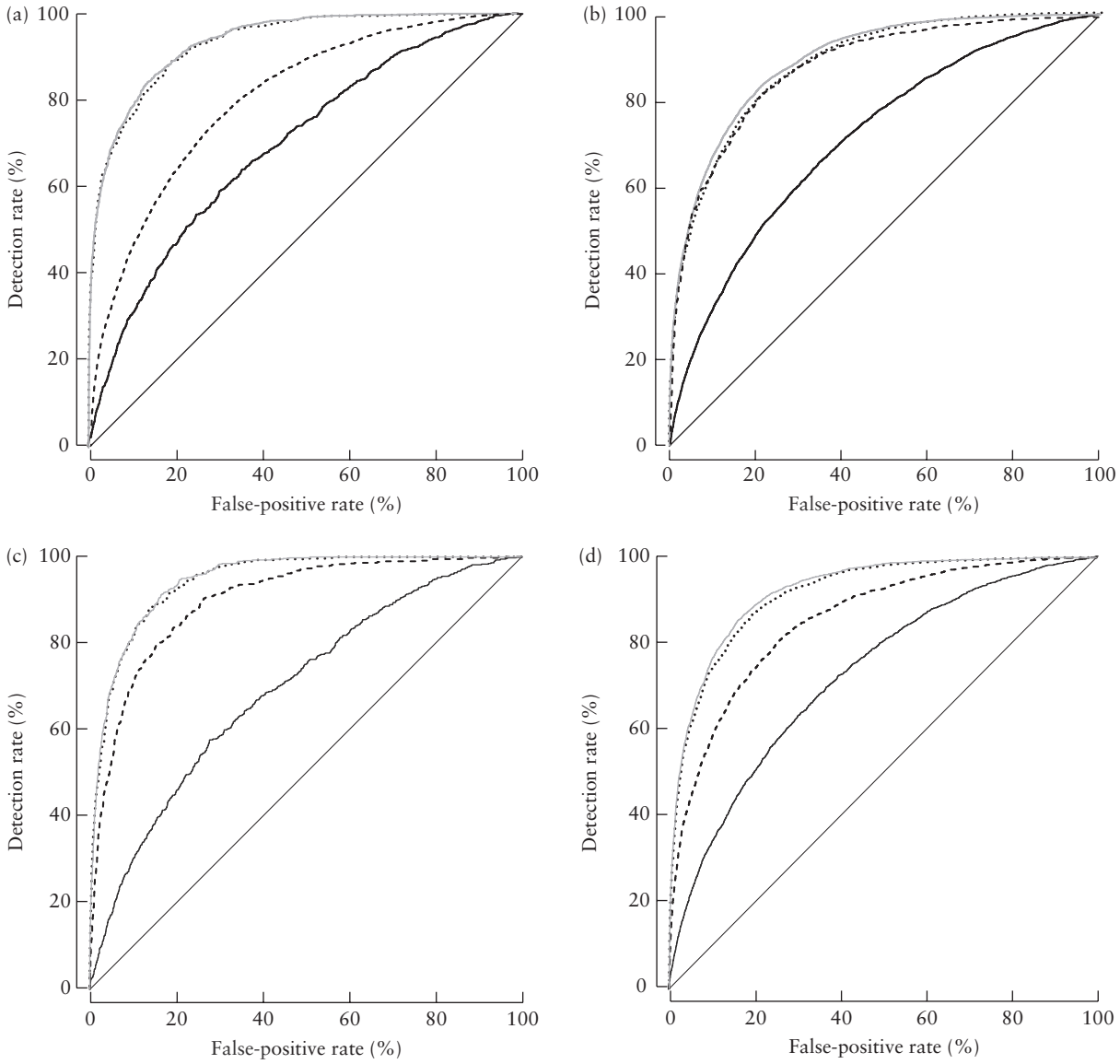


**Figure 1** Receiver–operating characteristics curves of maternal factors (——), estimated fetal weight at 35 + 0 to 36 + 6 weeks' gestation (·····), abdominal circumference growth velocity (- - - -) and combination of the three (——), in the prediction of small-for-gestational-age neonates with birth weight $< 10^{th}$ (a,b) and $< 3^{rd}$ (c,d) percentiles, delivered within 2 weeks (a,c) or at any time (b,d) after assessment.

**Table 2** Univariable and multivariable logistic regression analyses in prediction of small-for-gestational-age (SGA) neonate $<10^{th}$ and $<3^{rd}$ percentiles by maternal and pregnancy characteristics, estimated fetal weight (EFW) *Z*-score at 35 + 0 to 36 + 6 weeks' gestation, EFW growth velocity and abdominal circumference (AC) growth velocity

| | *Univariable* | | *Multivariable* | |
|---|---|---|---|---|
| *Characteristic* | *OR (95% CI)* | P | *OR (95% CI)* | P |
| SGA $<10^{th}$ percentile | | | | |
| Maternal factors | 17.98 (16.01–20.21) | < 0.001 | 6.82 (5.94–7.82) | < 0.001 |
| EFW *Z*-score | 0.15 (0.14–0.16) | < 0.001 | 0.18 (0.16–0.19) | < 0.001 |
| EFW growth velocity | $8.12e^{-41}$ ($3.16e^{-42}$–$2.08e^{-39}$) | < 0.001 | — | — |
| AC growth velocity | $8.46e^{-80}$ ($4.36e^{-82}$–$1.64e^{-77}$) | < 0.001 | $2.10e^{-04}$ ($7.50e^{-08}$–0.584) | 0.036 |
| SGA $<3^{rd}$ percentile | | | | |
| Maternal factors | 21.59 (18.07–25.08) | < 0.001 | 5.42 (4.41–6.67) | < 0.001 |
| EFW *Z*-score | 0.15 (0.14–0.16) | < 0.001 | 0.18 (0.17–0.20) | < 0.001 |
| EFW growth velocity | $9.18e^{-50}$ ($7.75e^{-52}$–$1.09e^{-47}$) | < 0.001 | — | — |
| AC growth velocity | $2.17e^{-91}$ ($1.06e^{-94}$–$4.45e^{-88}$) | < 0.001 | $4.47e^{-09}$ ($3.71e^{-14}$–0.001) | 0.001 |

OR, odds ratio.

**Table 3** Performance of prediction of small-for-gestational-age (SGA) neonate with birth weight $<10^{th}$ and $<3^{rd}$ percentiles, delivered within 2 weeks and at any stage after screening at 35 + 0 to 36 + 6 weeks' gestation

| | *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 | 0.933 (0.926–0.941) | 76.8 (74.4–79.0) | 0.945 (0.937–0.952) | 81.3 (78.2–84.0) |
| Maternal factors | 0.693 (0.675–0.710) | 30.3 (27.7–32.5) | 0.695 (0.673–0.717) | 30.3 (27.1–33.8) |
| EFW growth velocity | 0.828 (0.815–0.842) | 55.4 (53.6–57.1) | 0.856 (0.840–0.871) | 57.9 (54.4–60.7) |
| AC growth velocity | 0.884 (0.873–0.895) | 64.3 (62.0–66.7) | 0.900 (0.888–0.913) | 70.9 (67.1–73.4) |
| EFW *Z*-score + maternal factors | 0.936 (0.929–0.943) | 78.6 (76.1–80.7) | 0.946 (0.939–0.954) | 81.7 (78.7–84.5) |
| EFW *Z*-score + AC growth velocity + maternal factors | 0.936 (0.929–0.944) | 78.6 (76.1–80.7) | 0.947 (0.940–0.954) | 82.1 (79.1–84.9) |
| SGA at any stage | | | | |
| EFW *Z*-score | 0.883 (0.879–0.888) | 63.4 (62.0–64.7) | 0.918 (0.912–0.923) | 74.2 (72.2–76.1) |
| Maternal factors | 0.713 (0.706–0.721) | 31.6 (30.0–32.6) | 0.726 (0.715–0.738) | 33.9 (31.7–35.9) |
| EFW growth velocity | 0.737 (0.730–0.744) | 36.7 (34.2–38.5) | 0.793 (0.782–0.803) | 47.5 (45.2–49.7) |
| AC growth velocity | 0.808 (0.802–0.814) | 47.0 (45.1–49.4) | 0.855 (0.847–0.864) | 58.4 (56.1–60.7) |
| EFW *Z*-score + maternal factors | 0.895 (0.890–0.899) | 67.1 (65.9–68.4) | 0.924 (0.919–0.930) | 75.9 (74.0–77.8) |
| EFW *Z*-score + AC growth velocity + maternal factors | 0.895 (0.890–0.899) | 67.1 (65.9–68.4) | 0.925 (0.919–0.930) | 76.4 (74.5–78.3) |

Values in parentheses are 95% CI. AC, abdominal circumference; AUC, area under receiver–operating characteristics curve; DR, detection rate; EFW, estimated fetal weight; SPR, screen-positive rate.

improve the performance of screening that was achieved by EFW *Z*-score alone ($P = 0.148$) and addition of AC growth velocity did not improve the performance of screening that was achieved by a combination of maternal risk factors and EFW *Z*-score ($P = 0.058$) (Table 3).

The AUC for a SGA neonate $<10^{th}$ percentile born at any time after assessment in screening by a combination of maternal risk factors and EFW *Z*-score at 35 + 0 to 36 + 6 weeks (AUC, 0.895; 95% CI, 0.890–0.899) was significantly higher than that in screening by EFW *Z*-score alone (AUC, 0.883; 95% CI, 0.879–0.888) ($P < 0.0001$); this was also the case for a SGA neonate $<3^{rd}$ percentile (0.924; 95% CI, 0.919–0.930 *vs* 0.918; 95% CI, 0.912–0.923) ($P < 0.001$) (Table 3). Addition of AC growth velocity did not improve the performance of screening that was achieved by a combination of maternal risk factors and EFW *Z*-score for prediction of either SGA neonate $<10^{th}$ percentile ($P = 0.103$) or $<3^{rd}$ percentile ($P = 0.061$) (Table 3).

The detection rate, at a 10% screen-positive rate, of a SGA neonate $<10^{th}$ percentile born within 2 weeks following assessment in screening by EFW *Z*-score alone (76.8%) was marginally improved by the addition of maternal risk factors (78.6%), but addition of AC growth velocity (78.6%) did not improve the detection rate that was achieved by a combination of maternal risk factors and EFW *Z*-score. In the case of a SGA neonate $<3^{rd}$ percentile, the detection rate in screening by EFW *Z*-score alone (81.3%) was not improved by the addition of maternal risk factors (81.7%) or the addition of maternal risk factors and AC growth velocity (82.1%) (Table 3). The detection rate, at a 10% screen-positive rate, of a SGA neonate $<10^{th}$ percentile born at any stage after assessment in screening by EFW *Z*-score alone (63.4%) was significantly improved by the addition of maternal risk factors (67.1%), but addition of AC growth velocity (67.1%) did not improve the detection rate achieved by a combination of maternal risk factors and EFW

**Table 4** Screen-positive rate 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 | 16.0 (14.9–17.2) | 21.3 (20.0–22.6) | 31.2 (29.7–32.6) |
| EFW *Z*-score + maternal factors | 14.6 (13.5–15.7) | 20.7 (19.4–22.0) | 30.8 (29.3–32.2) |
| EFW *Z*-score + maternal factors + AC growth velocity | 14.4 (13.3–15.5) | 20.6 (19.3–21.9) | 30.5 (29.0–31.9) |
| SGA < 3rd percentile | | | |
| EFW *Z*-score | 12.5 (11.5–13.5) | 17.2 (16.1–18.4) | 24.0 (22.8–25.3) |
| EFW *Z*-score + maternal factors | 11.6 (10.7–12.6) | 16.0 (14.9–17.1) | 22.3 (21.1–23.5) |
| EFW *Z*-score + maternal factors + AC growth velocity | 11.4 (10.5–12.4) | 15.9 (14.8–17.0) | 21.2 (20.0–22.5) |
| SGA at any stage | | | |
| SGA < 10th percentile | | | |
| EFW *Z*-score | 26.3 (26.0–27.1) | 33.7 (33.2–34.2) | 46.3 (45.8–46.8) |
| EFW *Z*-score + maternal factors | 23.3 (22.8–23.7) | 31.0 (30.6–31.5) | 42.0 (41.5–42.4) |
| EFW *Z*-score + maternal factors + AC growth velocity | 23.0 (22.6–23.4) | 31.1 (30.7–31.6) | 41.8 (41.3–42.5) |
| SGA < 3rd percentile | | | |
| EFW *Z*-score | 17.7 (17.3–18.0) | 24.4 (24.1–24.9) | 35.4 (34.9–35.8) |
| EFW *Z*-score + maternal factors | 15.9 (15.6–16.3) | 20.8 (20.5–21.0) | 31.8 (31.4–32.2) |
| EFW *Z*-score + maternal factors + AC growth velocity | 15.8 (15.5–16.2) | 21.6 (21.2–22.0) | 32.5 (32.0–32.9) |

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

*Z*-score (Table 3). In the case of a SGA neonate < 3rd percentile, the detection rate, at a 10% screen-positive rate, in screening by EFW *Z*-score alone (74.2%), was marginally improved by the addition of maternal risk factors (75.9%), but addition of AC growth velocity (76.4%) did not improve the detection rate achieved by a combination of maternal risk factors and EFW *Z*-score (Table 3).

The screen-positive rates necessary to achieve prediction of 85%, 90% and 95% of SGA neonates delivered within 2 weeks and at any stage after assessment are shown in Table 4. If the desired detection rate of SGA neonate < 10th percentile born within 2 weeks following assessment was 90%, the necessary screen-positive rate in screening by maternal risk factors and EFW *Z*-score was not significantly different from that of screening by EFW *Z*-score alone (20.7% *vs* 21.3%); this was also the case for SGA neonate < 3rd percentile (16.0% *vs* 17.2%). However, for SGA neonate < 10th percentile born at any stage after assessment, the necessary screen-positive rate for a 90% detection rate in screening by maternal risk factors and EFW *Z*-score was lower than that in screening by EFW *Z*-score alone (31.0% *vs* 33.7%; $P < 0.001$); this was also the case for SGA neonate < 3rd percentile (20.8% *vs* 24.4%; $P < 0.001$).

## DISCUSSION

### Main findings

The findings of this study demonstrate the performance of screening for a SGA neonate by routine ultrasound examination at 35 + 0 to 36 + 6 weeks' gestation. Screening by EFW, at a 10% screen-positive rate, predicted 63% of neonates with birth weight < 10th percentile and 74% of those with birth weight < 3rd percentile born at any stage after screening; 44% of fetuses thought to be SGA were born with birth weight ≥ 10th percentile. The performance of EFW was better for babies born within 2 weeks following assessment, with prediction of 77% of neonates with birth weight < 10th percentile and 81% of those with birth weight < 3rd percentile. To accomplish a detection rate of 90% for SGA neonates at the 35 + 0 to 36 + 6-week scan, we would need to classify about 35% of the population as being screen positive.

The predictive performance for a SGA neonate of EFW at 35 + 0 to 36 + 6 weeks' gestation was improved by addition of maternal demographic characteristics and medical history; addition of maternal risk factors improved the prediction of a SGA neonate with birth weight < 10th percentile born at any stage after screening from 63% to 67%. We have reported previously that the risk of delivering a SGA neonate increases with maternal age, decreases with maternal weight and height, is higher in women of black, South Asian, East Asian and mixed racial origins than in white women, in cigarette smokers, in those with chronic hypertension and those with diabetes mellitus Type 2 and in parous women with history of SGA. The risk is lower in parous women without history of SGA and in those with diabetes mellitus Type 1[12].

The predictive performance for a SGA neonate of EFW at 35 + 0 to 36 + 6 weeks' gestation was not improved by addition of fetal growth velocity between 19 + 0 to 23 + 6 and 35 + 0 to 36 + 6 weeks' gestation.

### Comparison with findings of previous studies

Our finding that EFW < 10th percentile predicts 63% and 74% of neonates with birth weight < 10th and < 3rd percentile, respectively, is consistent with the results of previous late third-trimester studies. Fadigas *et al.* examined 5515 pregnancies at 35–37 weeks and reported that EFW, at a 10% screen-positive rate, predicted 63%

and 73% of neonates with birth weight < 10th and < 3rd percentile, respectively[8]. Triunfo *et al.* examined 946 pregnancies at 36–38 weeks and reported that EFW, at a 10% false-positive rate, predicted 59% and 83% of neonates with birth weight < 10th and < 3rd percentile, respectively[18]. Souka *et al.* examined 2288 pregnancies at 34–37 weeks and reported that EFW, at a 10% screen-positive rate, predicted 75% of neonates with birth weight < 5th percentile[7].

Our finding that the prediction of a SGA neonate provided by EFW is improved by the addition of maternal risk factors (63% to 67% for SGA < 10th percentile) is consistent with the results of Fadigas *et al.*, who reported that addition of maternal factors improved the prediction of a SGA neonate from 63% to 66%[8].

We found that growth velocity between the second and third trimesters did not improve the prediction of SGA neonate provided by EFW at 35 + 0 to 36 + 6 weeks' gestation. Studies examining fetal growth velocity and conditional fetal growth percentiles, which are calculated taking into account an EFW earlier in pregnancy, compared with conventional weight-for-gestational-age charts, have reported contradictory results in the prediction of adverse perinatal outcome[11,19–22]. However, the objective of our study was to predict SGA neonate rather than adverse perinatal outcome. Our results are consistent with those of two previous studies that examined 3440 and 2696 pregnancies, respectively[23,24], and reported that growth velocity, conditional growth percentiles or serial fetal biometry did not improve the prediction of SGA neonate provided by the last EFW alone.

## Implications for clinical practice

The proposed new pyramid of pregnancy care[25], an integrated clinic 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 preterm pre-eclampsia and/or SGA and, through pharmacological intervention, to reduce the prevalence of these complications[26–29]. The objectives of subsequent visits, at around 20 and 32 or 36 weeks' gestation, are to identify the high-risk group and, through close monitoring of such pregnancies, to minimize adverse perinatal events by determining the appropriate time and place for iatrogenic delivery. We have proposed previously that assessment at 20 weeks' gestation would stratify the population into a high-risk group, which would comprise < 0.5% of all pregnancies and contain all cases of SGA delivering < 32 weeks, a moderate-risk group, comprising about 15% of pregnancies and containing about 90% of cases of SGA delivering at 32–36 weeks, and a low-risk group that would contain all cases of SGA delivering at term[30]. The high-risk group would require reassessment at 26–30 weeks and again at 32 and 36 weeks if not delivered, the moderate-risk group would be reassessed at 32 and 36 weeks and the low-risk group would be reassessed at 36 weeks.

This study provides the necessary data for development of policies to achieve prenatal prediction of a desired percentage of SGA neonates near term. We have shown that the prediction of a SGA neonate achieved by EFW can be improved by maternal factors but not by growth velocity. In a previous study, we reported that the prediction by EFW and maternal factors can be improved marginally by the addition of biomarkers of impaired placentation, including serum placental growth factor and uterine artery and fetal middle cerebral artery pulsatility indices[12].

## Strengths and limitations

The strengths of this screening study for SGA neonates are, first, examination of a large population of pregnant women attending for routine assessment of fetal growth and wellbeing at both 19 + 0 to 23 + 6 and 35 + 0 to 36 + 6 weeks' gestation, second, that trained sonographers carried out fetal biometry according to a standardized protocol and use of a widely used model for calculation of EFW[14], which has been shown to be the most accurate one among 70 previously reported models[13], and, third, use of the Fetal Medicine Foundation fetal and neonatal reference ranges which have a common median[15].

A potential limitation of the study 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 additional contribution of growth velocity to the prediction of a SGA neonate over that provided by EFW at 35–37 weeks alone. This was the consequence of the design of our study, which relied on data obtained from two routine ultrasound examinations in pregnancy. The extent to which a shorter interval between the two scans improves the contribution of growth velocity to the prediction of SGA remains to be determined. The second potential limitation of the study is the use of growth velocity rather than more complex methods of evaluating longitudinal growth; however, there is no evidence of superiority of the latter over the former[24,31–33].

## Conclusions

The performance of sonographic EFW for the prediction of a SGA neonate is highest if the interval between assessment and birth is short. Since 85% of SGA neonates are born at ≥ 37 weeks' gestation, a routine third-trimester scan is best performed at 36 rather than at 32 weeks' gestation. The performance of screening by EFW at 35 + 0 to 36 + 6 weeks is improved by maternal demographic characteristics and medical history but not by growth velocity between the second and third trimesters. Our results suggest that, to accomplish a detection rate of 90% for SGA neonates at the 35 + 0 to 36 + 6-week scan, we would need to classify about 35% of the population as being screen positive. Future studies will investigate whether growth velocity improves the performance of the 35 + 0 to 36 + 6-week scan in the prediction of adverse perinatal outcome.

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