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Prediction of large-for-gestational-age neonate by routine third-trimester ultrasound

N. KHAN[1,2,3], A. CIOBANU[3], T. KARAMPITSAKOS[1,2,3], R. AKOLEKAR[1,2] and K. H. NICOLAIDES[3]

[1]*Fetal Medicine Unit, Medway Maritime Hospital, Gillingham, UK;* [2]*Institute of Medical Sciences, Canterbury Christ Church University, Chatham, UK;* [3]*Fetal Medicine Research Institute, King's College Hospital, London, UK*

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

ABSTRACT

Objectives *First, 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 large-for-gestational-age (LGA) neonate born at ≥ 37 weeks' gestation. Second, to assess the additive value of fetal growth velocity between 32 and 36 weeks' gestation to the performance of EFW at 35 + 0 to 36 + 6 weeks' gestation for prediction of a LGA neonate. Third, to define the predictive performance for a LGA neonate of different EFW cut-offs on routine ultrasound examination at 35 + 0 to 36 + 6 weeks' gestation. Fourth, to propose a two-stage strategy for identifying pregnancies with a LGA fetus that may benefit from iatrogenic delivery during the 38th gestational week.*

Methods *This was a retrospective study. First, data from 21 989 singleton pregnancies that had undergone routine ultrasound examination at 31 + 0 to 33 + 6 weeks' gestation and 45 847 that had undergone routine ultrasound examination at 35 + 0 to 36 + 6 weeks were used to compare the predictive performance of EFW and AC for a LGA neonate with birth weight > 90th and > 97th percentiles born at ≥ 37 weeks' gestation. Second, data from 14 497 singleton pregnancies that had undergone routine ultrasound examination at 35 + 0 to 36 + 6 weeks' gestation and had a previous scan at 30 + 0 to 34 + 6 weeks were used to determine, through multivariable logistic regression analysis, whether addition of growth velocity, defined as the difference in EFW Z-score or AC Z-score between the early and late third-trimester scans divided by the time interval between the scans, improved the performance of EFW at 35 + 0 to 36 + 6 weeks in the prediction of delivery of a LGA neonate at ≥ 37 weeks' gestation. Third, in the database of the 45 847 pregnancies that had undergone routine ultrasound examination at 35 + 0 to 36 + 6 weeks' gestation, the screen-positive and detection rates for a LGA neonate born at ≥ 37 weeks' gestation and ≤ 10 days after the initial scan were calculated for different EFW percentile cut-offs between the 50th and 90th percentiles.*

Results *First, the areas under the receiver–operating characteristics curves (AUC) of screening for a LGA neonate were significantly higher using EFW Z-score than AC Z-score and at 35 + 0 to 36 + 6 than at 31 + 0 to 33 + 6 weeks' gestation (*$P < 0.001$ *for all). Second, the performance of screening for a LGA neonate achieved by EFW Z-score at 35 + 0 to 36 + 6 weeks was not significantly improved by addition of EFW growth velocity or AC growth velocity. Third, in screening by EFW > 90th percentile at 35 + 0 to 36 + 6 weeks' gestation, the predictive performance for a LGA neonate born at ≥ 37 weeks' gestation was modest (65% and 46% for neonates with birth weight > 97th and > 90th percentiles, respectively, at a screen-positive rate of 10%), but the performance was better for prediction of a LGA neonate born ≤ 10 days after the scan (84% and 71% for neonates with birth weight > 97th and > 90th percentiles, respectively, at a screen-positive rate of 11%). Fourth, screening by EFW > 70th percentile at 35 + 0 to 36 + 6 weeks' gestation predicted 91% and 82% of LGA neonates with birth weight > 97th and > 90th percentiles, respectively, born at ≥ 37 weeks' gestation, at a screen-positive rate of 32%, and the respective values of screening by EFW > 85th percentile for prediction of a LGA neonate born ≤ 10 days after the scan were 88%, 81% and 15%. On the basis of these results, it was proposed that routine fetal biometry at 36 weeks'*

Correspondence to: Prof. K. H. Nicolaides, Fetal Medicine Research Institute, King's College Hospital, 16–20 Windsor Walk, Denmark Hill, London SE5 8BB, UK (e-mail: kypros@fetalmedicine.com)

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gestation is a screening rather than diagnostic test for fetal macrosomia and that EFW $> 70^{th}$ percentile should be used to identify pregnancies in need of another scan at 38 weeks, at which those with EFW $> 85^{th}$ percentile should be considered for iatrogenic delivery during the 38^{th} week.

Conclusions *First, the predictive performance for a LGA neonate by routine ultrasonographic examination during the third trimester is higher if the scan is carried out at 36 than at 32 weeks, the method of screening is EFW than fetal AC, the outcome measure is birth weight $> 97^{th}$ than $> 90^{th}$ percentile and if delivery occurs within 10 days than at any stage after assessment. Second, prediction of a LGA neonate by EFW $> 90^{th}$ percentile is modest and this study presents a two-stage strategy for maximizing the prenatal prediction of a LGA neonate.*

INTRODUCTION

Large-for-gestational-age (LGA) neonates with birth weight $> 90^{th}$ percentile are at increased risk of perinatal death, birth injury and adverse neonatal outcome[1–5]. Such risks could potentially be reduced by elective Cesarean section or early induction of labor to limit the inevitable increase in fetal size with advancing gestational age[6–8]. However, there is uncertainty as to the best approach for identifying such LGA 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, the lack of consistent data on the performance of estimated fetal weight (EFW) *vs* fetal abdominal circumference (AC) for prediction of a LGA neonate, fourth, the limited data on the best timing for a universal third-trimester scan at 32 *vs* 36 weeks' gestation, and, fifth, the performance of sonographic fetal biometry in the prediction of a LGA neonate.

First, 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[9]. Second, there is some evidence that the predictive performance for a LGA neonate is better by universal sonographic fetal biometry during the third trimester than by the traditional method of selective ultrasonography based on maternal risk factors and the results of measurements of symphysis–fundus height[10]. Third, a systematic review of 36 articles reported that there was no difference in accuracy between ultrasonographic EFW and AC in the prediction of a macrosomic neonate at birth[11]. 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.*[12], which incorporates measurements of head circumference (HC), AC and femur length (FL)[13]. Fourth, on the issue of timing of the third-trimester scan, there is some evidence that the predictive performance of a scan for LGA neonates at 36 weeks' gestation may be superior to that at 32 weeks[14,15]. Fifth, there is uncertainty as to the additive value for prediction of a LGA neonate of fetal growth velocity to the performance of EFW during the late third trimester[16–18].

The objectives of this study were, first, 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 LGA neonate born at ≥ 37 weeks' gestation, second, to assess the additive value of fetal growth velocity between 32 and 36 weeks' gestation to the performance of EFW at 35 + 0 to 36 + 6 weeks' gestation for prediction of a LGA neonate, third, to define the predictive performance for a LGA neonate of different EFW cut-offs on routine ultrasound examination at 35 + 0 to 36 + 6 weeks' gestation, and, fourth, to propose a two-stage strategy for identifying pregnancies with a LGA fetus that may benefit from iatrogenic delivery during the 38^{th} gestational week.

METHODS

There are three parts to this study. First, data from 21 989 singleton pregnancies that had undergone routine ultrasound examination at 31 + 0 to 33 + 6 weeks' gestation and 45 847 that had undergone routine ultrasound examination at 35 + 0 to 36 + 6 weeks were used to compare the predictive performance of EFW and AC for a LGA neonate with birth weight $> 90^{th}$ and $> 97^{th}$ percentiles. The patients were examined 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 the 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 for fetal anatomy and measurement of fetal HC, AC and FL for calculation of EFW using the formula of Hadlock *et al.*[12]. Gestational age was determined by the measurement of fetal crown–rump length at 11–14 weeks or fetal HC at 19–24 weeks[19,20]. 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 from the patients included in this study were the subject of previous publications[4,15,21–27].

Second, data from 14 497 singleton pregnancies that had undergone routine ultrasound examination at 35 + 0 to 36 + 6 weeks' gestation and had a previous scan at least 2 weeks earlier at 30 + 0 to 34 + 6 weeks were used to determine whether addition of growth velocity between the early and late third-trimester scans improved the performance of EFW at 35 + 0 to 36 + 6 weeks in the prediction of delivery of a LGA neonate.

Third, the database of the 45 847 pregnancies that had undergone routine ultrasound examination at 35 + 0 to 36 + 6 weeks' gestation was used to define the predictive performance of different EFW cut-offs for a LGA neonate.

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 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 and diabetes mellitus, and obstetric history including parity (parous or nulliparous if no previous pregnancy at ≥ 24 weeks' gestation) and previous pregnancy with LGA. Maternal weight and height were measured at the time of the ultrasound examinations.

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 > 90^{th} and > 97^{th} percentiles born at ≥ 37 weeks' gestation, based on The Fetal Medicine Foundation fetal and neonatal population weight charts[9].

Statistical analysis

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

Study 1

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[9]. Similarly, AC was converted to *Z*-scores and percentiles adjusted for gestational age, according to the reference ranges of Snijders and Nicolaides[20]. Logistic regression analysis was undertaken to determine the significance of the contribution of AC *Z*-score and EFW *Z*-score in the prediction of delivery of a LGA neonate with birth weight > 90^{th} and > 97^{th} percentiles at ≥ 37 weeks' gestation. The performance of screening was determined by receiver–operating characteristics (ROC) curves and the areas under the ROC curves (AUC) of screening at 31 + 0 to 33 + 6 and 35 + 0 to 36 + 6 weeks' gestation in the prediction of a LGA neonate were compared.

Study 2

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[9,20]. 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. Multivariable regression analysis was carried out to determine whether the addition of AC growth velocity and EFW growth velocity to EFW *Z*-score at 35 + 0 to 36 + 6 weeks' gestation improved the performance of screening for a LGA neonate with birth weight > 90^{th} and > 97^{th} percentiles born at ≥ 37 weeks' gestation. The performance of screening was determined by ROC-curve analysis.

Study 3

The screen-positive and detection rates for a LGA neonate with birth weight > 90^{th} and > 97^{th} percentiles born at ≥ 37 weeks' gestation and ≤ 10 days after the initial scan, at different EFW percentile cut-offs between the 50^{th} and 90^{th} percentiles, were estimated.

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 scan periods, in the group of neonates with birth weight > 90^{th} percentile, compared to those with birth weight ≤ 90^{th} percentile, median maternal age, weight and height, EFW *Z*-score, AC *Z*-score and birth-weight *Z*-score were higher, fewer women were of non-white racial origin and were smokers, and more women had pre-existing diabetes mellitus Type 1 and were parous with a previous pregnancy with a LGA neonate.

Delivery at ≥ 37 weeks' gestation occurred in 20 901 (95.1%) of the 21 989 pregnancies examined at 31 + 0 to 33 + 6 weeks' gestation and in 44 918 (98.0%) of the 45 847 examined at 35 + 0 to 36 + 6 weeks' gestation.

Performance of screening for LGA neonate

Screening at 35 + 0 to 36 + 6 vs *31 + 0 to 33 + 6 weeks and by EFW* vs *fetal AC*

The AUCs of screening for a LGA neonate born at ≥ 37 weeks' gestation were significantly higher if, first, the scan was carried out at 35 + 0 to 36 + 6 weeks' gestation than at 31 + 0 to 33 + 6 weeks, second, the method of assessment was EFW *Z*-score than AC *Z*-score, and, third, the outcome measure was birth weight > 97th than > 90th percentile (Table 2 and Figure 1).

Effect of growth velocity on prediction of LGA neonate

In the dataset with paired measurements of fetal biometry at 30 + 0 to 34 + 6 and 35 + 0 to 36 + 6 weeks' gestation, multivariable logistic regression analysis demonstrated that, in the prediction of a LGA neonate with birth weight > 90th percentile born at ≥ 37 weeks' gestation, there was no significant improvement in the performance of

Table 1 Maternal and pregnancy characteristics of study population, according to gestational age (GA) at screening and delivery of large-for-gestational-age (LGA) neonate with birth weight > 90th percentile

	Screening at 31 + 0 to 33 + 6 weeks		*Screening at 35 + 0 to 36 + 6 weeks*	
Characteristic	*Non-LGA (n = 20 124)*	*LGA (n = 1865)*	*Non-LGA (n = 41 618)*	*LGA (n = 4229)*
Maternal age (years)	30.5 (25.9–34.4)	31.3 (26.9–35.1)‡	31.5 (27.2–35.3)	32.2 (28.3–35.8)‡
Maternal weight (kg)	76.0 (68.0–86.2)	85.0 (76.0–96.0)‡	78.2 (70.0–89.0)	88.0 (78.5–100.0)‡
Maternal height (cm)	164 (160–168)	167 (163–171)‡	165 (160–169)	167 (163–171)‡
Racial origin				
White	13 927 (69.2)	1497 (80.3)‡	30 677 (73.7)	3483 (82.4)‡
Black	4393 (21.8)	270 (14.5)‡	6708 (16.1)	488 (11.5)‡
South Asian	908 (4.5)	36 (1.9)‡	2085 (5.0)	100 (2.4)†
East Asian	427 (2.1)	27 (1.4)	882 (2.1)	57 (1.3)†
Mixed	469 (2.3)	35 (1.9)	1266 (3.0)	101 (2.4)*
Cigarette smoker	2269 (11.3)	118 (6.3)‡	3565 (8.6)	158 (3.7)‡
Conception				
Natural	19 550 (97.1)	1812 (97.2)	40 205 (96.6)	4065 (96.1)
Ovulation drugs	171 (0.8)	15 (0.8)	228 (0.5)	29 (0.7)
In-vitro fertilization	403 (2.0)	38 (2.0)	1185 (2.8)	135 (3.2)
Medical condition				
Chronic hypertension	279 (1.4)	27 (1.4)	530 (1.3)	50 (1.2)
Diabetes mellitus Type 1	65 (0.3)	17 (0.9)‡	118 (0.3)	49 (1.2)‡
Diabetes mellitus Type 2	123 (0.6)	12 (0.6)	169 (0.4)	39 (0.9)‡
Obstetric history				
Nulliparous	9945 (49.4)	635 (34.0)	19 456 (46.7)	1404 (33.2)
Parous with prior LGA	950 (4.7)	439 (23.5)‡	1825 (4.4)	956 (22.6)‡
Parous without prior LGA	9229 (45.9)	791 (42.4)†	20 337 (48.9)	1869 (44.2)‡
GA at screening (weeks)	32.2 (32.0–32.6)	32.3 (32.0–32.6)*	36.1 (35.9–36.4)	36.1 (35.9–36.4)
EFW *Z*-score	−0.09 (−0.75 to 0.57)	1.04 (0.51 to 1.59)‡	−0.03 (−0.66 to 0.57)	1.21 (0.71 to 1.75)‡
AC *Z*-score	−0.19 (−0.62 to 0.28)	0.56 (0.14 to 0.96)‡	−0.09 (−0.59 to 0.40)	0.86 (0.40 to 1.33)‡
GA at delivery (weeks)	40.0 (39.0–40.9)	40.0 (39.0–40.9)	39.9 (39.0–40.8)	40.0 (39.1–40.9)‡
Birth-weight *Z*-score	−0.17 (−0.85 to 0.43)	1.63 (1.43 to 1.95)‡	−0.13 (−0.79 to 0.45)	1.63 (1.44 to 1.93)‡
Birth weight (g)	3343 (3038–3630)	4245 (4054–4420)‡	3365 (3070–3645)	4240 (4065–4400)‡

Data are given as median (interquartile range) or *n* (%). Compared to pregnancies with non-LGA neonate: *$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$. AC, fetal abdominal circumference; EFW, estimated fetal weight.

Table 2 Comparisons of areas under the receiver–operating characteristics curves in screening for large-for-gestational-age (LGA) neonate with birth weight > 90th and > 97th percentiles delivered at ≥ 37 weeks' gestation, by estimated fetal weight and fetal abdominal circumference, according to gestational age at screening

Outcome	*Estimated fetal weight*	*Abdominal circumference*	P
Screening at 35 + 0 to 36 + 6 weeks			
LGA > 90th percentile	0.861 (0.856–0.867)	0.837 (0.831–0.843)	< 0.001
LGA > 97th percentile	0.902 (0.894–0.910)	0.882 (0.872–0.891)	< 0.001
Screening at 31 + 0 to 33 + 6 weeks			
LGA > 90th percentile	0.815 (0.806–0.825)	0.790 (0.780–0.800)	< 0.001
LGA > 97th percentile	0.853 (0.838–0.868)	0.828 (0.812–0.845)	< 0.001

Values in parentheses are 95% CI.

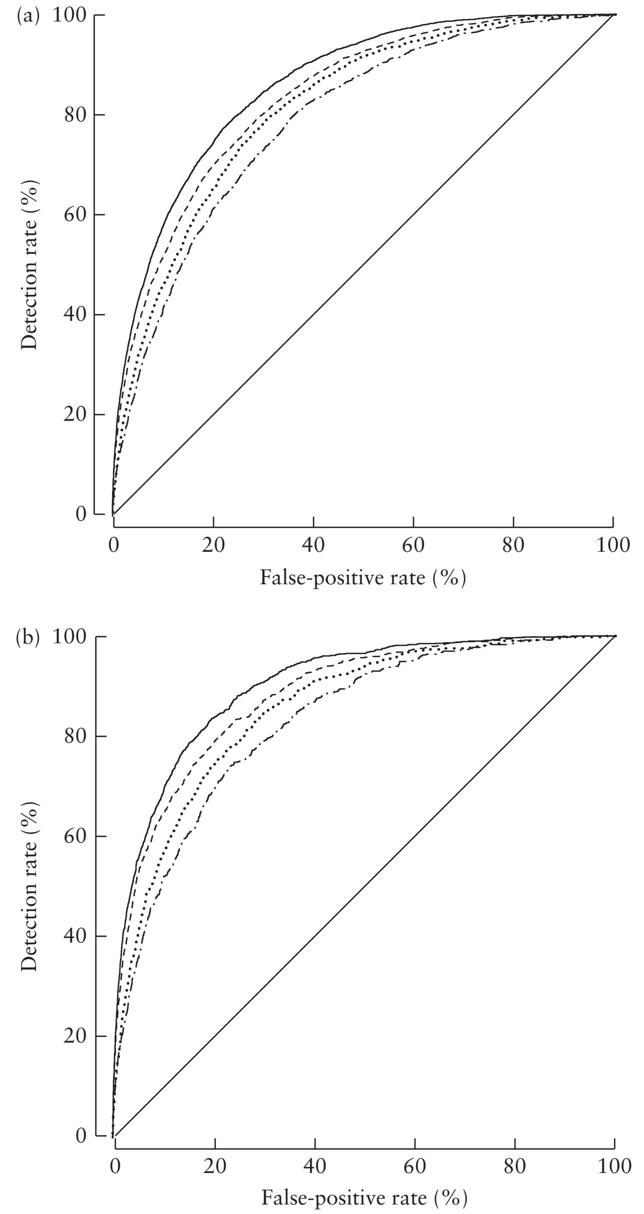

Figure 1 Receiver–operating characteristics curves of estimated fetal weight and fetal abdominal circumference at 35 + 0 to 36 + 6 weeks' gestation (—— and - - -, respectively) and at 31 + 0 to 33 + 6 weeks (····· and — · —, respectively), in prediction of large-for-gestational-age neonate with birth weight > 90th (a) and > 97th (b) percentiles, delivered at ≥ 37 weeks' gestation.

screening by addition of either AC growth velocity or EFW growth velocity to EFW *Z*-score at 35 + 0 to 36 + 6 weeks' gestation (AUC, 0.891; 95% CI, 0.883–0.899 *vs* 0.887; 95% CI, 0.879–0.896 and 0.892; 95% CI, 0.884–0.900 *vs* 0.887; 95% CI, 0.879–0.896, respectively); the detection rates, at a 10% false-positive rate, were 66%, 66% and 65%, respectively. Similarly, in the prediction of a LGA neonate with birth weight > 97th percentile born at ≥ 37 weeks' gestation, there was no significant improvement in the performance of screening by addition of either AC growth velocity or EFW growth velocity to EFW *Z*-score at 35 + 0 to 36 + 6 weeks' gestation (AUC, 0.921; 95% CI, 0.909–0.933 *vs* 0.919; 95% CI, 0.906–0.931 and 0.922; 95% CI, 0.910–0.934 *vs* 0.919; 95% CI, 0.906–0.931, respectively); the detection rates, at a 10% false-positive rate, were 75%, 76% and 75%, respectively.

Screening at different EFW percentile cut-offs in births at ≥ 37 weeks' gestation

The predictive performance for a LGA neonate with birth weight > 90th and > 97th percentiles delivered at ≥ 37 weeks' gestation in screening by EFW at a series of cut-offs between the 50th and 90th percentiles at 35 + 0 to 36 + 6 weeks' gestation is shown in Table 3 and the ROC curves of such screening are shown in Figure 2. Screening by EFW > 90th percentile predicted 65% of neonates with birth weight > 97th percentile and 46% of those with birth weight > 90th percentile, with respective positive predictive values of 17% and 43%. The respective values in screening by EFW > 70th percentile were 91% and 82%, and 7% and 24%. In the population of 44 918 pregnancies delivering at ≥ 37 weeks' gestation, the median interval between the scan and delivery was 3.9 (range, 0.1–7.6) weeks.

Screening at different EFW percentile cut-offs in births ≤ 10 days after scan

The predictive performance for a LGA neonate with birth weight > 90th and > 97th percentiles delivered ≤ 10 days after the scan at 35 + 0 to 36 + 6 weeks' gestation in screening by EFW at a series of cut-offs between the 50th and 90th percentiles is shown in Table 3 and the ROC curves of such screening are shown in Figure 2. Screening by EFW > 90th percentile predicted 84% of neonates with birth weight > 97th percentile and 71% of those with birth weight > 90th percentile, with respective positive predictive values of 28% and 51%. The respective values in screening by EFW > 85th percentile were 88% and 81%, and 22% and 43%.

Proposed strategy for management of LGA fetuses

On the assumption that, in pregnancies with suspected fetal macrosomia, iatrogenic delivery by induction of labor or elective Cesarean section during the 38th gestational week, compared to expectant management, would reduce the risk of associated perinatal death, birth injury and adverse neonatal outcome, we propose a two-stage strategy for identifying pregnancies that could potentially benefit from such intervention. The first stage is routine ultrasound examination at 35 + 0 to 36 + 6 weeks' gestation to identify pregnancies with EFW > 70th percentile (Table 3). In the second stage, these pregnancies with EFW > 70th percentile are offered a second ultrasound examination at the beginning of 38 weeks and those with EFW > 85th percentile (Table 3) are offered iatrogenic delivery.

On the basis of the results in Table 3, it is anticipated that about 30% of pregnancies will have EFW > 70th

Table 3 Predictive performance for large-for-gestational-age (LGA) neonate with birth weight $> 90^{th}$ and $> 97^{th}$ percentiles delivered at ≥ 37 weeks and ≤ 10 days after scan in screening by estimated fetal weight at 35 + 0 to 36 + 6 weeks' gestation

		LGA > 90^{th} percentile		*LGA > 97^{th} percentile*	
Estimated fetal weight	*SPR (n (%; 95% CI))*	*DR (n (%; 95% CI))*	*PPV (% (95% CI))*	*DR (n (%; 95% CI))*	*PPV (% (95% CI))*
Birth at ≥ 37 weeks	n = *45 847*	n = *4229*		n = *1190*	
$> 90^{th}$ percentile	4503 (9.8; 8.9–10.7)	1944 (46; 44–48)	43 (42–44)	775 (65; 62–68)	17 (16–18)
$> 85^{th}$ percentile	7096 (15.5; 14.7–16.3)	2535 (60; 58–62)	36 (35–37)	916 (77; 74–80)	13 (12–14)
$> 80^{th}$ percentile	9630 (21.0; 20.1–21.8)	2927 (69; 67–71)	30 (29–31)	992 (83; 80–86)	10 (9–11)
$> 75^{th}$ percentile	12 131 (26.5; 25.4–27.2)	3238 (77; 75–79)	27 (26–28)	1050 (88; 85–91)	9 (8–10)
$> 70^{th}$ percentile	14 626 (31.9; 30.8–32.3)	3455 (82; 80–84)	24 (23–25)	1085 (91; 88–94)	7 (6–8)
$> 65^{th}$ percentile	17 070 (37.2; 36.8–38.5)	3653 (86; 84–88)	21 (20–22)	1121 (94; 91–97)	7 (6–8)
$> 60^{th}$ percentile	19 498 (42.5; 41.3–42.7)	3800 (90; 88–92)	20 (19–21)	1142 (96; 93–99)	6 (5–7)
$> 55^{th}$ percentile	21 931 (47.8; 47.1–48.5)	3912 (93; 91–95)	18 (17–19)	1150 (97; 94–100)	5 (4–6)
$> 50^{th}$ percentile	24 269 (52.9; 52.2–53.6)	3992 (94; 92–96)	16 (15–17)	1156 (97; 94–100)	5 (4–6)
Birth ≤ 10 days after scan	n = *2901*	n = *236*		n = *110*	
$> 90^{th}$ percentile	325 (11.2; 10.1–12.4)	167 (71; 65–77)	51 (46–56)	92 (84; 77–91)	28 (23–33)
$> 85^{th}$ percentile	445 (15.3; 14.0–16.6)	190 (81; 76–86)	43 (38–48)	97 (88; 82–94)	22 (17–27)
$> 80^{th}$ percentile	564 (19.4; 18.0–20.8)	204 (86; 82–90)	36 (32–40)	99 (90; 84–96)	18 (15–21)
$> 75^{th}$ percentile	665 (22.9; 21.4–24.4)	217 (92; 89–95)	33 (29–37)	101 (92; 87–97)	15 (12–18)
$> 70^{th}$ percentile	795 (27.4; 25.8–29.0)	222 (94; 91–97)	28 (25–31)	103 (94; 90–98)	13 (11–15)
$> 65^{th}$ percentile	925 (31.9; 30.2–33.6)	228 (97; 95–99)	25 (22–28)	106 (96; 92–100)	11 (9–13)
$> 60^{th}$ percentile	1039 (35.8; 34.1–38.5)	229 (97; 95–99)	22 (20–24)	107 (97; 94–100)	10 (8–12)
$> 55^{th}$ percentile	1162 (40.0; 38.2–41.8)	231 (98; 96–100)	20 (18–22)	107 (97; 94–100)	9 (7–11)
$> 50^{th}$ percentile	1271 (43.8; 42.0–45.6)	231 (98; 96–100)	18 (16–20)	107 (97; 94–100)	8 (7–9)

DR, detection rate; PPV, positive predictive value; SPR, screen-positive rate.

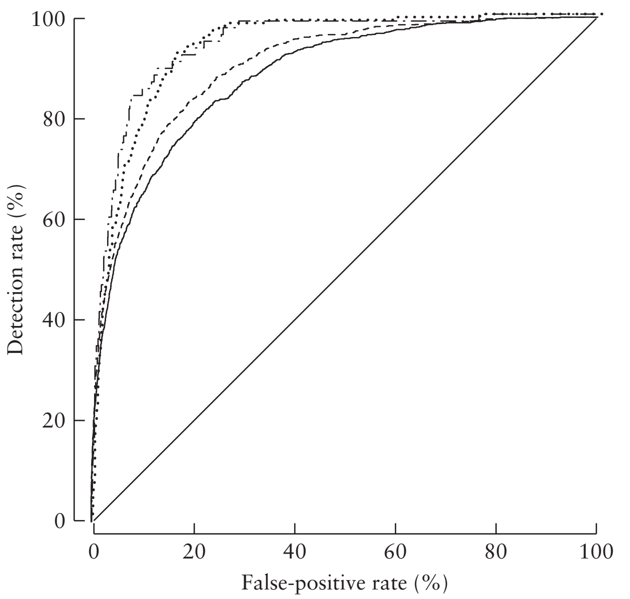

Figure 2 Receiver–operating characteristics curves of estimated fetal weight in prediction of large-for-gestational-age neonate with birth weight $> 90^{th}$ and $> 97^{th}$ percentiles, delivered at ≥ 37 weeks' gestation (—— and - - -, respectively) and within 10 days after assessment (····· and — · –, respectively).

percentile and will therefore be offered another scan at 38 weeks, and about 15% of the total would undergo iatrogenic delivery during the 38^{th} week. However, in our study population, 21.6% (9885/45 847) of pregnancies delivered < 39 weeks' gestation, including 20.9% (3050/14 626) of those with EFW > 70^{th} percentile at the 35 + 0 to 36 + 6-week scan. Future implementation studies are necessary to define the exact proportion of the population that would be stratified into the different management groups.

DISCUSSION

Main findings

The findings of this study demonstrate that the predictive performance for a LGA 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 $> 97^{th}$ than $> 90^{th}$ percentile, and, fourth, if delivery occurs within 10 days than at any stage after assessment. The predictive performance for a LGA neonate of EFW at 35 + 0 to 36 + 6 weeks is not improved by the addition of fetal growth velocity.

We found that screening by EFW $> 90^{th}$ percentile at 35 + 0 to 36 + 6 weeks' gestation predicted 65% of neonates with birth weight $> 97^{th}$ percentile born at ≥ 37 weeks' gestation and 46% of those with birth weight $> 90^{th}$ percentile, with respective positive predictive values of 17% and 43%. The respective values in screening by EFW > 70^{th} percentile were 91% and 82%, and 7% and 24%.

Comparison with previous studies

We found that the predictive performance for a LGA 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[13].

Our finding that the predictive performance for a LGA 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 comparing the performance of ultrasonographic fetal biometry in 3690 pregnancies at 30 + 0 to 33 + 6 weeks' gestation to that in 2288 at 34 + 0 to 37 + 0 weeks[14], and of another study comparing the performance of fetal biometry in 25 727 pregnancies at 30 + 0 to 34 + 6 weeks' gestation to that in 6181 at 34 + 0 to 37 + 6 weeks[15].

Our finding that the addition of growth velocity between 32 and 36 weeks' gestation did not improve the prediction of a LGA neonate provided by EFW at 36 weeks alone is consistent with the results of a study that examined 3440 pregnancies and reported that serial fetal biometry did not improve the prediction of a LGA neonate provided by the last EFW before delivery alone[17], and of another study that examined 2696 pregnancies and reported that AC growth velocity between 22 and 32 weeks did not improve the prediction of a LGA neonate provided by AC at 32 weeks[18]. Similarly, in previous studies, we reported that growth velocity between 22 and 36 weeks and between 32 and 36 weeks did not improve the predictive performance for small-for-gestational-age (SGA) neonates provided by EFW at 36 weeks[23,24]. Salomon *et al.*, examined 356 pregnancies at 11–14, 20–24 and 30–34 weeks' gestation and, on the basis of fetal biometry and growth velocity between ultrasound examinations, developed models that provided modest prediction of SGA and LGA neonates[16].

Implications for clinical practice

All pregnant women should be offered a routine third-trimester scan because such policy is more effective at identifying both LGA and SGA fetuses than is selective ultrasonography based on maternal risk factors and the results of measurements of symphysis–fundus height. As shown in this study, the best timing for performing such a scan is about 36 weeks' gestation. However, the scan should be considered to be a screening rather than diagnostic test for LGA neonates. Selection of EFW > 90^{th} percentile as the cut-off necessary to identify the high-risk group in need of further assessment and/or iatrogenic delivery during the 38^{th} gestational week, with the aim of reducing the risk of associated perinatal death, birth injury and adverse neonatal outcome, is inadequate because the majority of affected fetuses would be missed.

This study provides the framework for stratification of risk for LGA neonates and management of pregnancies undergoing routine fetal biometry at 36 weeks' gestation. We propose a two-stage strategy for identifying pregnancies that could potentially benefit from iatrogenic delivery during the 38^{th} gestational week. In the first stage, at 36 weeks' gestation, an EFW cut-off is selected to include the majority of expected LGA neonates at an acceptably low screen-positive rate; in the second stage the screen-positive group from first-stage screening have a second scan at the beginning of the 38^{th} week and those with EFW above a certain cut-off are offered iatrogenic delivery. We propose a pragmatic approach of selecting the EFW cut-off of the 70^{th} percentile for the first stage and the 85^{th} percentile for the second stage. However, the EFW cut-offs and protocols for management of the screen-positive groups will inevitably vary according to the findings of implementation studies, local preferences and health-economic considerations. Future studies will examine whether the implementation of such protocols could improve perinatal outcome.

Strengths and limitations

The strengths of this screening study for LGA 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, that trained sonographers carried out fetal biometry according to a standardized protocol[20], third, use of The Fetal Medicine Foundation fetal and neonatal reference ranges which have a common median[9], fourth, direct comparison of the predictive performance of EFW and fetal AC, and, fifth, presentation of a strategy for prenatal prediction of LGA neonates and the management of affected pregnancies.

A limitation of this study, in relation to the comparison of the predictive performance for a LGA neonate 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 are 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 LGA 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 LGA neonate by EFW > 90^{th} percentile is modest. This study presents a two-stage approach for stratifying pregnancies undergoing routine ultrasound examination at 36 weeks' gestation into management groups based on EFW. This approach is likely to have a higher predictive performance for LGA neonates than screening by EFW > 90^{th} percentile. Future implementation studies will define the impact of the proposed approach in prenatal prediction of a LGA neonate and reduction of adverse perinatal outcome.

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