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Routine ultrasound at 32 *vs* 36 weeks' gestation: prediction of small-for-gestational-age neonates

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KEYWORDS: adverse perinatal outcome; estimated fetal weight; fetal biometry; pyramid of pregnancy care; small-for-gestational age; symphysis–fundus height; third-trimester screening

ABSTRACT

Objective *To evaluate and compare the performance of routine ultrasonographic estimated fetal weight (EFW) and fetal abdominal circumference (AC) at 31 + 0 to 33 + 6 and 35 + 0 to 36 + 6 weeks' gestation in the prediction of a small-for-gestational-age (SGA) neonate.*

Methods *This was a prospective study of 21 989 singleton pregnancies undergoing routine ultrasound examination at 31 + 0 to 33 + 6 weeks' gestation and 45 847 undergoing routine ultrasound examination at 35 + 0 to 36 + 6 weeks' gestation. In each case, the estimated fetal weight (EFW) from measurements of fetal head circumference, AC and femur length was calculated using the Hadlock formula and expressed as a percentile according to The Fetal Medicine Foundation fetal and neonatal population weight charts. The same charts were used for defining a SGA neonate with birth weight < 10th and < 3rd percentiles. For each gestational-age window, the screen-positive and detection rates, at different EFW percentile cut-offs between the 10th and 50th percentiles, were calculated for prediction of delivery of a SGA neonate with birth weight < 10th and < 3rd percentiles within 2 weeks and at any stage after assessment. The areas under the receiver–operating characteristics curves (AUC) in screening for a SGA neonate by EFW and AC at 31 + 0 to 33 + 6 and at 35 + 0 to 36 + 6 weeks' gestation were compared.*

Results *First, the AUCs in screening by EFW for a 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 were significantly higher than those at 31 + 0 to 33 + 6 weeks (P < 0.001). Second, at both 35 + 0 to 36 + 6 and 31 + 0 to 33 + 6 weeks' gestation, the predictive performance for a SGA neonate with birth weight < 10th and < 3rd percentiles born at any stage after screening was significantly higher using EFW Z-score than AC Z-score. Similarly, at 35 + 0 to 36 + 6 weeks, but not at 31 + 0 to 33 + 6 weeks, the predictive performance for a SGA neonate with birth weight < 10th and < 3rd percentiles born within 2 weeks after screening was significantly higher using EFW Z-score than AC Z-score. Third, screening by EFW < 10th percentile at 35 + 0 to 36 + 6 weeks' gestation predicted 70% and 84% of neonates with birth weight < 10th and < 3rd percentiles, respectively, born within 2 weeks after assessment, and the respective values for a neonate born at any stage after assessment were 46% and 65%. Fourth, prediction of > 85% of SGA neonates with birth weight < 10th percentile born at any stage after screening at 35 + 0 to 36 + 6 weeks' gestation requires use of EFW < 40th percentile. Screening at this percentile cut-off predicted 95% and 99% of neonates with birth weight < 10th and < 3rd percentiles, respectively, born within 2 weeks after assessment, and the respective values for a neonate born at any stage after assessment were 87% and 94%.*

Conclusions *The predictive performance for a SGA neonate of routine ultrasonographic examination during the third trimester is higher if, first, the scan is carried out at 35 + 0 to 36 + 6 weeks' gestation than at 31 + 0 to 33 + 6 weeks, second, the method of screening is EFW than fetal AC, third, the outcome measure is birth weight < 3rd than < 10th percentile, and, fourth, if delivery occurs within 2 weeks than at any stage after assessment. Prediction of a SGA neonate by EFW < 10th percentile is modest and prediction of > 85% of cases at 35 + 0 to 36 + 6 weeks' gestation necessitates use of EFW < 40th percentile.*

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INTRODUCTION

National guidelines from many developed countries define fetal growth restriction on the basis of ultrasonographic estimated fetal weight (EFW) or fetal abdominal circumference (AC) $< 10^{th}$ percentile and severe growth restriction as EFW $< 3^{rd}$ percentile[1]. There are also extensive reports on how best to manage pregnancies with a small-for-gestational-age (SGA) fetus[1,2]. However, there is uncertainty as to the best approach for identifying such SGA fetuses, because of, first, the existence of a wide range of charts for fetal size and birth weight, second, the controversy of universal *vs* selective ultrasound examination based on maternal risk factors and the results of abdominal palpation or serial measurements of symphysis–fundus height, third, lack of consistent data on the performance of EFW *vs* AC for prediction of a SGA neonate, and, fourth, limited data on the best timing for a universal third-trimester scan at 32 *vs* 36 weeks' gestation.

We have addressed the issue of inconsistency between fetal and neonatal growth charts by developing EFW and birth-weight reference ranges with a common median[3]. Previous studies provided evidence that the predictive performance of the traditional method of identifying pregnancies with a SGA fetus by maternal abdominal palpation and serial measurements of symphysis–fundus height is poor[4,5]. There is some evidence that improved prediction of SGA is achieved by universal sonographic fetal biometry during the third trimester; a study of 3977 nulliparous women reported that universal third-trimester ultrasonography tripled the detection of SGA neonates compared to selective ultrasonography based on maternal risk factors and the results of measurements of symphysis–fundus height[6]. A recent systematic review and meta-analysis of 21 prospective and retrospective cohort studies of low-risk or non-selected singleton pregnancies with screening ultrasound performed at ≥ 32 weeks' gestation reported that the predictive performance for a SGA neonate of fetal AC and EFW was similar[7]. However, a study of 5163 singleton pregnancies with fetal biometry at 22–43 weeks' gestation and live birth of a phenotypically normal neonate within 2 days after the ultrasound examination reported that the most accurate formula for prediction of birth weight, among 70 models identified by systematic review of 45 studies, was that of Hadlock *et al.*[8], which incorporates measurements of head circumference (HC), AC and femur length (FL)[9]. As for the issue of timing of the third-trimester scan, there is some evidence that the predictive performance of a scan at 36 weeks may be superior to that at 32 weeks; a randomized study of 2586 low-risk singleton pregnancies reported that the predictive performance for a SGA neonate $< 10^{th}$ and $< 3^{rd}$ percentiles was superior at 36 compared to 32 weeks' gestation[10].

The objective of this study was to evaluate and compare the performance of routine ultrasonographic EFW and fetal AC at $31+0$ to $33+6$ and $35+0$ to $36+6$ weeks' gestation in the prediction of a SGA neonate born within 2 weeks and at any stage after assessment.

METHODS

This was a prospective study of 21 989 singleton pregnancies undergoing routine ultrasound examination at $31+0$ to $33+6$ weeks' gestation and 45 847 undergoing routine ultrasound examination at $35+0$ to $36+6$ weeks' gestation at King's College Hospital, London or Medway Maritime Hospital, Gillingham, UK. In the participating hospitals, all women with a singleton pregnancy are offered routine ultrasound examinations at $11+0$ to $13+6$ and at $19+0$ to $23+6$ weeks' gestation. During a period (May 2011 to March 2014), an additional scan was offered at $31+0$ to $33+6$ weeks, but subsequently (March 2014 to September 2018), this was changed to $35+0$ to $36+6$ weeks. In the selection of patients, care was taken to include only routine scans and not follow-up scans for maternal medical conditions or a suspected problem in fetal growth.

At the first- or second-trimester visit, we recorded maternal demographic characteristics and medical history and, at the third-trimester visits, we carried out an ultrasound examination of fetal anatomy and measurement of fetal HC, AC and FL for calculation of EFW using the formula of Hadlock *et al.*[8]. Gestational age was determined by the measurement of fetal crown–rump length at 11–14 weeks or fetal HC at 19–24 weeks[11,12]. The ultrasound examinations were carried out by examiners who had obtained The Fetal Medicine Foundation Certificate of Competence in ultrasound examination for fetal abnormalities. Data on the patients included in this study were the subject of previous publications[13–17].

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 $31+0$ to $33+6$ or $35+0$ to $36+6$ weeks' gestation and delivery of a non-malformed liveborn or stillborn neonate. We excluded pregnancies with aneuploidy or major fetal abnormality.

Patient characteristics

Patient characteristics recorded included maternal age and racial origin (white, black, South Asian, East Asian and 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 delivery of a neonate with birth weight $< 10^{th}$ or $< 3^{rd}$ percentile for gestational age[3].

Statistical analysis

Data were expressed as median (interquartile range) for continuous variables and *n* (%) for categorical variables. 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%.

The observed measurements of EFW and birth weight were converted to *Z*-scores and percentiles adjusted for gestational age according to The Fetal Medicine Foundation fetal and neonatal population weight charts[3]. Similarly, AC was converted to a *Z*-score and percentile adjusted for gestational age according to the reference ranges of Snijders and Nicolaides[12]. Logistic regression analysis was undertaken to determine the significance of the contribution of AC and EFW *Z*-scores in the prediction of delivery of a SGA neonate $< 10^{th}$ and $< 3^{rd}$ percentiles. The performance of screening was determined by receiver–operating characteristics (ROC) curves, and the areas under the ROC curves (AUC) in screening at $31+0$ to $33+6$ and $35+0$ to $36+6$ weeks' gestation in the prediction of a SGA neonate were compared[18]. For each gestational-age window, the screen-positive and detection rates, at different EFW percentile cut-offs between the 10^{th} and 50^{th} percentiles, were calculated for 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.

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

The characteristics of the study population are shown in Table 1. The characteristics of those with a scan at $31+0$ to $33+6$ weeks' gestation were similar to those with a scan at $35+0$ to $36+6$ weeks. In both study periods, in the group of neonates with birth weight $< 10^{th}$ percentile, compared to those with birth weight $\geq 10^{th}$ percentile, the median maternal age, weight and height, EFW *Z*-score, AC *Z*-score, birth-weight *Z*-score and gestational age at delivery were lower, more women were of non-white racial origin, were a smoker and were parous with a previous pregnancy affected by SGA, and fewer women were parous without previous SGA.

Table 1 Maternal and pregnancy characteristics in study population of 67 836 singleton pregnancies, according to gestational age (GA) at screening and delivery of small-for-gestational-age (SGA) neonate with birth weight $< 10^{th}$ percentile

	Screening at 31 + 0 to 33 + 6 weeks		*Screening at 35 + 0 to 36 + 6 weeks*	
Characteristic	*Non-SGA (n = 19 190)*	*SGA (n = 2799)*	*Non-SGA (n = 40 567)*	*SGA (n = 5280)*
Maternal age (years)	30.7 (26.1–34.5)	29.8 (24.9–34.2)*	31.7 (27.4–35.4)	30.9 (26.2–35.0)*
Maternal weight (kg)	77.1 (69.0–88.0)	72.0 (64.0–81.8)*	79.9 (71.5–91.0)	73.4 (65.5–83.2)*
Maternal height (cm)	165 (160–169)	163 (158–167)*	165 (161–170)	163 (158–167)*
Racial origin				
White	13 789 (71.9)	1635 (58.4)	30 812 (76.0)	3348 (63.4)*
Black	3864 (20.1)	799 (28.5)*	6065 (15.0)	1131 (21.4)*
South Asian	732 (3.8)	212 (7.6)*	1697 (4.2)	488 (9.2)*
East Asian	388 (2.0)	66 (2.4)	813 (2.0)	126 (2.4)
Mixed	417 (2.2)	87 (3.1)†	1180 (2.9)	187 (3.5)†
Cigarette smoker	1860 (9.7)	527 (18.8)*	2961 (7.3)	762 (14.4)*
Conception				
Natural	18 645 (97.2)	2717 (97.1)	39 190 (96.6)	5080 (96.2)
Ovulation drugs	162 (0.8)	24 (0.9)	223 (0.5)	34 (0.6)
In-vitro fertilization	383 (2.0)	58 (2.1)	1154 (2.8)	166 (3.1)
Medical condition				
Chronic hypertension	240 (1.3)	66 (2.4)*	490 (1.2)	90 (1.7)†
Diabetes mellitus Type 1	77 (0.4)	5 (0.2)	162 (0.4)	5 (0.1)†
Diabetes mellitus Type 2	112 (0.6)	23 (0.8)	189 (0.5)	19 (0.4)
Obstetric history				
Nulliparous	8978 (46.8)	1602 (57.2)	17 911 (44.2)	2949 (55.9)
Parous with prior SGA	1167 (6.1)	434 (15.5)*	3112 (7.7)	964 (18.3)*
Parous without prior SGA	9045 (47.1)	763 (27.3)*	19 544 (48.2)	1367 (25.9)*
GA at screening (weeks)	32.2 (32.0–32.6)	32.2 (32.0–32.6)	36.1 (35.9–36.4)	36.1 (35.9–36.4)
EFW *Z*-score	0.02 (−0.63 to 0.66)	−1.18 (−1.79 to −0.59)*	0.01 (−0.59 to 0.60)	−1.39 (−2.08 to −0.85)*
AC *Z*-score	−0.05 (−0.48 to 0.42)	−0.76 (−1.15 to −0.35)	0.00 (−0.47 to 0.49)	−1.02 (−1.49 to −0.57)*
GA at delivery (weeks)	40.4 (39.0–40.9)	39.5 (38.2–40.5)*	40.0 (39.1–40.9)	39.4 (38.2–40.3)*
Birth-weight *Z*-score	0.09 (−0.49 to 0.72)	−1.76 (−2.20 to −1.48)*	0.13 (−0.45 to 0.75)	−1.72 (−2.14 to −1.48)*
Birth weight (g)	3470 (3200–3770)	2710 (2460–2870)*	3490 (3220–3790)	2715 (2510–2860)*

Data are given as median (interquartile range) or *n* (%). On comparison with those delivering a non-SGA neonate: *$P < 0.01$; †$P < 0.05$.
AC, abdominal circumference; EFW, estimated fetal weight.

Delivery within 2 weeks after the ultrasound examination at 31 + 0 to 33 + 6 weeks' gestation occurred in 234 (1.1%) of the 21 989 pregnancies. These included 143 (61.1%) that delivered after spontaneous onset of labor and 91 (38.9%) that delivered after induction of labor or elective Cesarean section. The indications for iatrogenic delivery were: (1) severe pre-eclampsia and/or fetal growth restriction (78.0%); (2) antepartum hemorrhage due to placenta previa or placental abruption (11.0%); (3) non-SGA fetus with abnormal fetal Doppler, abnormal fetal heart-rate pattern or reduced fetal movements (4.4%); (4) fetal death (2.2%); (5) fetal anemia (2.2%); (6) obstetric cholestasis (1.1%); and (7) maternal pneumonia (1.1%).

Delivery within 2 weeks after the ultrasound examination at 35 + 0 to 36 + 6 weeks' gestation occurred in 5342 (11.7%) of the 45 847 pregnancies. These included 2988 (55.9%) that delivered after spontaneous onset of labor and 2354 (44.1%) that delivered after induction of labor or elective Cesarean section. The indications for iatrogenic delivery were: (1) chronic hypertension, pre-eclampsia, gestational hypertension, diabetes mellitus, gestational diabetes or obstetric cholestasis (40.1%); (2) other maternal medical condition or maternal request (6.1%); (3) SGA fetus with or without abnormal fetal Doppler findings (23.8%); (4) non-SGA fetus with abnormal fetal Doppler or fetal heart-rate pattern, reduced fetal movements or oligohydramnios (6.1%); (5) previous Cesarean section or myomectomy (8.8%); (6) antepartum hemorrhage due to placenta previa or placental abruption (5.6%); (7) breech or transverse lie (4.7%); (8) previous stillbirth or other adverse perinatal outcome (2.2%); (9) polyhydramnios and/or large-for-gestational age (2.1%); and (10) fetal death (0.5%).

Performance of screening for SGA neonate

Screening at 35 + 0 to 36 + 6 vs *31 + 0 to 33 + 6 weeks' gestation*

The AUCs in screening by EFW for a SGA neonate with birth weight < 10th percentile, delivered within 2 weeks and at any stage after screening at 35 + 0 to 36 + 6 weeks' gestation (0.933 (95% CI, 0.926–0.941) and 0.883 (95% CI, 0.879–0.888), respectively), were significantly higher than those at 31 + 0 to 33 + 6 weeks (0.906 (95% CI, 0.870–0.942); $P < 0.001$ and 0.822 (95% CI, 0.814–0.830; $P < 0.001$, respectively) (Table 2 and Figure 1a,b). Similarly, the AUCs in screening by EFW for a SGA neonate with birth weight < 3rd percentile, delivered within 2 weeks and at any stage after screening at 35 + 0 to 36 + 6 weeks' gestation (0.945 (95% CI, 0.937–0.952) and 0.918 (95% CI, 0.912–0.923), respectively), were significantly higher than those at 31 + 0 to 33 + 6 weeks (0.897 (95% CI, 0.857–0.937); $P = 0.034$ and 0.858 (95% CI, 0.847–0.869); $P < 0.001$, respectively) (Table 2 and Figure 1c,d).

Screening by EFW vs *fetal AC*

Comparison of the AUCs in screening for a SGA neonate by EFW and AC is shown in Table 2 and Figure 1. At both 35 + 0 to 36 + 6 and 31 + 0 to 33 + 6 weeks' gestation, the predictive performance for a SGA neonate with birth weight < 10th and < 3rd percentiles born at any stage after screening was significantly higher using EFW *Z*-score than AC *Z*-score. Similarly, at 35 + 0 to 36 + 6 weeks, but not at 31 + 0 to 33 + 6 weeks, the predictive performance for a SGA neonate with birth weight < 10th and < 3rd percentiles born within 2 weeks after screening was significantly higher using EFW *Z*-score than AC *Z*-score.

Screening at different EFW percentile cut-offs

The predictive performance for a SGA neonate with birth weight < 10th percentile in screening by EFW at a series of cut-offs between the 10th and 50th percentiles at 35 + 0 to 36 + 6 and 31 + 0 to 33 + 6 weeks' gestation is shown in Table 3; the respective values for a SGA neonate with birth weight < 3rd percentile are shown in Table 4. Screening by EFW < 10th percentile at 35 + 0 to 36 + 6 weeks' gestation predicted 70% and 84% of neonates with birth weight < 10th and < 3rd percentiles, respectively, born within 2 weeks after assessment, and the respective values for neonates born at any stage after assessment were 46% and 65%.

Prediction of > 85% of SGA neonates with birth weight < 10th percentile born at any stage after screening at

Table 2 Comparison of areas under the receiver–operating characteristics curves in screening for small-for-gestational-age (SGA) neonate with birth weight < 10th and < 3rd percentiles, by estimated fetal weight (EFW) and fetal abdominal circumference (AC), according to gestational age at screening

	Delivery ≤ 2 weeks after screening			*Delivery any time after screening*		
Outcome	*EFW*	*AC*	P	*EFW*	*AC*	P
Screening at 35 + 0 to 36 + 6 weeks						
SGA < 10th percentile	0.933 (0.926–0.941)	0.915 (0.906–0.924)	< 0.001	0.883 (0.879–0.888)	0.860 (0.854–0.865)	< 0.001
SGA < 3rd percentile	0.945 (0.937–0.952)	0.930 (0.920–0.939)	< 0.001	0.918 (0.912–0.923)	0.898 (0.891–0.905)	< 0.001
Screening at 31 + 0 to 33 + 6 weeks						
SGA < 10th percentile	0.906 (0.870–0.942)	0.895 (0.849–0.931)	0.256	0.822 (0.814–0.830)	0.795 (0.790–0.801)	< 0.001
SGA < 3rd percentile	0.897 (0.857–0.937)	0.892 (0.850–0.934)	0.607	0.858 (0.847–0.869)	0.831 (0.819–0.842)	< 0.001

Values in parentheses are 95% CI.

Table 3 Predictive performance for small-for-gestational-age (SGA) neonate with birth weight < 10th percentile delivered within 2 weeks and at any time after assessment in screening by estimated fetal weight (EFW) at 35 + 0 to 36 + 6 and 31 + 0 to 33 + 6 weeks' gestation

		SGA delivered ≤ 2 weeks after screening		*SGA delivered any time after screening*	
EFW cut-off	*Screen-positive rate*	*Detection rate*	*Positive predictive value (%)*	*Detection rate*	*Positive predictive value (%)*
35 + 0 to 36 + 6 weeks					
n	45 847	1156		5280	
< 10th percentile	4109 (9.0; 8.7–9.3)	804 (70; 67–72)	19.6 (17.4–21.3)	2429 (46; 45–47)	59.1 (57.6–61.2)
< 15th percentile	6125 (13.4; 13.1–13.7)	883 (76; 74–79)	14.4 (12.1–16.7)	3034 (57; 56–59)	49.5 (47.7–51.3)
< 20th percentile	8089 (17.6; 17.3–17.9)	952 (82; 80–85)	11.8 (9.7–13.4)	3483 (66; 65–67)	43.1 (41.5–45.6)
< 25th percentile	10 215 (22.3; 22.0–22.6)	1004 (87; 85–89)	9.8 (7.6–11.8)	3888 (74; 72–75)	38.1 (36.3–40.5)
< 30th percentile	12 402 (27.1; 26.8–27.4)	1044 (90; 89–92)	8.4 (6.5–10.2)	4192 (79; 78–81)	33.8 (31.6–35.7)
< 35th percentile	14 694 (32.1; 31.8–32.4)	1079 (93; 92–95)	7.3 (5.3–9.5)	4436 (84; 83–85)	30.2 (28.4–32.5)
< 40th percentile	16 918 (36.9; 36.6–37.2)	1101 (95; 94–96)	6.5 (4.4–8.7)	4619 (87; 87–88)	27.3 (25.8–29.6)
< 45th percentile	19 221 (41.9; 41.6–42.2)	1120 (97; 96–98)	5.8 (3.6–7.8)	4797 (91; 90–92)	25.0 (23.1–27.0)
< 50th percentile	21 536 (47.0; 46.7–47.3)	1127 (97; 97–98)	5.2 (3.3–7.5)	4926 (93; 93–94)	22.9 (21.8–24.6)
31 + 0 to 33 + 6 weeks					
n	21 989	93		2799	
< 10th percentile	2164 (9.8; 9.4–10.2)	72 (77; 69–86)	3.3 (2.6–4.0)	1072 (38; 36–40)	49.5 (47.6–51.4)
< 15th percentile	3306 (15.0; 14.6–15.4)	79 (85; 78–92)	2.4 (1.8–3.0)	1408 (50; 48–53)	42.6 (40.8–44.4)
< 20th percentile	4459 (20.3; 19.9–20.7)	83 (89; 83–96)	1.9 (1.3–2.5)	1638 (59; 56–61)	36.7 (34.9–38.5)
< 25th percentile	5578 (25.4; 25.0–25.8)	87 (94; 89–98)	1.6 (1.0–2.2)	1855 (66; 64–68)	33.3 (31.6–35.1)
< 30th percentile	6667 (30.3; 29.9–30.7)	88 (95; 90–98)	1.3 (0.7–1.9)	2032 (73; 71–75)	30.5 (28.8–32.2)
< 35th percentile	7773 (35.3; 34.9–35.7)	90 (97; 92–99)	1.2 (0.6–1.8)	2177 (78; 76–80)	28.0 (26.3–29.7)
< 40th percentile	8842 (40.2; 38.8–40.6)	92 (99; 95–100)	1.0 (0.5–1.6)	2295 (82; 80–84)	26.0 (24.4–27.6)
< 45th percentile	9940 (45.2; 44.8–45.6)	92 (99; 95–100)	0.9 (0.4–1.3)	2396 (86; 84–87)	24.1 (22.5–25.7)
< 50th percentile	11 035 (50.2; 49.8–50.6)	93 (100; 96–100)	0.8 (0.3–1.1)	2485 (89; 87–89)	22.5 (20.9–24.1)

Data are given as *n* (%; 95% CI) or with (95% CI).

Table 4 Predictive performance for small-for-gestational-age (SGA) neonate with birth weight < 3rd percentile delivered within 2 weeks and at any time after assessment in screening by estimated fetal weight (EFW) at 35 + 0 to 36 + 6 and 31 + 0 to 33 + 6 weeks' gestation

		SGA delivered ≤ 2 weeks after screening		*SGA delivered any time after screening*	
EFW cut-off	*Screen-positive rate*	*Detection rate*	*Positive predictive value (%)*	*Detection rate*	*Positive predictive value (%)*
35 + 0 to 36 + 6 weeks					
n	45 847	638		2017	
< 3rd percentile	1636 (3.6; 2.7–4.5)	437 (69; 65–72)	26.7 (23.7–29.7)	855 (42; 39–46)	52.3 (48.9–55.5)
< 10th percentile	4109 (9.0; 8.7–9.3)	535 (84; 82–86)	13.0 (10.4–15.6)	1308 (65; 62–68)	31.8 (29.8–33.8)
< 15th percentile	6125 (13.4; 13.1–13.7)	569 (89; 87–92)	9.3 (7.1–11.6)	1513 (75; 73–77)	24.7 (22.9–26.5)
< 20th percentile	8089 (17.6; 17.3–17.9)	588 (92; 90–94)	7.3 (5.3–9.3)	1630 (81; 79–83)	20.2 (18.5–21.9)
< 25th percentile	10 215 (22.3; 22.0–22.6)	608 (95; 94–97)	6.0 (4.1–7.8)	1741 (86; 85–88)	17.0 (15.4–18.6)
< 30th percentile	12 402 (27.1; 26.8–27.4)	619 (97; 96–98)	5.0 (3.3–6.7)	1810 (90; 88–91)	14.6 (13.1–16.0)
< 35th percentile	14 694 (32.1; 31.8–32.4)	629 (99; 97–99)	4.3 (2.7–5.8)	1867 (93; 92–94)	12.7 (11.3–14.1)
< 40th percentile	16 918 (36.9; 36.6–37.2)	632 (99; 98–100)	3.7 (2.2–5.1)	1900 (94; 93–95)	11.2 (9.9–12.6)
< 45th percentile	19 221 (41.9; 41.6–42.2)	635 (100; 99–100)	3.3 (1.9–4.7)	1942 (96; 96–97)	10.1 (8.8–11.4)
< 50th percentile	21 536 (47.0; 46.7–47.3)	635 (100; 99–100)	2.9 (1.6–4.2)	1961 (97; 97–98)	9.1 (7.8–10.2)
31 + 0 to 33 + 6 weeks					
n	21 989	73		1155	
< 3rd percentile	766 (3.5; 2.2–4.8)	49 (67; 58–76)	6.4 (4.7–8.0)	340 (29; 26–33)	44.4 (41.1–47.7)
< 10th percentile	2164 (9.8; 9.4–10.2)	60 (82; 74–90)	2.8 (1.9–3.8)	603 (52; 49–55)	27.9 (25.3–30.4)
< 15th percentile	3306 (15.0; 14.6–15.4)	64 (88; 81–94)	1.9 (1.1–2.7)	736 (64; 61–67)	22.3 (19.9–24.7)
< 20th percentile	4459 (20.3; 19.9–20.7)	66 (90; 84–96)	1.5 (0.8–2.2)	816 (71; 68–73)	18.3 (16.1–20.5)
< 25th percentile	5578 (25.4; 25.0–25.8)	68 (93; 88–97)	1.2 (0.6–1.8)	894 (77; 75–80)	16.0 (13.9–18.1)
< 30th percentile	6667 (30.3; 29.9–30.7)	69 (95; 90–98)	1.0 (0.4–1.6)	954 (83; 80–85)	14.3 (12.3–16.3)
< 35th percentile	7773 (35.3; 34.9–35.7)	71 (97; 94–98)	0.9 (0.4–1.4)	1002 (87; 85–89)	12.9 (11.0–14.8)
< 40th percentile	8842 (40.2; 38.8–40.6)	72 (99; 95–100)	0.8 (0.3–1.3)	1039 (90; 88–92)	11.8 (9.9–13.7)
< 45th percentile	9940 (45.2; 44.8–45.6)	72 (99; 95–100)	0.7 (0.2–1.2)	1062 (92; 90–94)	10.7 (8.9–12.5)
< 50th percentile	11 035 (50.2; 49.8–50.6)	73 (100; 96–100)	0.7 (0.3–1.2)	1081 (94; 92–95)	9.8 (8.1–11.5)

Data are given as *n* (%; 95% CI) or with (95% CI).

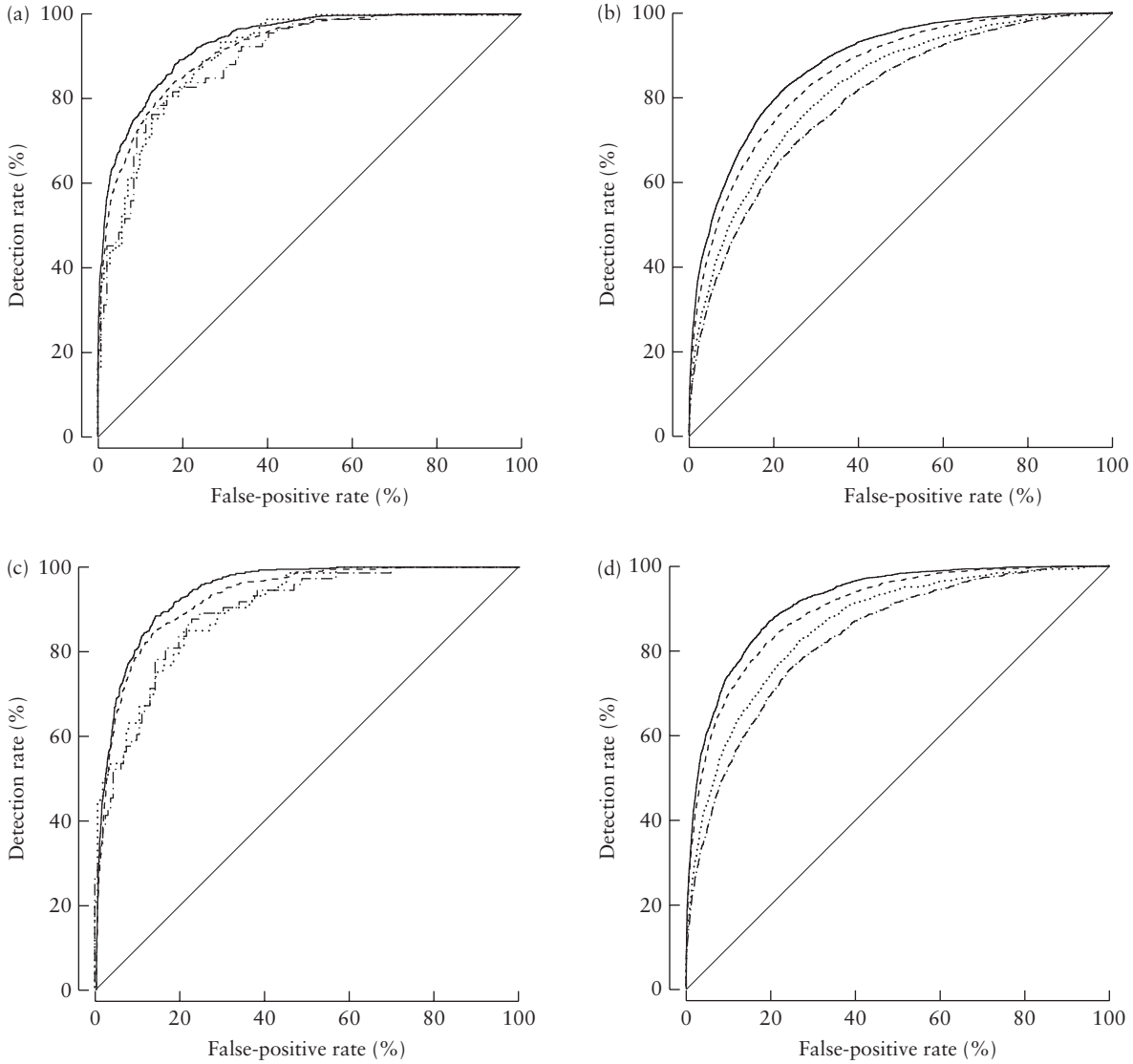

Figure 1 Receiver–operating characteristics curves of estimated fetal weight and fetal abdominal circumference at 35 + 0 to 36 + 6 weeks' gestation (—— and - - -, respectively) and at 31 + 0 to 33 + 6 weeks (····· and – · –, respectively), in prediction of small-for-gestational-age neonates with birth weight < 10th (a,b) and < 3rd (c,d) percentiles, delivered within 2 weeks (a,c) and at any time (b,d) after assessment.

35 + 0 to 36 + 6 weeks' gestation requires use of EFW < 40th percentile. Screening at this percentile cut-off predicted 95% and 99% of neonates with birth weight < 10th and < 3rd percentiles, respectively, born within 2 weeks after assessment, and the respective values for neonates born at any stage after assessment were 87% and 94%.

DISCUSSION

Main findings

The findings of this study demonstrate that the predictive performance for a SGA neonate of routine ultrasonographic examination during the third trimester is higher if, first, the scan is carried out at 35 + 0 to 36 + 6 weeks' gestation than at 31 + 0 to 33 + 6 weeks, second, the method of screening is EFW than fetal AC, third, the outcome measure is birth weight < 3rd than < 10th percentile, and, fourth, delivery occurs within 2 weeks than at any stage after assessment. Prediction of a SGA neonate by EFW < 10th percentile is modest and prediction of > 85% of cases at 35 + 0 to 36 + 6 weeks' gestation necessitates use of EFW < 40th percentile.

For a SGA neonate born within 2 weeks after assessment at 31 + 0 to 33 + 6 weeks' gestation, there was no significant difference in the predictive performance between EFW and fetal AC. This is not surprising because, in about 30% of the neonates born within 2 weeks after assessment, delivery was iatrogenic because of severe pre-eclampsia and/or fetal growth restriction and, in such cases, fetal AC would be affected more than HC and FL. In contrast, at 35 + 0 to 36 + 6 weeks' gestation, in only about 10% of neonates born within 2 weeks after assessment, delivery was iatrogenic for fetal growth restriction.

Screening by EFW < 10th percentile at 35 + 0 to 36 + 6 weeks' gestation predicted 70% and 84% of neonates with birth weight < 10th and < 3rd percentiles, respectively,

born within 2 weeks after assessment, with positive predictive values of 19.6% and 13.0%, respectively. The respective values for neonates born at any stage after assessment were 46%, 65%, 59.1% and 31.8%. Screening by EFW $< 40^{th}$ percentile at $35+0$ to $36+6$ weeks predicted 95% and 99% of neonates with birth weight $< 10^{th}$ and $< 3^{rd}$ percentiles, respectively, born within 2 weeks after assessment, with positive predictive values of 6.5% and 3.7%, respectively; the respective values for neonates born at any stage after assessment were 87%, 94%, 27.3% and 11.2%.

Comparison with previous studies

We found that the predictive performance for a SGA neonate of EFW is superior to that of fetal AC. This finding is consistent with the results of a study that investigated the ability of ultrasonographic fetal biometry to predict birth weight in neonates born within 2 days after the ultrasound examination and reported that models incorporating measurements of fetal HC, AC and FL were superior to those using AC alone or AC and FL[9]. Our finding that the predictive performance for a SGA neonate of fetal biometry at $35+0$ to $36+6$ weeks' gestation is superior to that at $31+0$ to $33+6$ weeks is consistent with the results of a previous study of 2288 pregnancies undergoing ultrasound examination at both of these gestational-age windows[19] and those of a randomized trial comparing the performance of ultrasound examination at 36 *vs* 32 weeks' gestation[10].

Implications for clinical practice

Justification of prenatal screening for a SGA fetus is based on, first, evidence that such fetuses are at increased risk of stillbirth and adverse perinatal outcome[20–23] and, second, the expectation that these risks can be reduced by medical intervention, such as early delivery[1]. In this respect, all pregnant women should be offered a routine third-trimester scan because such policy is more effective in identifying SGA fetuses than is selective ultrasonography based on maternal risk factors and the results of measurements of symphysis–fundus height[6].

Since 85% of SGA neonates are born at term[17] and the predictive performance for a SGA neonate is highest if the scan is carried out close to the time of birth, the best timing for a routine scan is about 36 weeks' gestation. Identification of SGA fetuses born before 36 weeks' gestation would require ultrasound scans at 26–28 and 30–32 weeks and we have proposed previously that selection of the subgroup of the population requiring such additional scans should be based on stratification of risk at 20 weeks' gestation[24]. In relation to SGA fetuses born < 32 weeks' gestation, there is evidence of a high association with pre-eclampsia and that the risk can be reduced by first-trimester screening for pre-eclampsia and treatment of the high-risk group with aspirin[25–30].

The findings of this study highlight that a routine third-trimester ultrasound scan constitutes a screening rather than diagnostic test for SGA neonates and that the EFW cut-off of the 40^{th} rather than the 10^{th} percentile should be used to identify a group in need of further investigations. However, only about one in four of such fetuses would actually be SGA at birth and the objective of further investigations would be to distinguish between true and false positives. Such an objective could potentially be achieved by serial ultrasound scans to define subsequent growth and wellbeing; supportive evidence for such expectation is that the predictive performance for SGA neonates is considerably higher in pregnancies delivering within 2 weeks after assessment than in those with a longer interval. Alternative strategies, including addition of fetal growth velocity between 20 or 32 and 36 weeks' gestation and addition of maternal risk factors, serum placental growth factor, uterine artery pulsatility index and the cerebroplacental ratio, had limited success in improving the predictive performance for a SGA neonate of EFW at 36 weeks[15–17,31,32].

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 either $31+0$ to $33+6$ or $35+0$ 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[8] which has been shown to be the most accurate among 70 models reported previously[9], third, use of The Fetal Medicine Foundation fetal and neonatal reference ranges which have a common median[3], and, fourth, direct comparison of the predictive performance of EFW and fetal AC.

A limitation of the study, in relation to the comparison of the predictive performance for SGA neonates of the scan at $31+0$ to $33+6$ *vs* that at $35+0$ to $36+6$ weeks' gestation, is that it was not a randomized study. However, the findings should be valid because, during the two consecutive periods of study, the characteristics of the population were similar, the two hospitals were the same and the ultrasonographers carrying out the scans had received the same training and followed the same protocol for conducting the scan.

Conclusions

The predictive performance for a SGA neonate of routine ultrasonographic examination during the third trimester is higher if the scan is carried out at $35+0$ to $36+6$ weeks' gestation than at $31+0$ to $33+6$ weeks, but prediction of a SGA neonate by EFW $< 10^{th}$ percentile is modest and prediction of $> 85\%$ of cases at $35+0$ to $36+6$ weeks necessitates use of EFW $< 40^{th}$ percentile for selecting the group in need of further assessment. Future studies should investigate potential methods for reducing the false-positive rate in the group with EFW $< 40^{th}$ percentile.

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