Original Research

A Comparison of Methods for the Diagnosis of Fetal Growth Restriction Between the Royal College of Obstetricians and Gynaecologists and the American College of Obstetricians and Gynecologists

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OBJECTIVE: The Royal College of Obstetricians and Gynaecologists (RCOG) defines fetal growth restriction as ultrasound-estimated fetal weight less than the 10th percentile or abdominal circumference less than the 10th percentile; the American College of Obstetricians and Gynecologists (ACOG) defines fetal growth restriction as estimated fetal weight less than the 10th percentile alone. We compared each method's ability to predict small for gestational age (SGA) at birth.

METHODS: For this retrospective study of diagnostic accuracy, we reviewed deliveries at the University of New Mexico Hospital from January 1, 2013, to March 31, 2017. We included mothers with singleton, well-dated pregnancies and nonanomalous fetuses undergoing indicated fetal growth restriction surveillance with an ultrasound-estimated fetal weight within 30 days of delivery. Estimated fetal weights and percentiles were calculated using the Hadlock intrauterine growth curve. Small for gestational age was defined as birth weight less than the 10th percentile based on a recent, sex-specific curve. We calculated the area under the curve, sensitivity, specificity, and positive and negative likelihood ratios for various approaches using abdominal circumference and estimated fetal weight to diagnose fetal growth restriction, including the definitions endorsed by ACOG and RCOG.

RESULTS: We included 1,704 pregnancies with a mean ultrasonography-to-delivery interval of 14.0 days (±8.6). There were 235 SGA neonates (13.8%). The rate of fetal growth restriction was 13.6% when using ACOG's criteria and 16.9% according to RCOG's criteria (P=.007). The area under the curve of RCOG's diagnostic approach was 0.78 (95% CI 0.76–0.80), which was higher than ACOG's (0.76, 95% CI 0.74–0.78, P=.01). Sensitivities and specificities of the various methods were similar. Adopting estimated fetal weight or abdominal circumference less than the 10th percentile instead of estimated fetal weight alone to predict SGA at birth would correctly identify one additional case of SGA for each 14 patients assessed.

CONCLUSION: The diagnostic approach endorsed by RCOG is a marginally better predictor of SGA at birth compared with the method endorsed by ACOG. Future research should consider the potential benefits and harms of the different methods in different populations.

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Small for gestational age (SGA), usually defined as birth weight less than the 10th percentile, is associated with adverse neonatal outcomes and cardiovascular and metabolic diseases in adulthood.[1,2] The intrauterine diagnosis of fetal growth restriction is

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used to predict SGA at birth and is associated with intrauterine fetal death. The goal of screening for fetal growth restriction is to identify the fetus at increased risk for intrauterine demise to institute antenatal surveillance with the goal of decreasing perinatal death.[3] The standard estimated fetal weight is calculated using Hadlock formula, which incorporates the fetal biparietal diameter, head circumference, abdominal circumference, and femur length.[4,5]

The American College of Obstetricians and Gynecologists' (ACOG) Practice Bulletin on fetal growth restriction supports the use of estimated fetal weight less than the 10th percentile to diagnose fetal growth restriction, considering fetuses with an abdominal circumference less than the 10th percentile but an estimated fetal weight greater than the 10th percentile as normal.[4] In contrast, the Royal College of Obstetricians and Gynaecologists' (RCOG) criteria include either estimated fetal weight less than the 10th percentile or abdominal circumference less than the 10th percentile, considering a fetus with a small abdominal circumference but a normal estimated fetal weight to have fetal growth restriction.[6] The diagnostic accuracy of a small abdominal circumference in the setting of a normal estimated fetal weight has been tested only in limited populations, and the significance of this finding remains unclear.[7–9] Therefore, we set out to compare the diagnostic accuracies of the approaches recommended by ACOG and RCOG to predict SGA at birth with a secondary aim of testing the intermediate approach of estimated fetal weight less than the 10th percentile or abdominal circumference less than the fifth percentile. We hypothesized that RCOG's diagnostic approach (estimated fetal weight or abdominal circumference less than the 10th percentile) would be comparable with or better than ACOG's (estimated fetal weight less than the 10th percentile alone) to predict SGA at birth.

MATERIALS AND METHODS

For this study of diagnostic accuracy, we obtained approval by our institutional review board to retrospectively review all consecutive deliveries at our institution occurring between January 1, 2013, and March 31, 2017. We included neonates who both had an ultrasonographic estimated fetal weight performed within 30 days before delivery and were delivered at our institution. Exclusion criteria were multiple gestations, fetal hydrops, intrauterine fetal demise, inconsistent gestational age documentation, missing ultrasound or birth weight data, and congenital anomalies not allowing for accurate assessment of the biparietal diameter, head circumference, abdominal circumference, or femur length (eg, hydrocephalus or severe ventriculomegaly, holoprosencephaly, bony cranial abnormality, abdominal wall defect, limb–body wall anomaly, skeletal dysplasia, and caudal regression syndrome). Because neither ACOG nor RCOG specifies a gestational age range at which their criteria are valid, ultrasound assessments were not limited to specific gestational age ranges as long as they occurred within 30 days of delivery.

At our institution, third-trimester ultrasonography is performed only when indicated and fetal growth restriction is diagnosed using ACOG's criteria. Fetuses with a small abdominal circumference but normal estimated fetal weight do not undergo additional surveillance unless otherwise indicated. Starting in 2015, gestational age was determined using criteria recommended by ACOG.[10] Before 2015, gestational age was determined by last menstrual period as long as the earliest and best ultrasonographic gestational age estimate was within 8% of the gestational age at the time of the examination. When the ultrasonography–last menstrual period discrepancy was greater than 8% of the gestational age, the due date was determined by the ultrasonogram. Estimated fetal weights were calculated and estimated fetal weight or abdominal circumference percentiles assigned using the Hadlock estimated fetal weight and z score formulas, which are not sex-specific.[11,12] All values were calculated using the raw measurements to avoid error from varying use of different formulas or growth curves. Calculation of estimated fetal weights, estimated fetal weight and birth weight percentiles, and application of each diagnostic method occurred retrospectively and so were not available to clinicians.

Birth weight percentiles were assigned using recent, sex-specific curves based on a nationwide cohort of births in the United States that are not specific to race or ethnicity.[13] We chose this birth weight reference standard because it is comprised of a large, updated sample of nationally representative births. These birth weight percentile tables included data for completed weeks of gestation only, so to determine the percentiles using gestational weeks+days, cubic splines were used to interpolate the whole-week LMS (lambda, the power transformation; mu, the median; sigma, the coefficient of variation) curves to derive LMS data points for each gestational day. Cubic splines are preferred over linear interpolation because they generate a smooth curve that passes through all provided data points. We then used the LMS z score formula ($z = [\{X/M\}^{L} - 1]/LS$, where X is birth weight in kilograms) to calculate percentiles specific to the gestational day.[14] Small for gestational age was defined as birth weight less than the 10th percentile.

To characterize the overall test performance of the diagnostic approaches endorsed by ACOG (estimated fetal weight less than the 10th percentile) and RCOG (estimated fetal weight or abdominal circumference less than the 10th percentile) to predict SGA at birth, we plotted the receiver operator characteristics (true-positive rates plotted as a function of false-positive rates) and calculated the area under the curve (AUC) and positive and negative likelihood ratios with 95% CIs for each approach. Although receiver operator curves are normally generated by plotting the characteristics of multiple thresholds of a single continuous parameter, the methods being compared in our analysis are comprised of multiple parameters and so could only be plotted as a single point. Therefore, the "curves" for each method were generated by drawing straight lines from (0,0) to each method's plotted point to (1,1) with the AUC being the area under the lines. We also calculated the sensitivity and specificity with 95% CIs. As part of the secondary objective, the following diagnostic approaches were analyzed and compared against both ACOG's and RCOG's approaches: estimated fetal weight less than the 10th percentile or abdominal circumference less than the fifth percentile, estimated fetal weight and abdominal circumference less than the 10th percentile, abdominal circumference less than the 10th percentile interpreted independently of estimated fetal weight, and abdominal circumference less than the fifth percentile independent of estimated fetal weight.

Lastly, we compared the rates of the following neonatal outcomes among neonates prenatally predicted to be SGA by ACOG and RCOG: preterm birth at less than 37 weeks of gestation, neonatal intensive care unit admission, neonatal intensive care unit stay greater than 48 hours, mechanical ventilation for greater than 24 hours, necrotizing enterocolitis, death before discharge, and need for supplemental oxygen, bag–mask ventilation, endotracheal intubation, or chest compressions in the delivery room. Statistical significance was inferred by χ^2 for dichotomous variables and paired t test or analysis of variance with appropriate post hoc tests for continuous variables. Areas under the curve were compared using the DeLong method and NCSS 11.[15] We were unable to find an expected difference between methods in the literature to inform a power analysis and so did not calculate a prespecified sample size.

RESULTS

We identified 1,704 neonates that underwent an ultrasonographic estimated fetal weight within 30 days of delivery. In our sample, the mean interval from ultrasonography to delivery was 14.0 days (±8.6), and the rate of SGA at birth was 13.8% (n=235). Demographic characteristics are summarized in Table 1. The racial makeup of our study population was different from that of the cohort in the birth weight norms. Our sample had a higher proportion of Hispanic women (49.5% vs 24.4%) and lower proportions of non-Hispanic white women (23.8% vs 50.6%) and black women (1.9% vs 15.7%, $P<.01$ for all comparisons). The most common indications for an ultrasound examination were "size not equal to dates" (n=596 [35.0%]) and "maternal condition" (n=589 [34.6%]; Table 2).

To predict SGA at birth, the approach recommended by RCOG (estimated fetal weight greater

Table 1. Study Population Demographic Characteristics (N=1,704)

Characteristic	Value
Maternal age (y)	28.8±6.5
Ethnicity	
White	406 (23.8)
Hispanic	844 (49.5)
Native American	184 (10.8)
Black	32 (1.9)
Asian	41 (2.4)
Other or missing	195 (11.4)
Parity	
Nulliparous	461 (27.1)
Parous	1,243 (72.9)
Grand multiparous	56 (3.3)
Diabetes	360 (21.1)
Pregestational DM	81 (4.8)
Gestational DM	279 (16.4)
Hypertensive disorder	293 (17.2)
Chronic HTN	62 (3.6)
Preeclampsia	223 (13.1)
HELLP	6 (0.4)
Eclampsia	2 (0.1)
Tobacco use	239 (14.0)
Illicit drug use	275 (16.1)
Heroin	69 (4.0)
Amphetamine	60 (3.5)
Marijuana	63 (3.7)
Cocaine	13 (0.8)
Opioid replacement	149 (8.7)
Gestational age at delivery (wk)	37.7±2.8
US–delivery interval (d)	14.0±8.6
Mean birth weight (g)	2,960±865
Female fetal sex	824 (48.4)
Preterm birth	386 (22.7)
SGA	235 (13.8)

DM, diabetes mellitus; HTN, hypertension; HELLP, hemolysis, elevated liver enzymes, and low platelet count; US, ultrasonography; SGA, small for gestational age.
Data are mean±SD or n (%).

Table 2. Indications for Ultrasound Examination (N=1,704)

Indication	n (%)
Size not equal to dates	596 (35.0)
Maternal condition*	589 (34.6)
Fetal evaluation	249 (14.6)
Obstetric complication	177 (10.4)
Unclear	93 (5.5)

* Maternal conditions include advanced maternal age, chronic disease, smoking, diabetes, drug use, uterine abnormality, maternal infection, poor prenatal care, poor weight gain, poor obstetric history, prior cesarean delivery, or teen pregnancy.

than the 10th percentile or abdominal circumference less than the 10th percentile) yielded an AUC of 0.78 (95% CI 0.76–0.80), demonstrating better overall performance than the ACOG approach (AUC 0.76, 95% CI 0.74–0.78). This difference was statistically significant (P=.01). There was no difference between the two methods for any of the remaining parameters (as demonstrated by overlapping confidence intervals; Table 3). The receiver operator characteristics of each method are plotted in Figure 1, demonstrating the performance of estimated fetal weight less than the 10th percentile, estimated fetal weight or abdominal circumference less than the 10th percentile, and estimated fetal weight less than the 10th percentile or abdominal circumference less than the fifth percentiles.

Of the 235 SGA neonates, 80 (35%) were not identified by either method before delivery. The diagnostic criteria endorsed by RCOG led to 16.9% (95% CI 15.2–18.8%, n=289) of the cohort being diagnosed with fetal growth restriction compared with 13.6% (95% CI 12.0–15.3%, n=232) when using ACOG's criteria. This difference was statistically significant (P=.007). Although fetuses prenatally diagnosed with fetal growth restriction by ACOG's or RCOG's criteria had higher rates of neonatal morbidities than normally grown fetuses (Table 4), the fetuses identified as having fetal growth restriction by RCOG's but not ACOG's criteria (those with abdominal circumference less than the 10th percentile and estimated fetal weight greater than the 10th percentile) did not have different outcomes than fetuses with normal growth, although our study was not powered for this comparison. When analyzed separately, the additional cases of SGA identified by RCOG's criteria also did not have higher rates of adverse neonatal outcomes than those already identified by ACOG's criteria. When the analysis was performed excluding all anomalous fetuses rather than just those described in the exclusion criteria previously, the results were unchanged.

The alternate method of estimated fetal weight less than the 10th percentile or abdominal circumference less than the fifth percentile had better performance than ACOG's but was not different from

Table 3. Test Characteristics of Diagnostic Approaches for Fetal Growth Restriction

Diagnostic Approach	AUC (95% CI)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	+LR (95% CI)	−LR (95% CI)
ACOG (EFW less than 10th percentile)	0.76 (0.74–0.78)	58.7 (52.1–65.1)	93.6 (92.2–94.8)	9.2 (7.3–11.5)	0.44 (0.38–0.51)
RCOG (EFW less than 10th percentile or AC less than 10th percentile)	0.78* (0.76–0.80)	66.0 (59.5–72.0)	90.9 (89.3–92.3)	7.2 (6.0–8.7)	0.37 (0.31–0.45)
EFW less than 10th percentile or AC less than 5th percentile	0.77† (0.75–0.79)	62.1 (55.6–68.4)	92.7 (91.3–94.0)	8.5 (6.9–10.5)	0.41 (0.35–0.48)
EFW less than 10th percentile and AC less than 10th percentile	0.73‡ (0.71–0.75)	51.5 (44.9–58.0)	94.8 (93.6–95.9)	10.0 (7.7–12.8)	0.51 (0.45–0.58)
AC less than 10th percentile	0.75§ (0.73–0.77)	58.7 (52.1–65.1)	92.1 (90.6–93.4)	7.44 (6.1–9.1)	0.45 (0.38–0.52)
AC less than 5th percentile	0.71‡ (0.69–0.73)	46.8 (40.3–53.4)	95.4 (94.4–96.5)	10.3 (7.8–13.5)	0.56 (0.49–0.63)
AC less than 10th percentile, normal EFW	0.52‡ (0.50–0.54)	7.2 (4.3–11.3)	97.3 (96.3–98.1)	2.7 (1.5–4.6)	0.60 (0.55–0.65)
AC less than 5th percentile, normal EFW	0.51‡ (0.49–0.53)	3.4 (1.5–6.6)	99.1 (98.5–99.5)	3.8 (1.6–9.2)	0.97 (0.95–1.0)

AUC, area under the curve; +LR, positive likelihood ratio; −LR, negative likelihood ratio; ACOG, American College of Obstetricians and Gynecologists; EFW, estimated fetal weight; AC, abdominal circumference; RCOG, Royal College of Obstetricians and Gynaecologists.
* P=.01 when compared against ACOG approach using the DeLong method.
† P=.04 when compared against ACOG approach, P=.13 when compared against RCOG approach using the DeLong method.
‡ P<.01 when compared against ACOG approach using the DeLong method.
§ P=.56 when compared against ACOG approach, P<.01 when compared against RCOG approach using the DeLong method.

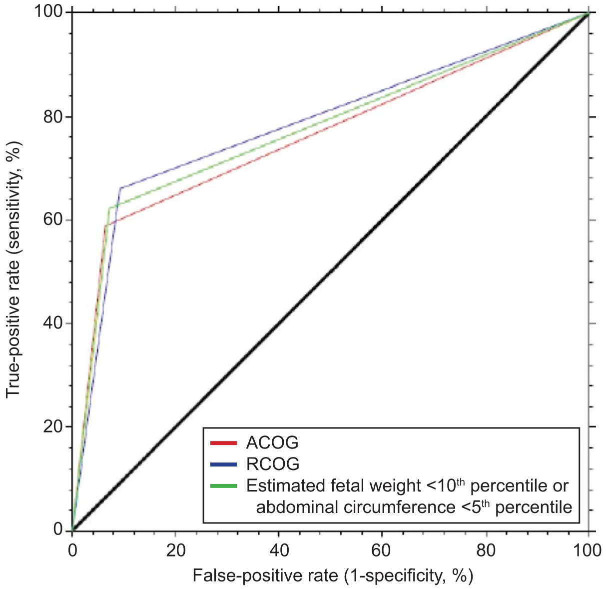

Fig. 1. Receiver operator characteristics of criteria for fetal growth restriction. The *diagonal line* represents diagnostic approaches that are no better than chance at predicting small for gestational age. A greater area under the curve represents a better balance of true- and false-positives. ACOG, American College of Obstetricians and Gynecologists; RCOG, Royal College of Obstetricians and Gynaecologists.

Blue. Methods for Diagnosing Fetal Growth Restriction. Obstet Gynecol 2018.

RCOG's with no differences in any other test parameter (Table 3). When analyzing the additional diagnostic criteria outlined in the secondary objectives, the AUCs of all other methods were lower than ACOG's, with the exception of abdominal circumference less than the 10th percentile interpreted independently of estimated fetal weight, which was no different (AUC 0.75, 95% CI 0.73–0.77, P=.6; Table 3). As expected, more inclusive diagnostic criteria were associated with weaker positive likelihood ratios and stronger negative likelihood ratios, although none were statistically different.

Fifty-seven pregnancies (3.3%, 95% CI 2.5–4.3%) had an abdominal circumference less than the 10th percentile in the presence of an estimated fetal weight greater than the 10th percentile, which represent the difference between RCOG's and ACOG's fetal growth restriction rates. Only 1.2% (95% CI 0.8–1.9%, n=21) had an abdominal circumference less than the fifth percentile in the presence of an estimated fetal weight greater than the 10th percentile. Adopting use of RCOG's method over ACOG's, the number needed to treat to correctly identify one additional case of SGA would be 14, whereas the number needed to harm to falsely identify one additional normal fetus as growth-restricted would be 18. Using estimated fetal weight less than the 10th percentile or abdominal circumference less than the 5th percentile rather than ACOG's method, the number needs to treat would be 30 with a number needed to harm of 57. Raw numbers of true- and false-positives and -negatives are reviewed in Table 5.

DISCUSSION

We found that in a population undergoing indicated fetal growth surveillance, the method endorsed by RCOG for the intrauterine diagnosis of fetal growth

Table 4. Neonatal Outcomes by Fetal Growth Status

Neonatal Outcome	EFW Greater Than 10th Percentile (n=1,415)	FGR by ACOG (n=232)	FGR by RCOG (n=289)	*P*
PTB	304 (21.5)	72 (31.0)	82 (28.4)	<.01
GA at delivery (wk)	37.9±2.7	36.7±3.2	36.9±3.1	<.01
Birth weight (g)	3,076±686	2,315±1,436	2,392±1,315	<.01
NICU admission	271 (19.2)	66 (28.4)	79 (27.3)	<.01
NICU stay greater than 48 h	262 (18.5)	65 (28)	78 (27.0)	<.01
RDS	79 (5.6)	22 (9.5)	24 (8.3)	.03
NEC	20 (1.4)	2 (0.9)	2 (0.7)	.52
Mechanical ventilation greater than 24 h	32 (2.3)	15 (6.5)	15 (5.2)	<.01
Supplemental O_2	164 (11.6)	47 (20.3)	54 (18.7)	<.01
Bag–mask ventilation	70 (4.9)	22 (9.5)	24 (8.3)	.02
Intubation	30 (2.1)	14 (6.0)	14 (4.8)	<.01
Chest compressions	5 (0.4)	2 (0.9)	2 (0.7)	.47
Death before discharge	0 (0)	0 (0)	0 (0)	—

EFW, estimated fetal weight; FGR, fetal growth restriction; ACOG, American College of Obstetricians and Gynecologists; RCOG, Royal College of Obstetricians and Gynaecologists; PTB, preterm birth; GA, gestational age; NICU, neonatal intensive care unit; RDS, respiratory distress syndrome; NEC, necrotizing enterocolitis; O_2, oxygen.
Data are n (%) or mean±SD unless otherwise specified.

Table 5. Distribution of Small-for-Gestational-Age and Non–Small-for-Gestational-Age Fetuses by Diagnostic Method

Diagnostic Approach	TP	FP	TN	FN
ACOG (EFW less than 10th percentile)	138	94	1,375	97
EFW less than 10 or AC less than 5th percentile	146	107	1,362	89
RCOG (EFW or AC less than 10th percentile)	155	134	1,335	80
EFW less than 10th percentile and AC less than 10th percentile	121	76	1,393	114
AC less than 10th percentile	138	116	1,353	97
AC less than 5th percentile	110	67	1,402	125
AC less than 10th percentile, normal EFW	17	40	1,429	218
AC less than 5th percentile, normal EFW	8	13	1,456	227

TP, true-positive; FP, false-positive; TN, true-negative; FN, false-negative; ACOG, American College of Obstetricians and Gynecologists; EFW, estimated fetal weight; AC, abdominal circumference; RCOG, Royal College of Obstetricians and Gynaecologists.
Data are n.

restriction performs better than the method endorsed by ACOG in the prediction of SGA at birth. As expected, application of more inclusive diagnostic criteria led to a higher rate of fetal growth restriction and the identification of additional cases of SGA that would have been missed by more restrictive diagnostic schemes. This is an important finding given that the antenatal surveillance of SGA fetuses who are correctly identified may reduce the risk of stillbirth and, when coupled with referral to appropriately resourced secondary or tertiary centers, confers an absolute risk reduction in perinatal death of 5 per 1,000.[3] The observation that our analysis did not show any difference in neonatal outcomes between normally grown fetuses and those with fetal growth restriction by RCOG's criteria but not ACOG's criteria should be interpreted with caution because the small number of those fetuses did not allow for sufficient power to detect a difference. Additionally, our analysis applied multiple diagnostic criteria retrospectively and so clinical care was guided only by the diagnostic method in use at that time, precluding any potential for outcomes to be altered by application of an alternate method. A large, prospective trial would be required to demonstrate a difference in neonatal outcomes among fetuses identified with fetal growth restriction according to the differing definitions. In addition, more research is necessary to ascertain whether the additional fetuses classified with fetal growth restriction identified by the more liberal RCOG criteria are more likely to be pathologically or constitutionally small. This distinction is important to establish because constitutionally small fetuses are not at increased risk for adverse outcomes of pregnancy and thus might not benefit from increased identification.[16]

Of interest is whether fetal growth-restricted cases identified by the more inclusive schemes are more likely to be true- or false-positives. Because additional true-positives identified by more inclusive diagnostic methods are inevitably accompanied by false-positives, more inclusive methods or thresholds may not always represent improved performance, leading some to choose the more restrictive approach as a result of concerns regarding the potential risks of additional false-positives. As a metric of test performance, the AUC accounts for this by incorporating both the true-positive rate and the false-positive rate, thereby providing an assessment of overall performance that takes both measures into account. In our comparison of AUCs, the RCOG method had statistically better overall performance than the ACOG method. Although overlapping CIs is one way to assess for statistically significant differences between proportions, the DeLong analysis was designed to compare AUCs derived from two tests applied to one study population (as was the case in our study) and has demonstrated a statistical difference.

Our study had multiple strengths. It was comprised of a large cohort of well-dated pregnancies from a single center, and the recalculation of estimated fetal weights and percentiles standardized the process and minimized bias. The use of cubic splines to interpolate birth weight whole-gestational week norms added granularity and clinical applicability. Study limitations included our inability to quantify the rate of fetal death among at-risk fetuses as a result of the nature of our database-driven chart review. Our population had a racial and geographic makeup that may not be nationally representative, although data previously reported from our institution demonstrated comparable mean birth weights to other geographic regions within the United States.[17]

Perhaps the most important limitation is that the retrospective nature of our study did not allow us to ascertain whether the application of different fetal growth restriction diagnostic methods affected neonatal outcomes. We would not expect this to alter the principal comparison of diagnostic criteria for fetal growth restriction, however, because both sets of criteria were applied to the same study population and would therefore be equally affected by any potential bias.

In summary, our study provided an important first step in addressing the difference in the fetal growth restriction diagnostic criteria recommended by ACOG and RCOG, demonstrating marginally superior performance of RCOG's criteria of estimated fetal weight or abdominal circumference less than the 10th percentile to predict SGA at birth. The adoption of the RCOG method may represent an opportunity to improve outcomes for a group of at-risk neonates, especially because it only requires an adjustment in interpretation of ultrasound parameters that are already part of standard intrauterine growth assessments. This approach falls short of what is ultimately required, however, because adjusting the thresholds of an inherently limited modality can only offer limited gains in SGA prediction. These limitations are exemplified by the high rate of SGA cases not identified by either method in our study. This underscores the need for research into and development of better diagnostic methods than those that rely on the use of traditional estimated fetal weight parameters and intrauterine growth curves alone. The diagnostic approach endorsed by RCOG is a marginally better predictor of SGA at birth compared with the method endorsed by ACOG. Future research should consider the potential benefits and harms of the different methods in different populations.

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