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Routine third-trimester ultrasound for the detection of small-for-gestational age in low-risk pregnancies (ROTTUS study): randomized controlled trial

S. Z. WANYONYI[1], J. ORWA[2], H. OZELLE[1], J. MARTINEZ[5], E. ATSALI[3], S. VINAYAK[4], M. TEMMERMAN[1] and F. FIGUERAS[5]

[1]*Department of Obstetrics and Gynaecology, Aga Khan University, Nairobi, Kenya;* [2]*Department of Population Health Sciences, Aga Khan University, Nairobi, Kenya;* [3]*School of Nursing and Midwifery, Aga Khan University, Nairobi, Kenya;* [4]*Department of Radiology and Imaging, Aga Khan University, Nairobi, Kenya;* [5]*Fetal Medicine Research Center, BCNatal, Barcelona Center for Maternal–Fetal and Neonatal Medicine, Hospital Clínic and Hospital Sant Joan de Déu, Institut Clínic de Ginecologia, Obstetrícia i Neonatologia, University of Barcelona, Barcelona, Spain*

KEYWORDS: fetal growth restriction; low-risk pregnancy; small-for-gestational age; third-trimester ultrasound

CONTRIBUTION

What are the novel findings of this work?
The use of a routine late third-trimester ultrasound-based protocol in well-selected low-risk pregnancies significantly increases the detection rate of small-for-gestational-age (SGA) neonates compared with a selective symphysis–fundus height measurement-based approach.

What are the clinical implications of this work?
Considering the association between stillbirth and undetected fetal growth abnormalities, especially in underserved areas, we recommend routine third-trimester ultrasound in low-risk pregnancies to detect SGA. This justifies the routine use of ultrasound for fetal growth monitoring between 36 + 0 and 37 + 6 weeks.

ABSTRACT

Objective *To compare the proportion of small-for-gestational-age (SGA) infants detected by routine third-trimester ultrasound* vs *those detected by selective ultrasound based on serial symphysis–fundus height (SFH) measurements (standard care) in low-risk pregnancy.*

Methods *This was an open-label randomized controlled trial conducted at a hospital in Kenya between May 2018 and February 2020. Low-risk pregnant women were randomly allocated (ratio of 1:1) to routine ultrasound for fetal growth assessment between 36 + 0 and 37 + 6 weeks' gestation (intervention group) or to standard care, which involved a selective growth scan on clinical suspicion of fetal growth abnormality based on serial SFH measurements (control group). During ultrasound examination, fetal growth was assessed by measurement of the abdominal circumference (AC), and AC < 10th centile was used to diagnose a SGA fetus. The main prespecified outcomes were the detection of neonatal SGA, defined as birth weight < 10th centile, and of severe neonatal SGA, defined as birth weight < 3rd centile. The predictive performance of routine third-trimester ultrasound and selective ultrasound based on serial SFH measurements was determined using receiver-operating-characteristics (ROC)-curve analysis.*

Results *Of 566 women assessed for eligibility, 508 (89.8%) were randomized, of whom 253 were allocated to the intervention group and 255 to the control group. Thirty-six babies in the intervention group and 26 in the control group had a birth weight < 10th centile. The detection rate of SGA infants by routine third-trimester ultrasound* vs *that by standard care was 52.8% (19/36)* vs *7.7% (2/26)* (P < *0.001) and the specificity was 95.5% (191/200) and 97.9% (191/195), respectively* (P = *0.08). The detection rate of severe SGA was 66.7% (12/18) by routine ultrasound* vs *8.3% (1/12) by selective ultrasound based on SFH measurements* (P < *0.001), with specificities of 91.7% (200/218) and 98.1% (205/209), respectively* (P = *0.006). The area under the ROC curve of routine third-trimester ultrasound in prediction of SGA was significantly greater than that of selective ultrasound based on SFH measurements (0.92 (95% CI, 0.87–0.96)* vs *0.68 (95% CI, 0.58–0.77);* P < *0.001).*

Correspondence to: Dr S. Z. Wanyonyi, Department of Obstetrics and Gynaecology, Aga Khan University, Nairobi, Kenya (e-mail: sikolia.wanyonyi@aku.edu)

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Conclusions *In low-risk pregnancy, routine ultrasound performed between 36 + 0 and 37 + 6 weeks is superior to selective ultrasound based on serial SFH measurements for the detection of true SGA, with high specificity.* © *2021 International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

Existing evidence does not support the use of routine third-trimester ultrasound in low-risk pregnant women with the sole aim of improving perinatal outcome[1–5]. However, this evidence comes from early studies, which arguably hold limited contemporary validity. As a result, there is large inconsistency between countries in their third-trimester ultrasound policy.

The rationale to offer routine fetal growth scans in the third trimester is driven by the observation that, even in low-risk populations, the risk of stillbirth is higher in babies that were not suspected prenatally to be growth restricted (hazard ratio, 5.0 (95% CI, 3.6–7.0)) compared with those identified as growth restricted during pregnancy (hazard ratio, 3.5 (95% CI, 1.9–6.4))[6]. Indeed, meta-analysis of the four large population-based series addressing the risk of stillbirth in non-suspected *vs* suspected small-for-gestational-age (SGA) fetuses shows that the risk is 2-fold higher in undetected SGA (risk ratio (RR), 2.1 (95% CI, 1.5–2.9)) (Table S1 and Figure S1)[6–9]. Furthermore, ultrasound remains the only reliable means of assessing fetal growth, considering the poor predictive ability of symphysis–fundus height (SFH) measurement and abdominal palpation[10,11]. The best observational evidence on the benefits of routine third-trimester ultrasound comes from a prospective cohort study that showed that, compared with selective clinically indicated ultrasound, routine scanning triples the detection rate of SGA infants[12]. A recent cluster randomized trial showed that, compared with clinically indicated ultrasound, routine third-trimester ultrasonography resulted in a modest improvement in the detection of SGA (19% *vs* 32%)[13]. However, there is no recent evidence from individual randomized trials.

We therefore sought to compare the proportion of SGA infants detected in low-risk pregnancies by routine third-trimester ultrasound *vs* those detected by the existing standard of care, in which ultrasound is offered only to pregnancies with suspicion of growth restriction based on serial SFH measurements.

PATIENTS AND METHODS

Study design

This open-label randomized controlled trial was conducted at the Aga Khan University Hospital, Nairobi, Kenya, between May 2018 and February 2020. The Aga Khan University Hospital is a private tertiary institution in which the majority of patients are of middle to high socioeconomic status. The patients are predominantly of African origin. During the study period, 5108 deliveries occurred, of which 4188 (82%) were of low-risk pregnancies.

In this study, low-risk pregnant women were randomly allocated to either a routine late third-trimester ultrasound scan for fetal growth assessment or the current local practice, which includes a growth scan only if the attending practitioner suspects a small fetus based on serial SFH measurements.

The trial was registered with the Pan African Clinical Trial Registry (PACTR201802003075138). The study and reporting of the results adhered to the CONSORT guidelines.

Eligibility criteria

At 32 + 0 to 35 + 6 weeks' gestation (when the distinction of low-risk from high-risk women was assumed to be certain), women were invited to participate in the study if they met the following criteria: (1) age ≥ 18 and < 40 years; (2) singleton pregnancy with no fetal malformation; (3) known last menstrual period with regular cycles or had dating ultrasound between 11 and 14 weeks; (4) low-risk result on first-trimester aneuploidy screening (combined test) and pregnancy associated plasma protein-A > 0.6 multiples of the median; (5) no relevant medical history and no need for long-term medication other than iron, folate, calcium, iodine or multivitamin supplements; (6) no smoking or consumption of recreational drugs or alcohol during pregnancy; (7) no more than two miscarriages in the three previous consecutive pregnancies; (8) no history of previous pregnancy affected by pre-eclampsia/eclampsia, HELLP syndrome or a related pregnancy-associated condition and no history of preterm birth or fetal growth restriction (FGR); (9) negative urinalysis during pregnancy; (10) no diagnosis or treatment for anemia 3 months before or after becoming pregnant; (11) not in an occupation with risk of exposure to chemicals or toxic substances, or very physically demanding activity; (12) normal glucose tolerance test in the current pregnancy; and (13) absence of any form of pregnancy-induced hypertension, suspected early-onset FGR, cholestasis or low-lying placenta/placenta previa. Patients unable to communicate in English or Swahili were excluded.

Sample-size calculation

The detection rate of SGA using the SFH measurement (local standard of care) was estimated to be 32%[11]. We hypothesized that using ultrasound would improve the detection rate to 45% (13% difference). This was based on the 14% improvement reported in a similar trial performed in Norway[14]. Using a superiority design with a power of 90% and 5% alpha-risk, we aimed to recruit at least 251 women to each arm of the study. We provided for a 10% attrition rate and therefore needed to recruit at least 552 women.

Randomization

After providing written informed consent, eligible women were randomly assigned to either the standard prenatal care protocol (controls) or the routine third-trimester ultrasound protocol (intervention). This was done in blocks of 10 using a sequence generated by a free online randomization service (www.randomisation.com). An allocation ratio of 1:1 was used to assign the women to the two study arms. The random allocation sequence was generated by the principal investigator (S.Z.W.) and the research assistant enrolled the participants and sequestered the randomization sequence. Owing to the nature of the intervention, it was not possible to blind the patients, attending professionals or researchers involved in this study.

Intervention and measurements

Women in the intervention arm were offered a growth scan between 36 + 0 and 37 + 6 weeks. The women in the control group were allowed to continue with the standard care (serial SFH measurements) and only had a growth scan if the attending obstetrician or midwife found it necessary owing to a difference between SFH (in cm) and gestational age (in completed weeks) greater than 2, or a stationary SFH between two consecutive visits of more than 2 weeks apart.

Abdominal circumference (AC) was measured, adhering to standard recommendations[15]. The AC plane had to be symmetrical, with the stomach bubble and portal sinus visible. The abdomen had to occupy more than half of the image with no kidneys visible. The calipers and the dotted lines were placed over the skin and the measurements obtained were transformed into centiles[15]. All ultrasound images were subjected to institutional quality-control checks.

Umbilical artery (UA), middle cerebral artery (MCA) and uterine artery pulsatility indices (PI) were obtained, adhering to the International Society of Ultrasound in Obstetrics and Gynecology guidelines on Doppler evaluation[16]. The cerebroplacental ratio was calculated as the ratio of MCA-PI to UA-PI. The single deepest vertical pocket was used to assess the amniotic fluid volume. These measurements were obtained to inform management decisions in cases with a suspicion of SGA. In accordance with protocol, women with a prenatal diagnosis of FGR were delivered at 37 + 0 weeks, and those meeting the criteria for SGA only were monitored weekly and delivered at 40 + 0 weeks[17]. This protocol was applied to all patients, regardless of the study-group allocation.

The birth-weight centiles for all the study participants were derived from the Fetal Medicine Foundation (FMF) birth-weight charts[18].

Study outcomes

The primary prespecified outcome measures were the detection rate of neonatal SGA, defined as birth weight $< 10^{th}$ centile, and of severe neonatal SGA, defined as birth weight $< 3^{rd}$ centile (according to the FMF birth-weight charts). Detection of SGA was defined as AC $< 10^{th}$ centile on the growth scan (both for routine and selective ultrasound), using Hadlock's formula[19].

Secondary prespecified outcomes included: emergency Cesarean section and operative vaginal delivery, 5-min Apgar score < 7, admission to the neonatal intensive care unit and perinatal death.

Ethical considerations

The study complied with the international ethical guidelines for biomedical research involving human subjects[20]. Ethical approval was obtained from the Aga Khan University research ethics committee (No. 2018/REC-41(v2)). Written informed consent was obtained from all women enrolled in the study.

All information collected for each patient was available for clinical use; however, privacy rules were followed with respect to use of the data for research purposes. As such, all individual data were anonymized to ensure confidentiality and data were stored, transmitted and analyzed anonymously by the research assistant.

Statistical analysis

Analysis was on an intention-to-treat basis. Comparison of variables between the two groups was performed using Student's *t*-test, the χ^2 test or Fisher's exact test, as appropriate. The predictive performance of the two methods (routine third-trimester ultrasound and selective ultrasound based on SFH measurements) was determined using receiver-operating-characteristics (ROC)-curve analysis. Total and partial (between 0% and 15% of false-positive rate) paired areas under the ROC curves (AUC) were compared using the DeLong method with binomial smoothing[21]. For ROC curve analysis, the AC measurements of women in the control group who did not undergo a growth scan were imputed using the sex-specific median, as done in previous studies[12]. Analysis was performed using STATA version 13.0 (StataCorp., College Station, TX, USA) and R3.5.1 (pROC package; R Foundation, Vienna, Austria); $P < 0.05$ was considered statistically significant.

RESULTS

Of 566 women assessed for eligibility, 508 were randomized, of whom 253 were allocated to the intervention group and 255 to the control group. Of these, 51 women were lost to follow-up, leaving 457 (236 in the intervention group and 221 in the control group) for the analysis (Figure 1). Table 1 shows the baseline characteristics of the women included in the study. The characteristics of the women who were lost to follow-up are presented in Table S2. There was no significant difference with respect to baseline characteristics between the included patients and those lost to follow-up.

In the control group, 44 (19.9%) women underwent a growth scan for clinical suspicion of SGA. On average, this scan was performed at 35.3 ± 1.5 weeks. In the intervention group, all but four women underwent the routine ultrasound scan, on average at 36.4 ± 0.8 weeks.

A total of 62 (13.6%) babies had a birth weight < 10th centile, comprising 36 in the intervention group and 26 in the control group. Of the 36 SGA babies in the intervention group, 19 were detected prenatally by an AC < 10th centile on ultrasound (detection rate of 52.8%) whereas only two of the 26 SGA babies in the control group were detected prenatally (detection rate of 7.7%); the detection rates were statistically significantly different between the two groups ($P < 0.001$). The specificity of routine third-trimester ultrasound for the detection of SGA was 95.5% (191/200) and that of the standard care was 97.9% (191/195) ($P = 0.08$).

A total of 30 (6.6%) babies had a birth weight < 3rd centile, including 18 in the intervention group and 12 in the control group. Of the 18 babies with severe SGA in the intervention group, 12 were prenatally detected by an AC < 10th centile on ultrasound (detection rate of 66.7%) whereas only one of the 12 newborns with severe SGA in the control group was identified prenatally (detection

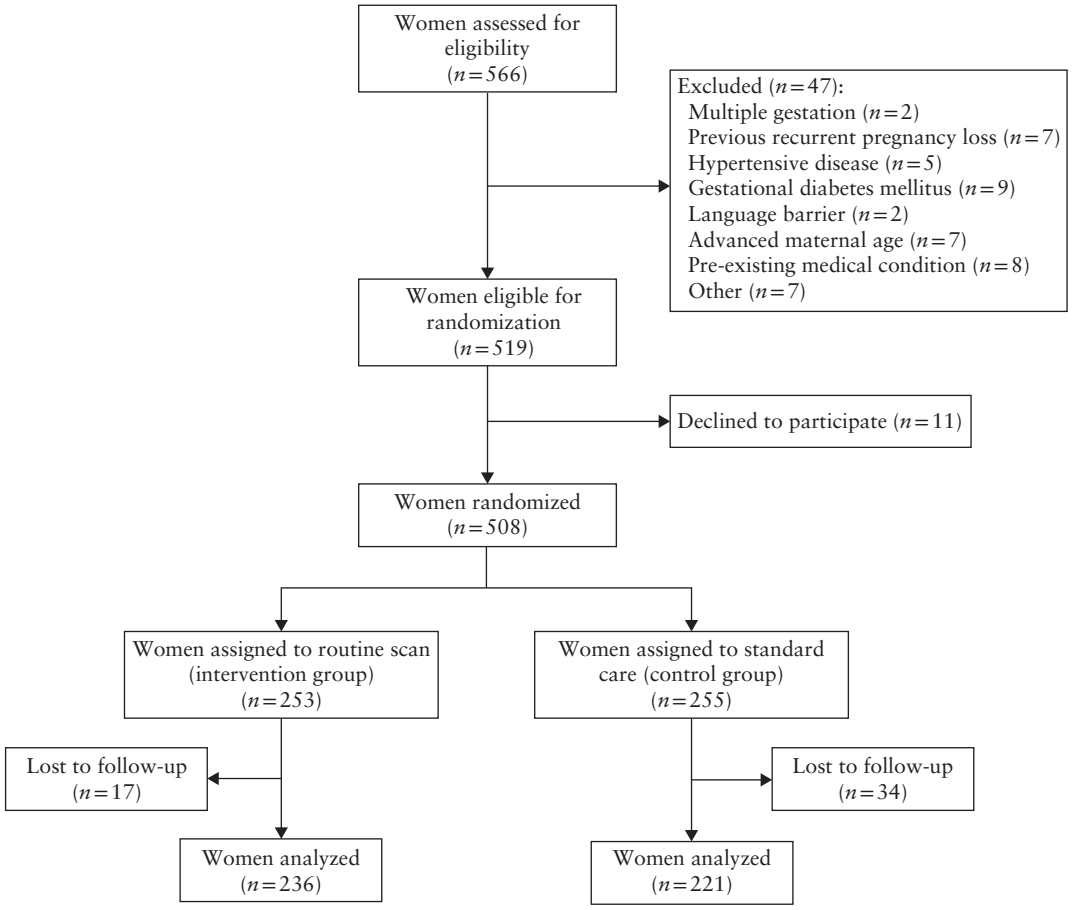

Figure 1 Flowchart showing inclusion in the trial of low-risk pregnancies and their randomization to routine ultrasound for fetal growth assessment (intervention group) or standard care involving selective fetal growth scans based on serial symphysis–fundus height measurements (control group) in the third trimester.

Table 1 Baseline characteristics of 457 low-risk pregnant women included in study, overall and according to randomization to routine ultrasound for fetal growth (intervention group) or selective fetal growth scan based on serial symphysis–fundus height measurements (control group) in the third trimester

Characteristic	*Overall* (n = *457*)	*Intervention group* (n = *236*)	*Control group* (n = *221*)	P*
Maternal age (years)	31.3 ± 4.3	31.7 ± 4.2	31.0 ± 4.3	0.37
Body mass index (kg/m^2)	27.6 ± 3.4	26.8 ± 4.1	28.3 ± 1.1	0.14
Parity				0.007
Nulliparous	159 (34.8)	86 (36.4)	73 (33.0)	
Primiparous	148 (32.4)	74 (31.4)	74 (33.5)	
Multiparous	150 (32.8)	76 (32.2)	74 (33.5)	
Gestational age at scan (weeks)	36.1 ± 2.0	36.4 ± 0.8	35.3 ± 1.5	< 0.001

Data are given as mean ± SD or *n* (%). *Comparison between intervention and control groups.

rate of 8.3%); the detection rates were statistically significantly different between the two groups ($P < 0.001$). The specificity of routine third-trimester ultrasound for the detection of severe SGA was 91.7% (200/218) and that of selective ultrasound based on SFH measurements was 98.1% (205/209) ($P = 0.006$).

The number of women needed to undergo a routine third-trimester ultrasound scan to detect one additional case of SGA was 14 (95% CI, 9.1–29.8) and the number needed to detect one additional case of severe SGA was 21 (95% CI, 13–62).

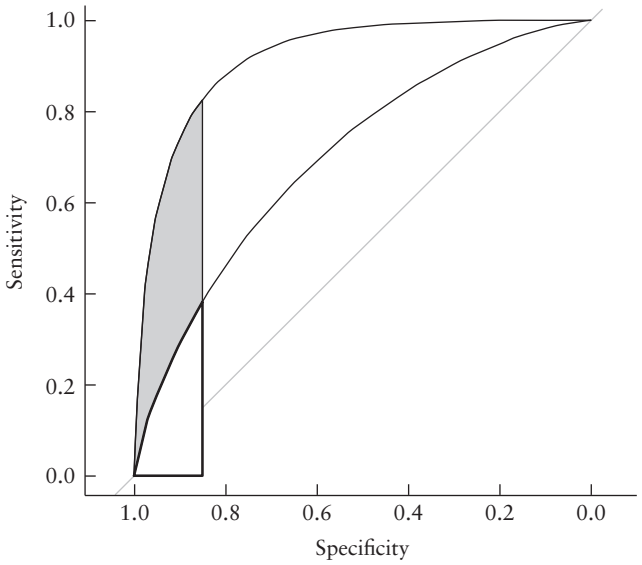

Figure 2 Receiver-operating-characteristics curves and partial areas under the curve (0–15% of false-positive rate) for prediction of small-for-gestational-age neonate by routine third-trimester ultrasound assessment of fetal growth (gray) and by selective fetal growth scan based on symphysis–fundus height measurements (unshaded).

Figure 2 shows the total and partial AUCs for the prediction of SGA by routine third-trimester ultrasound and standard care. The AUC of routine third-trimester ultrasound was significantly higher than that of selective ultrasound based on SFH measurements (0.92 (95% CI, 0.87–0.96) *vs* 0.68 (95% CI, 0.58–0.77); $P < 0.001$). The partial AUC corresponding to a false-positive rate of $\leq 15\%$ was also significantly higher for the routine ultrasound assessment of fetal growth compared with the selective SFH-based approach (0.13 (95% CI, 0.081–0.179) *vs* 0.03 (95% CI, 0.004–0.056); $P < 0.001$).

Table 2 details the perinatal outcomes by study group. The rate of adverse outcomes was similar between the intervention and control groups.

DISCUSSION

In this study, routine third-trimester ultrasound performed between 36 + 0 and 37 + 6 weeks in low-risk pregnant women significantly improved the detection rate of both SGA and severe-SGA babies when compared with a strategy of selective ultrasound based on serial SFH measurements.

The findings of our randomized trial are consistent with those of Sovio *et al.*[12], who found that, in nulliparous women, universal third-trimester growth ultrasound compared with selective screening tripled the detection rate of SGA fetuses, from 20% (95% CI, 15–24%) to 57% (95% CI, 51–62%). Likewise, a Norwegian trial reported that routine third-trimester ultrasound at 33 weeks improved the detection rate of SGA fetuses from 46% to 80% and increased even more the detection rate of large-for-gestational-age fetuses, from

Table 2 Perinatal outcomes of 457 low-risk pregnancies, overall and according to randomization to routine ultrasound for fetal growth (intervention group) or selective fetal growth scan based on serial symphysis–fundus height measurements (control group) in the third trimester

Outcome	*Overall (n = 457)*	*Intervention group (n = 236)*	*Control group (n = 221)*	*Relative risk (95% CI)*	P
GA at delivery (weeks)	39.6 ± 1.2	39.6 ± 1.2	39.7 ± 1.1	—	0.198
GA at delivery < 37 weeks	7 (1.5)	4 (1.7)	3 (1.4)	1.25 (0.25–5.51)	0.77
Mode of delivery					0.50
Spontaneous vaginal	264 (57.8)	129 (54.7)	135 (61.1)	0.89 (0.77–1.05)	
Assisted vaginal	15 (3.3)	8 (3.4)	7 (3.2)	1.07 (0.40–2.90)	
Emergency CS	69 (15.1)	37 (15.7)	32 (14.5)	1.08 (0.70–1.67)	
Non-emergency CS	109 (23.9)	62 (26.3)	47 (21.3)	1.24 (0.89–1.72)	
Onset of labor*					0.127
Spontaneous	257/450 (57.1)	122/233 (52.4)	135/217 (62.2)	0.85 (0.72–1.00)	
Induction of labor	84/450 (18.7)	49/233 (21.0)	35/217 (16.1)	1.31 (0.88–1.94)	
Elective CS	109/450 (24.2)	62/233 (26.6)	47/217 (21.7)	1.24 (0.89–1.72)	
Birth-weight centile					0.169
$< 10^{th}$	62 (13.6)	36 (15.3)	26 (11.8)	1.30 (0.81–2.07)	
10^{th} to 90^{th}	365 (79.9)	184 (78.0)	182 (82.4)	0.95 (0.86–1.04)	
$> 90^{th}$	30 (6.6)	16 (6.8)	13 (5.9)	1.16 (0.57–2.34)	
5-min Apgar score < 7	5 (1.1)	3 (1.3)	2 (0.9)	1.42 (0.24–8.33)	0.999‡
Admission to NICU	12 (2.6)	9 (3.8)	3 (1.4)	2.84 (0.77–10.2)	0.176‡
Neonatal death†	2/451 (0.4)	1/233 (0.4)	1/218 (0.5)	0.94 (0.06–14.9)	0.999‡

Data are given as mean ± SD, *n* (%) or *n*/*N* (%). *Data on onset of labor missing for seven participants. †Data on status at discharge missing for six neonates. ‡Fisher's exact test. CS, Cesarean section; GA, gestational age; NICU, neonatal intensive care unit.

36% to 91%[14]. However, these observational studies differ from ours since women were recruited as early as 18 weeks' gestation in a non-selected population. A nationwide cluster randomized trial conducted in 60 primary care midwifery practices in The Netherlands showed that routine third-trimester ultrasound compared with medically indicated ultrasonography based on serial SFH measurements increased the detection rate of SGA newborns (based on fetal AC $< 10^{th}$ centile and slow fetal abdominal growth) from 19% to 32%, but at the cost of increasing the false-positive rate from 3% to 10%[13]. In this study, women were recruited after the second-trimester anomaly scan. Recruitment in early to mid-pregnancy is a drawback of these studies, since it is well known that the risk profile in pregnancy can change over time. There are conditions that may develop later as the pregnancy advances that could affect fetal growth, such as pre-eclampsia, gestational diabetes, anemia or other external factors that interfere with the accelerative phase of fetal growth. In our study we included only women confirmed to be low risk at 32–35 week' gestation. It could be argued that this approach ensures a higher degree of external validity, since the decision to perform a routine or medically indicated third-trimester ultrasound scan in a real setting is contingent on the later development of conditions not present in the second trimester.

In a related study, Roma *et al.*[22] reported a higher detection rate of FGR when routine ultrasound for the assessment of fetal growth was performed at 36 weeks compared with at 32 weeks (38.8% *vs* 22.5%), with a positive likelihood ratio of 6.1 and negative likelihood ratio of 0.65. These findings informed our choice of 36–37 weeks as the optimum gestational-age window in which to perform growth ultrasound in low-risk pregnancies. Additional recent studies support the superiority of universal routine third-trimester ultrasound in detecting SGA fetuses, especially if done near term and combined with physiological parameters such as UA and MCA Doppler studies[23–25].

In our trial, the gestational age at delivery was similar in the two arms, with no significant difference in the proportion of women who delivered before 37 weeks' gestation. However, more women underwent induction of labor in the intervention arm than in the control arm (21% *vs* 16%; RR, 1.31 (95% CI, 0.88–1.94)). Even though this difference did not reach statistical significance, it could have been the result of the higher detection rate of SGA babies in the intervention group, which invariably led to higher rates of intervention, since the protocol used in this study recommends delivery after 37 weeks and by 40 weeks for severe SGA and SGA, respectively[17].

Despite our positive findings, it should be borne in mind that the use of fetal biometry alone may not be adequately sensitive for the prediction and identification of babies with a birth weight $< 10^{th}$ centile. It has been shown that the inclusion of maternal characteristics and biochemical markers alongside biophysical measurements may improve the accuracy of fetal biometry[26–31]. The third-trimester ultrasound scan, however, had in our series reasonably good specificity in both arms of the study (for SGA, 95.5% and 97.9% in the intervention and control groups, respectively; for severe SGA, 91.7% and 98.1%, respectively). Therefore, the finding of normal fetal growth on late third-trimester ultrasound is reassuring. However, we should caution that an appropriate-for-gestational-age fetus alone does not translate into 'zero risk' of term stillbirth, as there are other biological factors that could result in a poor outcome even against a background of normal growth.

The main strength of this study is the inclusion of a population in which routine third-trimester ultrasonography is not widespread, which allowed effective randomization of the study participants. It is noteworthy that the risk of contamination bias (by which women in the control group would be more likely to have an ultrasound scan) was unlikely in our study, since only 20% of the women had an ultrasound examination. Unlike previous studies, we used standard consensus definitions of SGA and severe SGA to define our outcomes and incorporated measures of functionality such as Doppler studies, as opposed to biometry alone, to inform management.

Limitations of our study include that it was performed in a single private tertiary center and included a population that was comprehensively screened and correctly identified as truly low risk. This may be difficult to achieve in routine clinical practice in most underserved regions and should be borne in mind when implementing our findings in low- and middle-income settings. Moreover, although our study was not aimed at detecting, nor powered to detect, differences in perinatal outcomes, we acknowledge that a Hawthorne effect (by which the included pregnancies may have been over-controlled) may have biased our finding of lack of differences in perinatal outcomes between the two groups.

In conclusion, in low-risk pregnancy, a routine late third-trimester ultrasound-based protocol significantly increases the detection of SGA fetuses compared with a selective SFH measurement-based approach. Considering the association between stillbirth and undetected fetal growth abnormalities, especially in underserved areas, the routine use of ultrasound for fetal growth monitoring between 36 + 0 and 37 + 6 weeks should be considered to inform prenatal management. The effect of this approach on perinatal outcomes needs to be further explored.

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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 Meta-analysis of adjusted measure of association of undetected *vs* detected small-for-gestational age with stillbirth

Table S2 Baseline characteristics of the 51 women who were lost to follow-up (LFU), overall and according to randomization group

Figure S1 Forest plot showing adjusted measure of association of undetected *vs* detected small-for-gestational age with stillbirth.

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Ecografía rutinaria del tercer trimestre para la detección de embarazos pequeños para la edad gestacional de bajo riesgo (estudio ROTTUS): un ensayo controlado aleatorizado

RESUMEN

Objetivo Comparar la proporción de niños pequeños para la edad gestacional (PEG) detectados durante la ecografía rutinaria del tercer trimestre frente a los que se detectaron mediante una ecografía selectiva basada en medidas en serie de la altura uterina (SFH, por sus siglas en inglés), es decir, la atención estándar, en embarazos de bajo riesgo.

Métodos Este estudio fue un ensayo controlado aleatorizado en abierto realizado en un hospital de Kenia entre mayo de 2018 y febrero de 2020. Las mujeres embarazadas de bajo riesgo fueron asignadas aleatoriamente (proporción de 1:1) a una ecografía de rutina para la evaluación del crecimiento fetal entre las 36+0 y las 37+6 semanas de gestación (grupo de intervención) o a la atención estándar, que consistía en una exploración selectiva del crecimiento cuando había sospecha clínica de una anomalía del crecimiento fetal en función de mediciones en serie de la SFH (grupo de control). Durante el examen ecográfico, se evaluó el crecimiento fetal por medio de la medición de la circunferencia abdominal (CA), mientras que la CA <10º percentil se utilizó como valor para diagnosticar un feto como PEG. Los principales resultados previstos por adelantado fueron la detección de la condición de PEG neonatal, definida como peso al nacer <10º percentil, y de la PEG neonatal grave, definida como peso al nacer <3er percentil. La eficacia predictiva de la ecografía rutinaria del tercer trimestre y de la ecografía selectiva basada en mediciones en serie de la SFH se determinó mediante el análisis de las características operativas del receptor (ROC, por sus siglas en inglés).

Resultados De las 566 mujeres evaluadas para la elegibilidad, 508 (89,8%) fueron aleatorizadas, de las cuales 253 fueron asignadas al grupo de intervención y 255 al grupo de control. El peso al nacer de 36 bebés del grupo de intervención y 26 del grupo de control fue <10º percentil. La tasa de detección de bebés PEG mediante ecografía rutinaria en el tercer trimestre frente a la de la atención estándar fue del 52,8% (19/36) frente al 7,7% (2/26) (P < 0,001) y la especificidad fue del 95,5% (191/200) y del 97,9% (191/195), respectivamente (P = 0,08). La tasa de detección de la condición de PEG grave mediante ecografía de rutina fue del 66,7% (12/18) frente al 8,3% (1/12) de la ecografía selectiva basada en las mediciones de la SFH (P < 0,001), con especificidades del 91,7% (200/218) y del 98,1% (205/209), respectivamente (P = 0,006). El área bajo la curva ROC de la ecografía rutinaria del tercer trimestre en la predicción del PEG fue significativamente mayor que la de la ecografía selectiva basada en las mediciones de la SFH (0,92 (IC 95%, 0,87–0,96) frente a 0,68 (IC 95%, 0,58–0,77) P<0,001).

Conclusiones En los embarazos de bajo riesgo, la ecografía de rutina realizada entre las semanas 36+0 y 37+6 es mejor que la ecografía selectiva basada en mediciones en serie de la SFH para la detección de la condición de PEG verdadera, con una alta especificidad.

晚期妊娠常规超声探测低风险怀孕中的小于胎龄儿（ROTTUS 研究）：随机对照试验

摘要

目的 对比晚期妊娠常规超声检查和因耻骨联合到宫底距离（SFH）测量（标准护理）而选中进行超声检查探测低风险怀孕中小于胎龄儿的比例。

方法 这项开放性随机对照试验于2018年5月至2020年2月之间在肯尼亚的一家医院内进行。该试验将低风险孕妇（按1：1的比例）随机分配到妊娠期36周至37+6周之间的常规超声评估胎儿生长发育（干预组）或标准护理，即涉及因耻骨联合到宫底距离（SFH）测量引发临床疑似胎儿生长异常而选中进行生长超声检查（控制组）。超声检查期间，胎儿生长发育通过测量异常腹围（AC）来评估，习惯上以AC小于第十百分位数来诊断小于胎龄儿。主要的预设结果将发现小于胎龄（SGA）新生儿定义为出生体重小于第十百分位数，而将严重小于胎龄新生儿定义为出生体重小于第三百分位数。晚期妊娠常规超声和由耻骨联合到宫底距离（SFH）测量而选中进行超声检查的预测表现，通过采用受试者操作特性（ROC）曲线分析来决定。

结果 在566名符合条件的孕妇中，对508名（89.8%）进行随机分配，其中253名被分配到干预组，255名被分配到控制组。干预组中的36个婴儿和控制组中的26个婴儿的出生体重小于第十百分位数。经晚期妊娠常规超声和标准护理对小于胎龄儿的检出率分别为52.8%（19/36）和7.7%（2/26）（P<0.001），特异性分别为95.5%（191/200）和97.9%（191/195）（P=0.08）。经晚期妊娠常规超声检测严重SGA的检出率为66.7%（12/18），而由SFH测量（P<0.001）而选中超声检测的检出率为8.3%（1/12），特异性分别为91.7%（200/218）和98.1%（205/209）（P=0.006）。由晚期妊娠常规超声预测SGA的ROC曲线下的区域远大于因SFH测量而选中超声检测所预测的（分别为0.92（95% CI, 0.87 – 0.96)和0.68（95% CI, 0.58 – 0.77）；P<0.001）。

结论 在低风险怀孕中，要检测出真正的SGA并具有高特异性，对妊娠期36周至37+6周之间进行常规超声优于因SFH测量而选中的超声检查。

