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# Ultrasound screening for fetal growth restriction at 36 *vs* 32 weeks' gestation: a randomized trial (ROUTE)

E. ROMA*, A. ARNAU†, R. BERDALA*, C. BERGOS*, J. MONTESINOS† and F. FIGUERAS‡

**Obstetrics and Gynecology Department, Althaia, Network Healthcare Manresa Foundation, Barcelona, Spain; †Research and Innovation Unit, Althaia, Network Healthcare Manresa Foundation, Barcelona, Spain; ‡BCNatal - Barcelona Center for Maternal-Fetal and Neonatal Medicine, Hospital Clínic and Hospital Sant Joan de Déu, IDIBAPS, University of Barcelona and Centre for Biomedical Research on Rare Diseases (CIBER-ER), Barcelona, Spain*

**KEYWORDS:** fetal development; fetal growth restriction; neonatal complications; placenta; ultrasonography

## ABSTRACT

***Objective*** *To compare the utility of routine third-trimester ultrasound examination at 36 weeks' gestation with that at 32 weeks in detecting fetal growth restriction (FGR).*

***Methods*** *This was an open-label parallel randomized trial (ROUTE study) conducted at a single general hospital serving a geographically well-defined catchment area in Barcelona, Spain, between May 2011 and April 2014. Women with no adverse medical or obstetric history and a singleton pregnancy without fetal abnormalities at routine second-trimester scan were assigned randomly to undergo a scan at 32 weeks' gestation (*n = *1272) or at 36 weeks' gestation (*n = *1314). Primary outcome measures were detection rates of FGR (customized birth weight < 10$^{th}$ centile) and severe FGR (customized birth weight < 3$^{rd}$ centile).*

***Results*** *There were no significant differences in perinatal outcome between those who underwent a scan at 32 weeks' gestation and those who underwent a scan at 36 weeks' gestation. Severe FGR at birth was associated significantly with emergency Cesarean delivery for fetal distress (odds ratio (OR), 3.4 (95% CI, 1.8–6.7)), neonatal admission (OR, 2.23 (95% CI, 1.23–4.05)), hypoglycemia (OR, 9.5 (95% CI, 1.8–49.8)) and hyperbilirubinemia (OR, 9.0 (95% CI, 4.6–17.6)). Despite similar false-positive rates (FPRs) (6.4%* vs *8.2%), FGR detection rates were superior at 36* vs *32 weeks' gestation (sensitivity, 38.8%* vs *22.5%;* P = *0.006), with positive and negative likelihood ratios of 6.1* vs *2.7 and 0.65* vs *0.84, respectively. In cases of severe FGR, FPRs for both scans were also similar (8.5%* vs *8.7%), but detection rates were superior at 36* vs *32 weeks' gestation (61.4%* vs *32.5%;* P = *0.008). Positive and negative likelihood ratios were 7.2* vs *3.7 and 0.4* vs *0.74, respectively.*

***Conclusion*** *In low-risk pregnancies, routine ultrasound examination at 36 weeks' gestation was more effective than that at 32 weeks' gestation in detecting FGR and related adverse perinatal and neonatal outcomes.* 

## INTRODUCTION

At a prevalence of 10%, over 500 000 pregnancies in Europe alone result in small-for-gestational-age (SGA) newborns each year[1]. Antenatal screening misses up to 75% of fetuses at risk of SGA[2,3]. In low-risk pregnancies, the detection rate is even lower (*c.* 15%)[4], which is of particular concern given that undetected SGA significantly increases the risk of adverse perinatal outcome and stillbirth[5,6]. By combining first- or second-trimester uterine artery Doppler findings with baseline maternal characteristics, the detection rate of early-onset fetal growth restriction (FGR) approaches acceptable levels[7]. Unfortunately, FGR in late pregnancy is largely overlooked[8], although it accounts for the largest fraction of adverse outcomes and stillbirths[9]. Within this subset, the main correlate of stillbirth, perinatal complications and abnormal neurodevelopment is severe FGR (generally birth weight < 3$^{rd}$ centile)[10–12]. Detecting late-onset FGR, especially severe cases, is therefore central to third-trimester screening.

Current third-trimester strategies to monitor growth involve symphysis–fundus height measurement. However, most SGA infants in low-risk populations are not detected in this manner[13]. Third-trimester ultrasound monitoring of fetal growth is routine in some countries, boosting detection rates to 40–80%[5,14]. However, the impact on perinatal outcome remains unclear. Moreover, the optimal gestational age for the third-trimester examination, in terms of detection, has not been addressed

*Correspondence to*: Dr E. Roma, Obstetrics and Gynecology Department, Althaia, Network Healthcare Manresa Foundation, 1–3 Dr. Joan Soler, 08243 Manresa, Barcelona, Spain (e-mail: eroma@althaia.cat)

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previously in any randomized study. Accordingly, this trial was conducted to compare the utility of routine third-trimester ultrasound examination at 36 with that at 32 weeks' gestation for detecting FGR.

## SUBJECTS AND METHODS

### Study population

Between May 2011 and April 2014, 2586 pregnant women were non-selectively enrolled into an open-label parallel randomized trial (Figure 1) confined to a geographical area of 206 129 inhabitants and 50 municipalities in Barcelona, Spain. All women were followed at 21 primary healthcare units within the catchment area of a single hospital (San Joan de Déu Hospital, Network Healthcare Manresa Foundation, Barcelona, Spain) where they delivered or to which they were referred for complications. Conforming to national guidelines, routine ultrasound scans were performed at $11+0$ to $13+6$ weeks' gestation for pregnancy dating, based on crown–rump length[15], and screening for congenital anomalies was performed at $19+0$ to $21+6$ weeks' gestation. After routine second-trimester scanning, women meeting the following inclusion criteria were eligible to participate in the study: 1) viable singleton non-anomalous fetus; 2) pregnancy dating by ultrasound performed before $13+6$ weeks; 3) maternal age at recruitment $\geq 18$ years; 4) absence of medical history of diabetes, autoimmune or renal diseases, hypertension or stillbirth. Each eligible woman was given an information sheet concerning the study protocol.

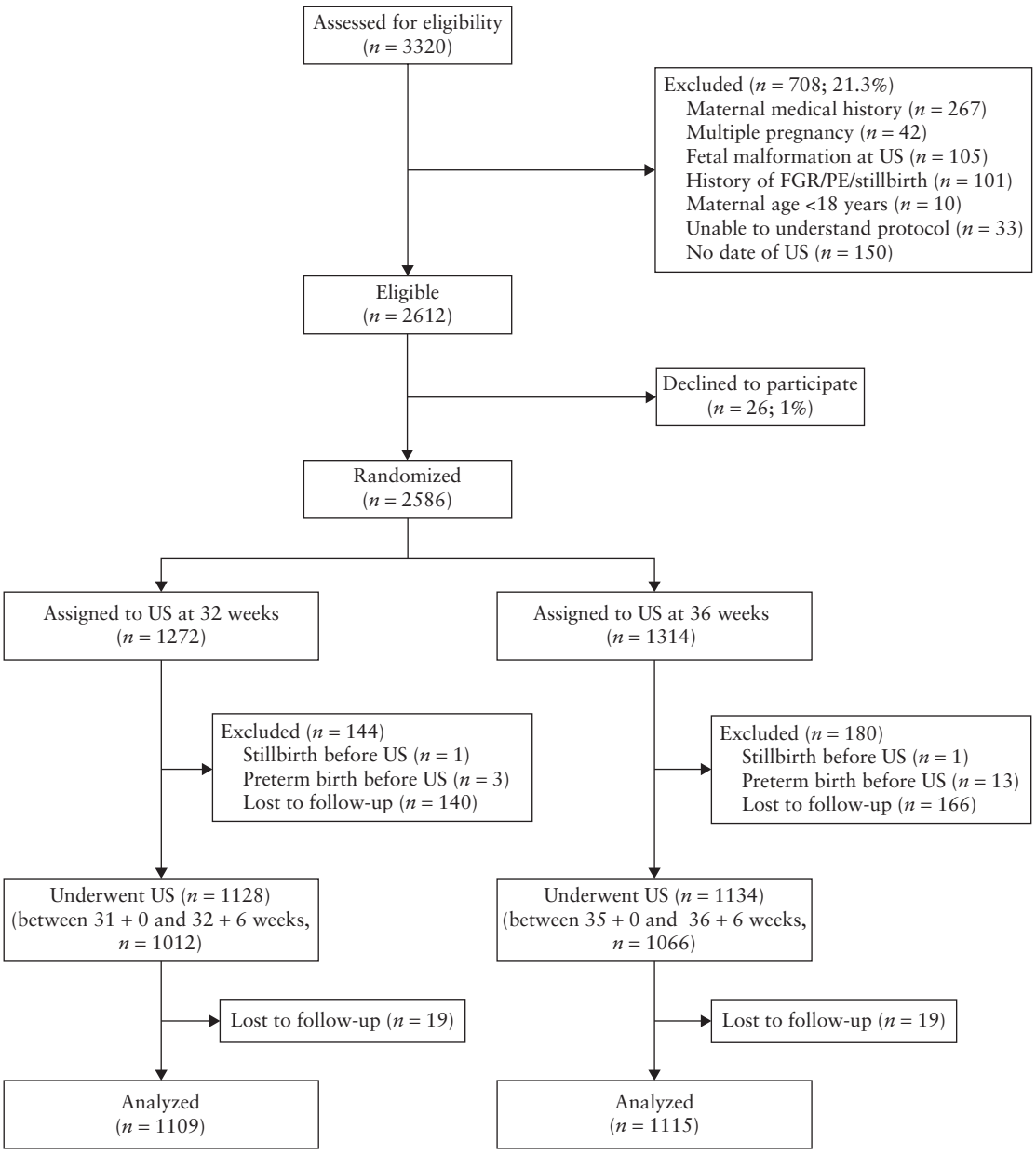


**Figure 1** Flowchart summarizing selection and grouping of study groups in the randomized controlled trial of pregnant women assigned to undergo ultrasound examination (US) at 32 or 36 weeks' gestation. FGR, fetal growth restriction; PE, pre-eclampsia.

Women participating in another clinical trial within the previous 3 months, those unable to understand the study protocol and those unwilling to give informed consent were excluded. The study protocol was approved by the Local Ethics Committee (IRB 11/17) and entered in the Current Controlled Trials Registry (ISRCTN17997330). The study design fulfilled CONSORT quality standard criteria for randomized trials.

*Randomization*

Using an online service (http://www.randomization.com), randomization sequences were generated in blocks of 100 participants to assure balanced distribution within study arms. The allocation sequence was sequestered internally by a Clinical Trials Unit (CTU). At the time of routine second-trimester scans and after participants were enrolled, recruiting physicians phoned the CTU for third-trimester scan allocation, at either 32 (± 1) or 36 (± 1) weeks' gestation, in a 1 : 1 allocation ratio. Women who declined consent for randomization but authorized the use of their medical data were included in the database. These data served in external validity testing of the trial. No participant refused both randomization and collection of identifiable data. It was not possible to blind participants, obstetricians or outcome assessors to the study group.

*Maternal and perinatal characteristics*

Data on maternal characteristics, including age, ethnicity, body mass index (BMI), nulliparity (no prior deliveries after 22 weeks' gestation), smoking status, medical and obstetric history, were recorded in the hospital database at inclusion in the study. In addition, all data pertaining to follow-up (development of complications, ultrasound evaluations and perinatal conditions) were collected prospectively.

*Ultrasound and Doppler measurements*

In all instances, ultrasound examinations were performed by one of 10 experienced and certified operators using an ultrasound machine (Siemens Sonoline Antares, Siemens Healthcare Diagnostics, Camberley, Surrey, UK; GE Voluson 730 Expert, GE Medical Systems, Zipf, Austria; or Toshiba Nemio 20, Toshiba Medical Systems, Tokyo, Japan) equipped with a 6–2-MHz linear curved-array transducer. Estimated fetal weight (EFW) was calculated from biparietal diameter, head and abdominal circumferences and femur length using the formula of Hadlock *et al.*[16]. EFW < 10$^{th}$ centile according to local standards[17] prompted Doppler examination of umbilical artery pulsatility index (UA-PI), measured from a free-floating portion of umbilical cord. Pulsed Doppler measurements were performed automatically, based on at least three consecutive waveforms, with angle of insonation as close to 0° as possible and always below 30°. A high-pass filter of 70 Hz was used to record low-flow velocities and to avoid artifacts.

*Outcome measures*

Pre-eclampsia (PE) was defined, according to criteria of the International Society for the Study of Hypertension in Pregnancy, as new-onset hypertension after 20 weeks' gestation, with systolic blood pressure (sBP) ≥ 140 mmHg and/or diastolic blood pressure (dBP) ≥ 90 mmHg on at least two occasions, 4 h apart and proteinuria ≥ 300 mg/24 h. Severe PE was defined as sBP/dBP ≥ 160/110 mmHg on two or more determinations and proteinuria ≥ 2 g/24 h or presence of maternal complications. Non-reassuring fetal status during labor was determined by pathological fetal heart rate or suspicious tracing[18] with fetal scalp blood pH < 7.15, or < 7.20 in two samples 30 min apart. Neonatal metabolic acidosis at birth was equated with umbilical arterial pH < 10$^{th}$ centile (< 7.15) and base excess > 90$^{th}$ centile (> 12 mEq/L)[19]. Neonatal hypothermia corresponded with a core temperature < 36.5 °C following appropriate warming measures. Criteria for admission to the neonatal unit were: 1) suspected infection, 2) persistent postprandial hypoglycemia (< 40 mg/dL), 3) low birth weight (< 2100 g), 4) prematurity (< 35 + 0 weeks), 5) severe acidosis at birth (arterial pH < 7.00) and 6) neurological symptoms (hypotonia, hypertonia or seizures). Mechanical ventilation and hypoxic-ischemic encephalopathy were grounds for admission to the intensive care unit.

*Management protocol*

Following assignment, participants were followed by midwives according to a standardized protocol, which included serial symphysis–fundus height measurements after 26 weeks' gestation. Suspected cases of SGA prompted weekly monitoring and elective induction at 37 + 1 weeks if UA-PI values were abnormal (> 95$^{th}$ centile); otherwise, monitoring was carried out every 2 weeks and delivery was induced at 40 + 1 weeks. Earlier delivery was indicated for (but not limited to) instances of suspected acidosis (i.e. abnormal fetal heart rate[18]), absent or reversed diastolic flow in the UA or development of severe PE.

*Sample size estimation and statistical analysis*

A sample size of 130 events (SGA at birth) in each study arm was deemed sufficient to identify a 20% increase, from 40% to 60%, in the rate of detecting birth weight < 10$^{th}$ centile, assuming a Type I error of 5% and aiming for a power of 90%. Given a 10% prevalence of SGA and an expected inclusion rate of 85%, a total of 3058 subjects (1529 per arm) were projected.

Analysis was based on originally-assigned groups (intention-to-treat). A binomial distribution model was used to determine 95% CIs of proportions. Student's *t*-test or the non-parametric Mann–Whitney *U*-test, and Pearson's chi-square or linear-by-linear association chi-square (for trends across ordered categories) test were performed for univariate between-group comparisons of quantitative and qualitative variables, respectively.

**Table 1** Characteristics of 2586 pregnant women assigned randomly to undergo ultrasound examination for detection of fetal growth restriction at either 32 or 36 weeks' gestation

| *Characteristic* | *32 weeks (n = 1272)* | *36 weeks (n = 1314)* | P* |
|---|---|---|---|
| Maternal age at delivery (years) | 31.3 ± 4.8 | 31.4 ± 4.8 | 0.63 |
| Maternal height (cm) | 162.4 ± 5.9 | 162.5 ± 6.2 | 0.74 |
| Maternal weight at booking (kg) | 64.5 ± 12.6 | 63.9 ± 12.1 | 0.49 |
| BMI at booking (kg/m$^2$) | 24.3 ± 4.6 | 24.2 ± 4.3 | 0.38 |
| Smoker at booking | 179 (14.1) | 235 (17.9) | 0.03 |
| Parity† | | | 0.49 |
| 0 | 591 (46.5) | 632 (48.1) | |
| 1 | 476 (37.5) | 500 (38.1) | |
| 2 | 147 (11.6) | 136 (10.4) | |
| ≥ 3 | 53 (4.2) | 44 (3.3) | |
| Ethnicity | | | 0.032 |
| White European | 906 (71.2) | 971 (73.9) | |
| South American | 76 (6.0) | 83 (6.3) | |
| Moroccan | 228 (17.9) | 224 (17.0) | |
| Black | 40 (3.1) | 29 (2.2) | |
| East Asian | 18 (1.4) | 6 (0.5) | |
| South Asian | 4 (0.3) | 1 (0.1) | |

Data are given as mean ± SD or *n* (%). *Continuous variables were compared using Student's *t*-test and categorical variables using Pearson's chi-square test. †Data on parity were not available for seven women. BMI, body mass index.

**Table 2** Perinatal outcome in 2224 women assigned randomly to undergo ultrasound examination for detection of fetal growth restriction at either 32 or 36 weeks' gestation

| *Outcome* | *32 weeks (n = 1109)* | *36 weeks (n = 1115)* | P* |
|---|---|---|---|
| Labor induction | 364 (32.8) | 400 (35.9) | 0.13 |
| GA at delivery (days) | 278.7 ± 9.4 | 279.1 ± 9 | 0.316 |
| Birth weight (g) | 3286 ± 459 | 3272 ± 453 | 0.467 |
| Male gender | 573 (51.7) | 553 (49.6) | 0.339 |
| Birth-weight centile | 48.4 ± 27.3 | 47 ± 27.6 | 0.25 |
| Birth weight | | | |
| < 10$^{th}$ centile | 109 (9.8) | 134 (12.0) | 0.098 |
| < 3$^{rd}$ centile | 40 (3.6) | 49 (4.4) | 0.34 |
| Instrumental delivery for NRFS | 88 (7.9) | 86 (7.7) | 0.845 |
| Cesarean delivery for NRFS | 54 (4.9) | 47 (4.2) | 0.459 |
| Neonatal acidosis‡ | 49 (4.8) | 47 (4.7) | 0.944 |
| 5-min Apgar score < 7 | 2 (0.2) | 4 (0.4) | 0.687† |
| Hypothermia | 4 (0.4) | 3 (0.3) | 0.725† |
| Hypoglycemia | 3 (0.3) | 2 (0.2) | 0.686† |
| Hyperbilirubinemia | 27 (2.4) | 30 (2.7) | 0.79 |
| Neonatal admission§ | 99 (8.9) | 89 (8.0) | 0.42 |
| NICU admission | 5 (0.5) | 1 (0.1) | 0.124† |

Data are given as mean ± SD or *n* (%). *Continuous variables were compared using Student's *t*-test and categorical variables using Pearson's chi-square or †Fisher's exact test. ‡UA-pH < 7.15. §Excluding neonatal admissions for low birth weight. GA, gestational age; NICU, neonatal intensive care unit; NRFS, non-reassuring fetal status during labor; UA, umbilical artery.

Open-source software (The R Foundation for Statistical Computing) was used for all computations and graph construction (R v2.15.1 and package pROC v1.7.2).

## RESULTS

Of the 3320 women assessed for eligibility, 2612 met the inclusion criteria; 26 declined to participate and had baseline characteristics similar to those of randomized participants (Table S1). A flowchart of participants, indicating reasons for exclusion, is shown in Figure 1. Baseline characteristics of 2586 subjects assigned randomly to scanning at 32 weeks' gestation ($n = 1272$) or 36 weeks' gestation ($n = 1314$) are detailed in Table 1. Of these women, 344 (13.3%) were lost to follow-up (306 before the scan and 38 during the scan-to-delivery interval). Again, baseline characteristics of participants lost to follow-up were comparable to the 2242 who completed all aspects of the study (Table S2), except for a significantly higher proportion of non-Caucasian women in the subset lost to follow-up. There were two stillbirths (one in each group) and 16 preterm deliveries (scan at 32 weeks' gestation, $n = 3$; scan at 36 weeks' gestation, $n = 13$) before the assigned ultrasound examination was performed. Table 2 summarizes perinatal and neonatal outcomes of the other 2224 pregnancies. Of note, perinatal outcomes did not differ between groups.

A total of 243 (10.9%) newborns were found to have FGR (customized birth weight < 10$^{th}$ centile). In 89 (4.0%) of these newborns, FGR was severe (birth weight < 3$^{rd}$ centile). Table S3 describes perinatal and neonatal outcomes according to birth-weight centile, showing more frequent adverse outcomes as the degree of FGR increases. Severe FGR at birth was associated significantly with emergency Cesarean delivery for fetal distress (odds ratio (OR), 3.4 (95% CI, 1.8–6.7)), neonatal admission (OR, 2.23 (95% CI, 1.23–4.05)), hypoglycemia (OR, 9.5 (95% CI, 1.8–49.8)) and hyperbilirubinemia (OR, 9.0 (95% CI, 4.6–17.6)).

Among the 2262 participants who underwent routine scans, imaging was performed outside the intended gestational age range of ± 1 week in 184 (8.1%) women, with scans performed for low fundal height in 53 women (in 21 at 32 weeks and in 32 at 36 weeks) and for superimposed maternal risk factor in 87 women. In 44 instances, the date of scanning was adjusted for participant convenience. Table 3 presents perinatal outcomes in instances in which scans were performed outside the intended range of gestational age.

Per protocol, 1012 and 1066 participants underwent a scan within 31 + 0 to 32 + 6 weeks and 35 + 0 to 36 + 6 weeks, respectively, and following analysis, a total of 97 (9.6%) and 112 (10.5%) fetuses with estimated weights < 10$^{th}$ centile, and 32 (3.2%) and 34 (3.2%) < 3$^{rd}$ centile were identified. Among fetuses with an estimated weight < 10$^{th}$ centile, 11 (11.3%) and 12 (10.7%) ($P = 0.89$) had increased UA-PI at 32 and 36 weeks' gestation, respectively.

For prediction of FGR, areas under the receiver–operating characteristics (ROC) curve (AUC) of estimated fetal-weight centile were 0.75 (95% CI, 0.71–0.79) for the scan at 32 weeks' gestation and 0.82 (95% CI, 0.78–0.85)

**Table 3** Baseline characteristics and perinatal outcomes according to whether ultrasound examinations were performed within or outside intended gestational age range of 31 + 0 to 32 + 6 or 35 + 0 to 36 + 6 weeks in 2262 women assigned randomly to undergo examination at either 32 or 36 weeks' gestation

| *Characteristic/ outcome* | *Outside range (n = 184)* | *Within range (n = 2078)* | P* |
|---|---|---|---|
| Maternal age at delivery (years) | 31.5 ± 5.2 | 31.3 ± 5.1 | 0.63 |
| BMI at booking (kg/m$^2$) | 24.9 ± 4.6 | 24.1 ± 4.3 | 0.046 |
| Nulliparous | 77 (41.8) | 999 (48.1) | 0.128 |
| Non-Caucasian | 128 (69.6) | 1526 (73.4) | 0.256 |
| Smoker at booking | 24 (13.0) | 326 (15.7) | 0.342 |
| Labor induction | 64 (34.8) | 700 (33.7) | 0.763 |
| GA at delivery (days) | 278.6 ± 9.8 | 279.9 ± 9 | 0.632 |
| Birth weight (g) | 3293 ± 509 | 3277 ± 451 | 0.684 |
| Male gender | 105 (57.1) | 1023 (49.2) | 0.032 |
| Birth-weight centile | 48.8 ± 27.4 | 47.6 ± 7.5 | 0.586 |
| Birth weight | | | |
| < 10$^{th}$ centile | 18 (9.8) | 224 (10.8) | 0.723 |
| < 3$^{rd}$ centile | 8 (4.3) | 57 (2.7) | 0.197 |
| Instrumental delivery for NRFS | 12 (6.5) | 162 (7.8) | 0.534 |
| Cesarean delivery for NRFS | 8 (4.3) | 93 (4.5) | 0.936 |
| Neonatal acidosis‡ | 7 (3.8) | 89 (4.3) | 0.76 |
| 5-min Apgar score < 7 | 1 (0.5) | 5 (0.2) | 0.399† |
| Hypothermia | 0 (0) | 5 (0.2) | 1† |
| Hypoglycemia | 0 (0) | 7 (0.3) | 1† |
| Hyperbilirubinemia | 5 (2.7) | 52 (2.5) | 0.805† |
| Neonatal admission§ | 13 (7.1) | 175 (8.4) | 0.523 |
| NICU admission | 0 (0) | 6 (0.3) | 1† |

Data are given as mean ± SD or *n* (%). *Continuous variables were compared using Student's *t*-test and categorical variables using Pearson's chi-square or †Fisher's exact test. ‡UA-pH < 7.15. §Excluding neonatal admissions for low birth weight. GA, gestational age; NICU, neonatal intensive care unit; NRFS, non-reassuring fetal status during labor; UA, umbilical artery.

for that at 36 weeks' gestation. For prediction of severe FGR, AUC of estimated fetal-weight centile were 0.82 (95% CI, 0.76–0.87) for the scan at 32 weeks' gestation and 0.86 (95% CI, 0.80–0.92) for that at 36 weeks' gestation. Figure 2 shows ROC curves of the scans at 32 and 36 weeks' gestation for predicting FGR and severe FGR and Table 4 demonstrates the performance of both approaches. Despite similar FPRs (6.4% *vs* 8.2%), FGR detection rates were superior at 36 weeks' gestation to those at 32 weeks' gestation (38.8% *vs* 22.5%; $P = 0.006$), with positive and negative likelihood ratios of 6.1 *vs* 2.7 and 0.65 *vs* 0.84, respectively. For severe FGR, false-positive rates were also similar (8.5% *vs* 8.7%), with improved detection of severe FGR at 36 as compared to 32 weeks' gestation (61.4% *vs* 32.5%; $P = 0.008$). Positive and negative likelihood ratios were 7.2 *vs* 3.7 and 0.4 *vs* 0.74, respectively.

A diagnosis of SGA at 32 weeks' gestation had an OR of 3.27 (95% CI, 1.97–5.43) for FGR and 5.07 (95% CI, 2.52–10.19) for severe FGR at birth. At 36 weeks' gestation, ORs were 9.31 (95% CI, 6.04–14.35) and 17.13 (95% CI, 8.98–32.7), respectively.

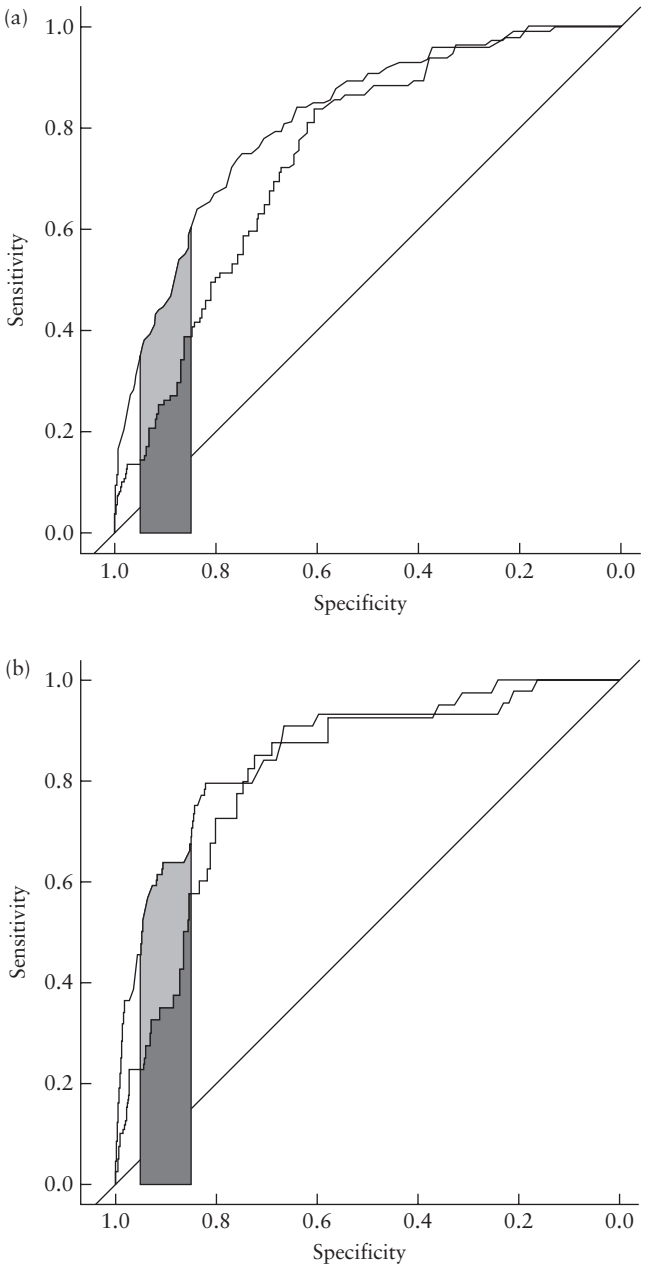


**Figure 2** Areas under the receiver–operating characteristics curve for ultrasound examinations at 32 (■) and 36 (□) weeks' gestation for prediction of fetal growth restriction (a) and severe fetal growth restriction (b). Shaded area indicates a 5–15% range of false-positive rate.

## DISCUSSION

Our study indicates that routinely performed late third-trimester scans (as opposed to mid third-trimester scans) yield improved rates of FGR detection, with no evident compensatory increase in risk of perinatal complications due to diagnostic delay. Although a meta-analysis of earlier randomized trials failed to demonstrate a real benefit of routine third-trimester scanning[20], it may be argued that the older pooled data are currently less valid because technology and expertise from the 1970s and 1980s do not translate

 

**Table 4** Performance of ultrasound examination at 32 or 36 weeks' gestation for detection of fetal growth restriction (FGR) or severe FGR*

| | *32 weeks* | *36 weeks* |
|---|---|---|
| Sensitivity (%) | | |
| FGR | 22.5 (15.7–31.1) | 38.8 (31.2–47.3) |
| Severe FGR | 32.5 (20.1–48.0) | 61.4 (46.6–74.3) |
| Specificity (%) | | |
| FGR | 91.8 (89.8–93.5) | 93.6 (91.8–95.0) |
| Severe FGR | 91.3 (89.4–93.0) | 91.5 (89.6–93.1) |
| PPV (%) | | |
| FGR | 25.8 (18.1–35.3) | 48.2 (39.2–57.4) |
| Severe FGR | 13.5 (8.1–21.8) | 24.1 (17.1–32.8) |
| NPV (%) | | |
| FGR | 90.4 (88.3–92.2) | 91.0 (88.9–92.6) |
| Severe FGR | 97.0 (95.7–97.9) | 98.2 (97.1–98.8) |
| LR+ | | |
| FGR | 2.7 | 6.1 |
| Severe FGR | 3.7 | 7.2 |
| LR− | | |
| FGR | 0.84 | 0.65 |
| Severe FGR | 0.74 | 0.40 |

Data in parentheses are 95% CIs. *FGR defined as birth weight < 10$^{th}$ centile and severe FGR as birth weight < 3$^{rd}$ centile. LR+, positive likelihood ratio; LR−, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

legitimately into current practice. Studies from that period also relied on outdated surrogates of fetal growth or formulae to estimate fetal weight[21,22]. Furthermore, many of the studies involved no change in management following a diagnosis of FGR, which does not reflect current practice. Finally, only three of the included trials[22–24] (accounting for 12% of subjects overall) included routine performance of ultrasound studies after 34 weeks' gestation, i.e. the gestational age at which FGR due to placental insufficiency is more likely to be apparent phenotypically and thus more readily detected by ultrasound.

Detecting FGR prior to delivery has several potential benefits. It prompts further investigation, e.g. UA Doppler, which has been shown to reduce the frequency of stillbirths by timely preterm delivery without increasing neonatal mortality[25]. It also alerts both the clinician and mother to the increased risk, enabling deliberations on the optimal timing of delivery. Depending on the severity of FGR, the risk of stillbirth may be increased 5- to 10-fold[9]. One randomized study reported no difference in perinatal mortality in fetuses with suspected late SGA delivered routinely at 37–38 weeks' gestation[26], although the study was underpowered for this outcome. A population-based study in the USA reported a significantly increased risk of stillbirth in pregnancies complicated by SGA when delivery was after the 37$^{th}$ week of pregnancy[27], and another in the UK[6], in which 92 218 normally-formed singletons (389 of them stillborn) were analyzed, found a reduced rate of stillbirth of 9.7 per 1000 births with antenatal FGR detection, compared with 19.8 when FGR was undetected. The impact of timely recognition and delivery of SGA fetuses is also underscored by the fact that, in this study, gestational age in instances of detected *vs* non-detected SGA status differed by only 10 days (270 *vs* 280 days) but resulted in a 50% lower incidence of stillbirths.

There is evidence that a declining growth rate in an SGA fetus during the third trimester imparts a higher risk of wasting at birth and of adverse perinatal outcome[28]. This is supported by findings of the DIGITAT study[26], in which there was a 2.5-fold increase in incidence of severe FGR with expectant management in SGA fetuses, compared to those delivered systematically after 36 weeks' gestation. It follows that the later the routine scan is performed, the more likely severe FGR will be detected. However, in most countries in which routine third-trimester scanning is advised, it is performed before 34 weeks' gestation[29]. Our findings support scanning later in the third trimester, at 37–38 weeks' gestation. Such a strategy does not seem to affect adversely perinatal outcome. On the other hand, further delay in routine scanning is controversial, given the evidence generated by large-population studies that the rate of stillbirths among severely growth-restricted fetuses markedly increases after this gestational age[27,30].

We acknowledge some limitations to our study. Primarily, our sample size was set *a priori* to prove differences in detection rates between scans at 32 and 36 weeks' gestation, which may be insufficient to assess differences in perinatal outcome, especially those events with low prevalence such as perinatal mortality or various neonatal complications. A study powered to detect differences in perinatal outcome would be more clinically relevant, as we took for granted in this study that detection of FGR is a desirable outcome in itself, which has only been proven in large observational studies[5,6].

It also seems plausible that a delayed diagnosis of early-onset FGR up to 36 weeks' gestation may result in poor neonatal outcome. However, we believe that most instances of early-onset FGR have been detected already by baseline risk factors and/or first- or second-trimester uterine artery Doppler[7], as well as by the strong association with PE. However, we would caution against generalization of our findings to high-risk pregnancies. Another criticism is that, in a setting in which fundal height measurement is performed more accurately, the differences between scans at 32 and 36 weeks' gestation in detecting FGR would be less pronounced. Our findings, however, reflect actual practice in which a policy of third-trimester scan is in place.

We also acknowledge that a strategy of serial scanning, combining the benefits of early and late third-trimester evaluation may further improve detection of FGR. However, Hedriana *et al.*[31] compared serial and one-time scanning in low-risk women at 28–42 weeks' gestation and found that, compared with a single evaluation, multiple ultrasound examinations did little to enhance prediction of birth weight.

In conclusion, our study shows that a strategy of routine third-trimester scanning at 36 as opposed to 32 weeks' gestation improves the detection rate of FGR.

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## SUPPORTING INFORMATION ON THE INTERNET

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

**Table S1** Baseline characteristics of all eligible candidates for a randomized controlled trial of women assigned to an ultrasound examination at either 32 or 36 weeks' gestation.

**Table S2** Baseline characteristics of 2586 pregnant women randomly assigned to undergo routine ultrasound examination at either 32 or 36 weeks' gestation according to follow-up status.

**Table S3** Perinatal outcomes in 2224 women randomly assigned to undergo routine ultrasound examination at either 32 or 36 weeks' gestation according to birth-weight percentile.

This article has been selected for Journal Club.

A slide presentation, prepared by Dr Aly Youssef, one of UOG's Editors for Trainees, is available online.

Chinese translation by Dr Yang Fang. Spanish translation by Dr Masami Yamamoto.