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Original Article

Clinical Utility of Prenatal Head-to-Abdominal Circumference Ratio for Prediction of Small-for-Gestational-Age Birth A Retrospective Study

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ABSTRACT

Background: Head-to-abdominal circumference (HC/AC) ratio on prenatal ultrasonography is useful for diagnosis of intrauterine growth retardation. This study assessed the utility of an HC/AC ratio cut-off point for predicting small-for-gestational-age (SGA) birth.

Methods: We retrospectively studied perinatal data from 177 neonates: 36 were classified as being SGA with systemic disease, 23 as SGA without systemic disease, 78 as appropriate-for-gestational-age (AGA) with systemic disease, and 40 as normal.

Results: HC/AC ratio correlated with gestational age ($r = -0.322$, $p = 0.024$) in the normal group but not in the other groups (SGA with disease group, $r = -0.116$, $p = 0.316$; SGA without disease, $r = -0.350$, $p = 0.085$; AGA with disease, $r = -0.121$, $p = 0.123$). An HC/AC ratio cut-off value of 1.15 identified risk of SGA at birth (sensitivity, 70%; specificity, 65%; $p < 0.0001$). An HC/AC ratio greater than 1.15 on follow-up ultrasonography was associated with increased risk of SGA at birth (odds ratio, 8.727; 95% confidence interval, 2.987 − 25.498; $p < 0.001$).

Conclusions: Prenatal HC/AC ratio did not decrease in SGA neonates. HC/AC ratio predicted the incidence of SGA at birth, regardless of gestational age.

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KEYWORDS: estimated fetal weight, intrauterine growth retardation, head-to-abdominal circumference ratio, small-for-gestational-age, ultrasonography

Perinatal mortality and morbidity are higher for small-for-gestational-age (SGA) neonates than for appropriate-for-gestational-age (AGA) neonates.[1–5] In addition, the incidences of non-reassuring fetal status and emergency cesarean delivery are higher for SGA neonates at term than for AGA neonates at term.[6] Furthermore, SGA at birth is

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associated with increased risk of neurological dysfunction and poor pulmonary outcomes, such as chronic lung disease, regardless of gestational age at birth.[7, 8] Thus, prenatal prediction of SGA at birth is of critical importance.

SGA at birth indicates that the fetus has failed to reach a specific biometric measure or estimated weight threshold by a specific gestational age. Abdominal circumference (AC) on ultrasonography and estimated fetal weight (EFW) calculated based on ultrasound measurements are the most accurate methods of predicting SGA. However, because calculation of AC and EFW uses gestational age at the time of ultrasonography to predict SGA at birth, the correct gestational age at the time of examination must be known. Thus, it is difficult to diagnose fetal intrauterine growth retardation (IUGR) and predict SGA at birth when gestational age cannot be accurately determined, as in cases of menoxenia, unknown last menstruation, and poor prenatal care.

The head-to-abdominal circumference (HC/AC) ratio on prenatal ultrasonography is useful for diagnosis of IUGR.[9–13] Although an IUGR diagnosis based on HC/AC ratio also incorporates gestational age at the time of ultrasonography, an elevated HC/AC ratio has been reported for singleton SGA fetuses.[14] Thus, HC/AC ratio might be a useful predictor of SGA at birth, regardless of gestational age. Furthermore, there is currently no HC/AC ratio cut-off value for predicting SGA at birth. In this study, we retrospectively assessed the utility of an HC/AC ratio cut-off for predicting the incidence of SGA at birth, regardless of gestational age.

Methods

The Institutional Ethics Committee of Toho University Omori Medical Center (Tokyo, Japan) approved this study (reference number, M16093; date of approval, 15 July 2016). We retrospectively analyzed data from a consecutive series of neonates who had undergone prenatal ultrasonography to evaluate abnormalities detected by primary screening at Toho University Omori Medical Center (Tokyo, Japan) between April 2010 and September 2015. We excluded neonates with missing data on antenatal biometry, perinatal diagnosis, and physical measurements. The patients were classified into four groups, namely, SGA with disease (SGA neonates with systemic diseases), SGA without disease (SGA neonates without systemic diseases), appropriate-for-gestational-age (AGA) with disease (AGA neonates with systemic diseases), or normal (AGA neonates without systemic disease).

Gestational age was determined on the basis of maternal menstrual history and early fetal ultrasonography. All ultrasound examinations were performed by experienced staff trained in ultrasound who used the same commercially available ultrasound system (XarioXG SSA-680A; Toshiba Medical Systems Corp., Tokyo, Japan or ACUSON SC 2000; Siemens AG, Berlin, Germany). Fetal measurements included biparietal diameter (BPD), occipitofrontal diameter (OFD), AC, femur length (FL), cerebellum transverse diameter, transverse cardiac diameter, cardiothoracic area ratio, and pulmonary artery/aorta/superior vena cava ratio. The detailed definitions of these measurements were based on guidelines standardized by the Japan Society of Ultrasonics in Medicine.[15, 16] Head circumference (HC) was calculated by using the formula $3.14 \times (BPD + OFD)/2$.[17] For AC measurement, we used the elliptical measurement at the transverse section of the fetal abdomen at the level of the stomach. The umbilical vein in the liver was considered to be one-third of the anteroposterior diameter of the fetal abdomen. EFW was calculated by using the formula $EFW = 1.07 \times BPD^3 + 0.30 \times AC^2 \times FL$.[15, 16] SGA at birth was defined as a birth weight less than the 10th percentile, corrected for gestational age, according to Japanese growth charts.[18] AGA at birth was defined as a birth weight from the 10th to the 90th percentiles, and large for gestational age at birth was defined as a birth weight greater than the 90th percentile. Maternal and neonatal data were collected from medical records.

Statistical analysis

Neonatal characteristics were analyzed with the Kruskal Wallis *H*-test. Spearman rank correlation was used to assess correlations of HC, AC, and HC/AC ratio with gestational age at the time of ultrasound. Differences between correlation coefficients were assessed with the Fisher *r*-to-*z* transformation. To test if HC/AC ratio predicted incidence of SGA at birth, the area under the receiver operating characteristics (ROC) curve of SGA at birth was calculated. The area under the curve (AUC) is a measure of the accuracy of a parameter (an AUC of 0.5 is no better than chance, and no prediction is possible; an AUC of 1.0 is the best possible prediction). The optimal cut-off point is the one that has the lowest false-positive and false-negative rates across a range of cut-off points. Odds ratios (ORs) with 95% confidence intervals (CI) of the HC/AC ratio cut-off level for predicting the incidence of SGA were calculated, as determined by ROC analysis and

an EFW greater than 1.5 standard deviations (SD) below the mean for gestational age among Japanese.[18] The abilities of the HC/AC ratio cut-off level determined by ROC analysis and the normal limits determined by Campbell et al[9] to predict SGA incidence were compared with the chi-square test or Fisher exact probability test, as appropriate. Statistical significance was defined as a p value less than 0.05. The SigmaPlot™ statistical software package for Windows (version 13.0, Systat Software Inc., San Jose, CA, USA) was used for statistical analysis.

Results

In total, 177 neonates were enrolled in the present study, and 315 ultrasound examinations were performed. None were excluded from the final analysis. Most neonates were diagnosed as having IUGR with coexisting disease or non-IUGR with coexisting disease (Fig. 1 and Table 1). Eighty-three neonates had undergone multiple prenatal ultrasound examinations: 45 neonates had undergone two examinations, 23 had undergone three, 13 had undergone four, and two neonates had undergone five examinations. Among the 31 fetuses who received a diagnosis of IUGR at primary scanning, 27 (87%) were diagnosed as having IUGR at our hospital. Among the 146 fetuses who were not diagnosed as having IUGR at primary scanning, 28 (19%) were diagnosed as having IUGR at our hospital. During the fetal period, IUGR was diagnosed in 23 (64%) of 36 SGA neonates with disease, 20 (87%) of 23 SGA neonates without disease, 8 (10%) of 78 AGA neonates with disease, and 4 (10%) of 40 normal neonates ($p < 0.001$). Among fetuses receiving a diagnosis of IUGR at primary screening and at our hospital, SGA at birth was noted in 84% (26/31) and 78% (43/55), respectively ($p = 0.723$). Among fetuses not receiving a diagnosis of IUGR at primary screening or at our hospital, SGA at birth was noted in 23% (34/146) and 13% (16/122), respectively ($p = 0.037$). In the normal group, six mothers with cardiac disease and/or collagen disease were included. One neonate classified as normal was large for gestational age.

Fig. 2 shows the correlations of HC, AC, and HC/AC ratio with gestational age at ultrasonography in the four groups. HC increased progressively during the fetal period in all groups, but HC at full term tended to be lower in SGA neonates with and without disease than in normal neonates (slope: $F = 0.3544$, $p = 0.5525$; intercepts: $F = 10.753$, $p = 0.0013$; Fig. 2A). AC progressively increased during the fetal period in all groups, but AC at full term tended to be lower in SGA neonates with and without disease than in normal neonates (slope: $F = 3.2784$, $p = 0.0723$; intercepts: $F = 55.4065$, $p < 0.0001$; Fig. 2B). The HC/AC ratio gradually decreased during the fetal period in normal neonates ($r = -0.322$, $p = 0.024$) but not in the other groups (SGA with disease group: $r = -0.116$, $p = 0.316$; SGA without disease group: $r = -0.350$, $p = 0.085$; AGA with disease group: $r = -0.121$, $p = 0.123$; Fig. 2C). Fig. 3 shows the HC/AC ratio at the time of ultrasound in normal neonates. Twelve (24%) of the 49 HC/AC ratios deviated from the normal limits established by Campbell et al,[9] but most such deviations were small.

ROC analysis revealed that HC/AC ratio at the time of ultrasound predicted SGA at birth (AUC, 0.7387; 95% CI, 0.6800 − 0.7975; $p < 0.0001$; Fig. 4). ROC analysis showed that an HC/AC ratio of 1.15 at ultrasonography predicted SGA at birth with a sensitivity of 70.0% (95% CI, 60.4% − 79.0%) and a specificity of 64.5% (95% CI, 57.7% − 70.9%). Regardless of gestational age, an HC/AC ratio greater than 1.15 was associated with increased risk of SGA at birth (OR, 4.297; 95% CI, 2.579 − 7.159; $p < 0.001$). In addition, an EFW 1.5 SD below the mean for gestational age was associated with increased risk of SGA at birth (OR, 17.812; 95% CI, 9.752 − 32.536; $p < 0.001$). For SGA neonates with and without disease, the accuracy of predicting SGA at birth did not differ between an EFW more than 1.5 SD below the mean for gestational age and an HC/AC ratio greater than 1.15. However, among AGA neonates with disease and normal neonates, an HC/AC ratio greater than 1.15 was not more accurate than an EFW more than 1.5 SD below the mean for gestational age in predicting SGA at birth (Table 2). Among 16 fetuses that were SGA neonates (structural chromosome aberration, 11; twin pregnancy, 3; no disease, 2), none had an EFW more than 1.5 SD below the mean for gestational age, but an HC/AC ratio greater than 1.15 was observed in 11 (69%) of these fetuses (structural chromosome aberration, 7; twin pregnancy, 2; no disease, 2).

Fig. 5 shows HC/AC ratios for 83 neonates who had undergone multiple prenatal ultrasound examinations. Among SGA neonates with and without disease, the HC/AC ratio did not decrease during the fetal period in 16 (67%) of 24; an HC/AC ratio greater than 1.15 was observed in 16 (67%) of 24 (Fig. 5A, 5B). Among AGA neonates with disease, the HC/AC ratio decreased during the fetal period in 41 (77%) of 53, and an HC/AC ratio greater than 1.15 was observed in 11 (21%) of 53 (Fig. 5C). In nor-

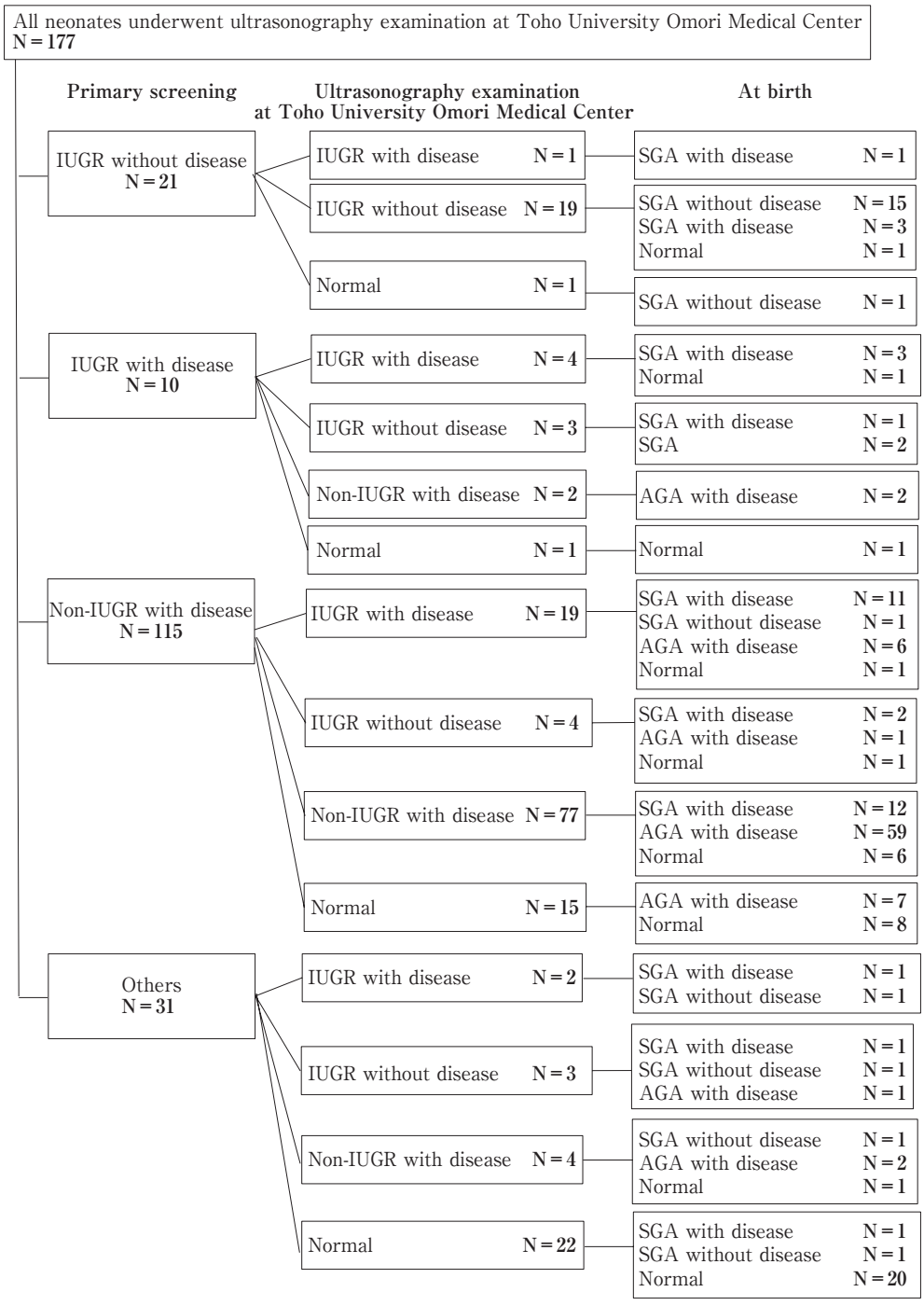

Fig. 1 CONSORT flow diagram of patients.
CONSORT: Consolidated Standards of Reporting Trials, IUGR: intrauterine growth retardation, SGA: small for gestational age, AGA: appropriate for gestational age.

mal neonates, the HC/AC ratio decreased in five (83%) of six during the fetal period, and an HC/AC ratio greater than 1.15 was observed in one (17%) of six (Fig. 5D). HC/AC ratios that deviated from the normal limits reported by Campbell et al[9] were observed in 20 (83%) of 24 SGA neonates with and without disease (Fig. 5A, 5B), in 24 (45%) of 53 AGA neonates with disease (Fig. 5C), and in two (33%) of six normal neonates (Fig. 5D). The ability to predict SGA at birth did not differ between an HC/AC ratio greater than 1.15 and the normal limits reported by

Table 1 Characteristics of patients

	SGA with disease (n = 36)	SGA without disease (n = 23)	AGA with disease (n = 78)	Normal (n = 40)	*P* value
Maternal age (years)	36 (26−45)	32 (21−40)	32 (19−44)	34 (17−44)	0.120
Fetal characteristics					
Gestational age at first examination (weeks)	28.6 (21.1−38.2)	31.0 (18.0−36.9)	31.1 (18.3−39.1)	29.5 (14.9−41.0)	0.061
Multiple examinations (n)	23 (64%)	1 (4%)	53 (68%)	6 (15%)	<0.001
Diagnosis at last examination (n)					<0.001
IUGR with disease	16 (44%)	2 (9%)	6 (8%)	2 (5%)	
IUGR without disease	7 (19%)	18 (78%)	2 (3%)	2 (5%)	
Non-IUGR with disease	12 (33%)	1 (4%)	63 (81%)	8 (40%)	
Normal	1 (3%)	1 (4%)	7 (10%)	28 (70%)	
Neonatal characteristics					
Gestational age at delivery (weeks)	37.2 (26.9−41.0)	37.1 (28.3−41.0)	38.1 (29.6−41.3)	38.6 (31.3−41.4)	<0.001
Preterm delivery (n)	16 (44%)	10 (44%)	12 (15%)	3 (8%)	<0.001
Birth weight (g)	1820 (637−2686)	1815 (405−2620)	2917 (1081−3793)	2989 (1207−4040)	<0.001
Birth height (cm)	41 (30−50)	42 (26−48)	48 (36−52)	49 (36−53)	<0.001
Birth head circumference (cm)	31 (23−36)	30 (21−34)	34 (26−38)	34 (28−37)	<0.001
Birth chest circumference (cm)	26 (19−31)	26 (15−31)	32 (21−36)	32 (21−37)	<0.001
Systemic disease (n)					
Cardiovascular	21 (58%)	-	37 (47%)	-	
Chromosomal	15 (42%)	-	6 (8%)	-	
Neurological	0 (0%)	-	13 (17%)	-	
Abdominal	10 (28%)	-	11 (14%)	-	
Renal	2 (6%)	-	13 (16%)	-	
Pulmonary	3 (8%)	-	7 (9%)	-	
Bone	1 (3%)	-	2 (3%)	-	

Data are presented as median (range) or number (proportion).
SGA: small for gestational age, AGA: appropriate for gestational age, IUGR: intrauterine growth retardation.

Campbell et al[9] in any group (SGA with and without disease group: $p = 0.317$; AGA with disease group: $p < 0.001$; normal group: $p = 1.000$). Regardless of the presence of systemic disease, fetuses with an HC/AC ratio that did not decrease during the fetal period and was greater than 1.15 at a follow-up ultrasound examination had an increased risk of SGA at birth (OR, 8.727; 95% CI, 2.987 − 25.498; $p < 0.001$).

Discussion

In the present study, HC/AC ratio did not decrease during the fetal period in SGA neonates with and without disease. An HC/AC ratio greater than 1.15 was associated with increased risk of SGA at birth, regardless of gestational age at the time of ultrasonography.

HC/AC ratio measured during prenatal ultrasound is useful for diagnosis of fetal IUGR.[9–13] Furthermore, David et al reported that the HC/AC ratio was elevated in 42% of singleton SGA fetuses and that such elevation was associated with increased perinatal mortality, lower birth weight, and lower gestational age at delivery.[14] The standard size of Japanese neonates is smaller than the values specified in the guidelines of the World Health Organization and Western countries.[19] In 1993, Wakatsuki reported that the HC/AC ratio during gestational weeks 15 to 30 is lower in Japanese than in Europeans.[20] However, in the present study, most HC/AC ratios for normal neonates were within the normal limits determined by Campbell et al,[9] and SGA neonates had elevated HC/AC ratios on prenatal ultrasonography. It should be noted that the present technique for AC measurement differs from the method used in a previous Japanese study.[20] In Thailand, the HC/AC ratio does not differ from those reported in Western countries, despite physical differences after birth in these

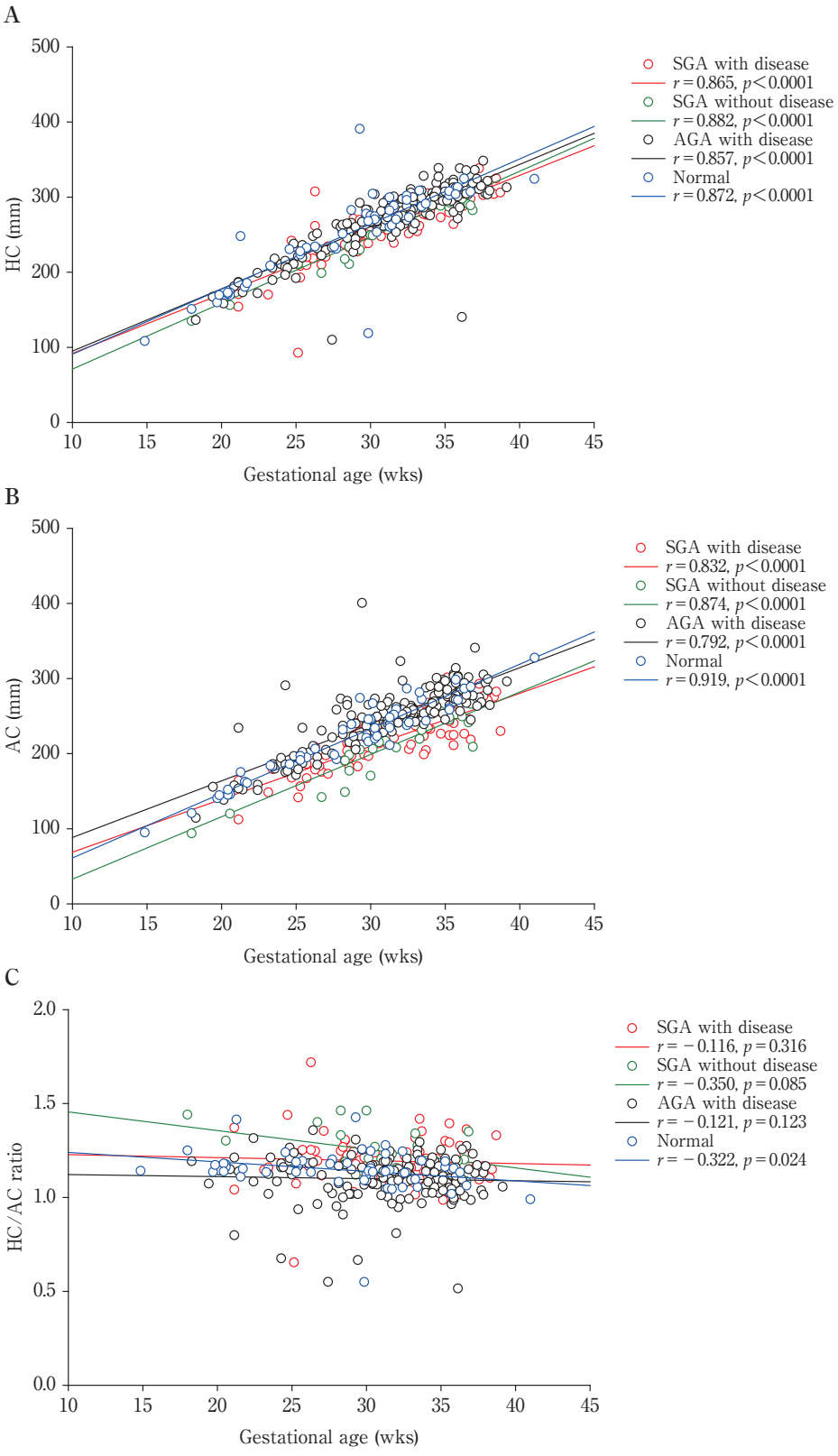

Fig. 2 Correlations of **(A)** head circumference (HC), **(B)** abdominal circumference (AC), and **(C)** HC/AC ratio with gestational age at the time of ultrasound examination for small-for-gestational-age (SGA) neonates with disease (red), SGA neonates without disease (green), appropriate-for-gestational-age neonates with disease (black), and normal neonates (blue).

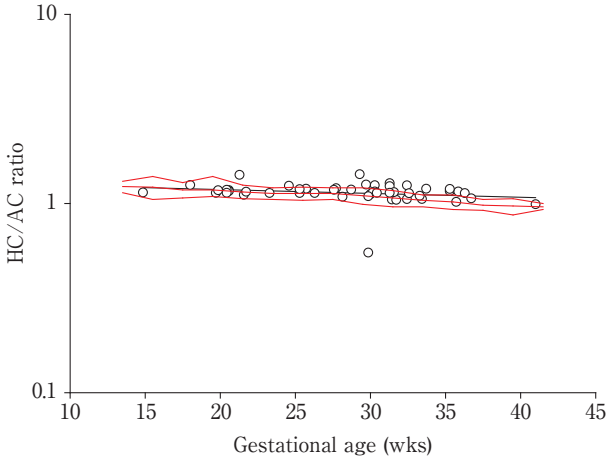

Fig. 3 Head-to-abdominal circumference ratio (HC/AC ratio) in normal neonates. Red lines represent mean HC/AC ratios with 5th and 95th percentile confidence limits, as reported by Campbell et al.[9]

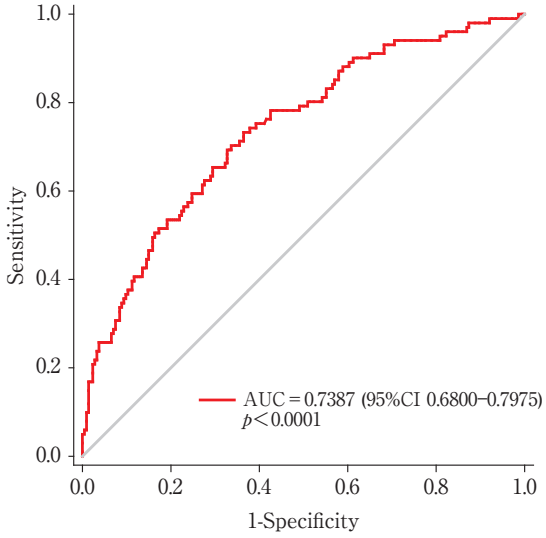

Fig. 4 Receiver operating characteristics curve for head-to-abdominal circumference ratio. The optimal cut-off value for predicting small for gestational age at birth was 1.15.
AUC: area under the curve, CI: confidence interval.

populations.[21] Nevertheless, HC/AC ratio appears to be a useful parameter for estimating fetal growth in Japanese. In addition, although HC and AC progressively increased during the fetal period in all neonates, HC and AC at term tended to be lower in SGA neonates with and without disease than in normal neonates. Elevation of the HC/AC ratio in SGA neonates with and without disease is likely attributable to unbalanced growth of the head and body, and specifically to poor growth of the abdominal region. Thus, our findings indicate that HC/AC ratio is useful for predicting the incidence of SGA at birth.

In the present study, an HC/AC ratio greater than 1.15 and an EFW more than 1.5 SD below the mean for gestational age were associated with increased risk of SGA at birth. The ability to predict SGA at birth was stronger for an EFW more than 1.5 SD below the mean for gestational age than for an HC/AC ratio greater than 1.15. In particular, an HC/AC ratio greater than 1.15 could not exclude non-SGA at birth more accurately than an EFW greater than 1.5 SD below the mean for gestational age. However, an HC/AC ratio greater than 1.15 could predict SGA at birth, regardless of gestational age at the time of ultrasonography, and an HC/AC ratio greater than 1.15 could predict the risk of SGA at birth without referring to the normal limits. Furthermore, in SGA neonates with and without disease, most HC/AC ratios at follow-up ultrasound examinations were greater than 1.15; however, in AGA neonates with disease and normal neonates, most HC/AC ratios at follow-up ultrasound examinations were lower than 1.15. Thus, regardless of the presence of systemic disease, an HC/AC ratio greater than 1.15 at multiple follow-up ultrasound examinations was strongly associated with increased risk of SGA at birth. In addition, in the present study, 70% of SGA neonates with an EFW not greater than 1.5 SD below the mean for gestational age had an HC/AC ratio greater than 1.15, and most of these neonates had structural chromosome aberrations. These results suggest that HC/AC ratio is useful for predicting SGA at birth in IUGR caused by fetal or maternal factors.

The limitations of the present study include its retrospective nature, patient selection bias, and lack of assessment of long-term postnatal neurodevelopmental dysfunction and mortality. Our results suggest that an HC/AC ratio greater than 1.15 at multiple ultrasound examinations is an accurate predictor of SGA at birth. However, the number of ultrasound examinations varied among the study patients, and most underwent only one examination. In addition, because the study patients were referred to our department for detailed examination of abnormalities detected by primary screening, we have limited information on normal neonates. In the present study, an HC/AC ratio greater than 1.15 was observed in 76 (36%) of 214 examinations of 118 non-SGA neonates. Patient selection bias might affect the ability to predict SGA risk at birth. However, as was the case in previous studies,[9–14, 20] an elevated

Table 2 Results of 315 fetal ultrasound examinations (n = 117).

	EFW > 1.5 SD below mean for gestational age	HC/AC ratio > 1.15	*P* value
SGA with disease (n = 77)	49 (64%)	50 (65%)	1.000
SGA without disease (n = 24)	20 (83%)	21 (88%)	1.001
AGA with disease (n = 165)	18 (11%)	53 (32%)	< 0.001
Normal (n = 49)	5 (10%) *	23 (47%)	0.001

Data are presented as number (proportion). *48 ultrasound examinations
SGA: small for gestational age, AGA: appropriate for gestational age, EFW: estimated fetal weight, HC/AC: head-to-abdominal circumference, SD: standard deviation

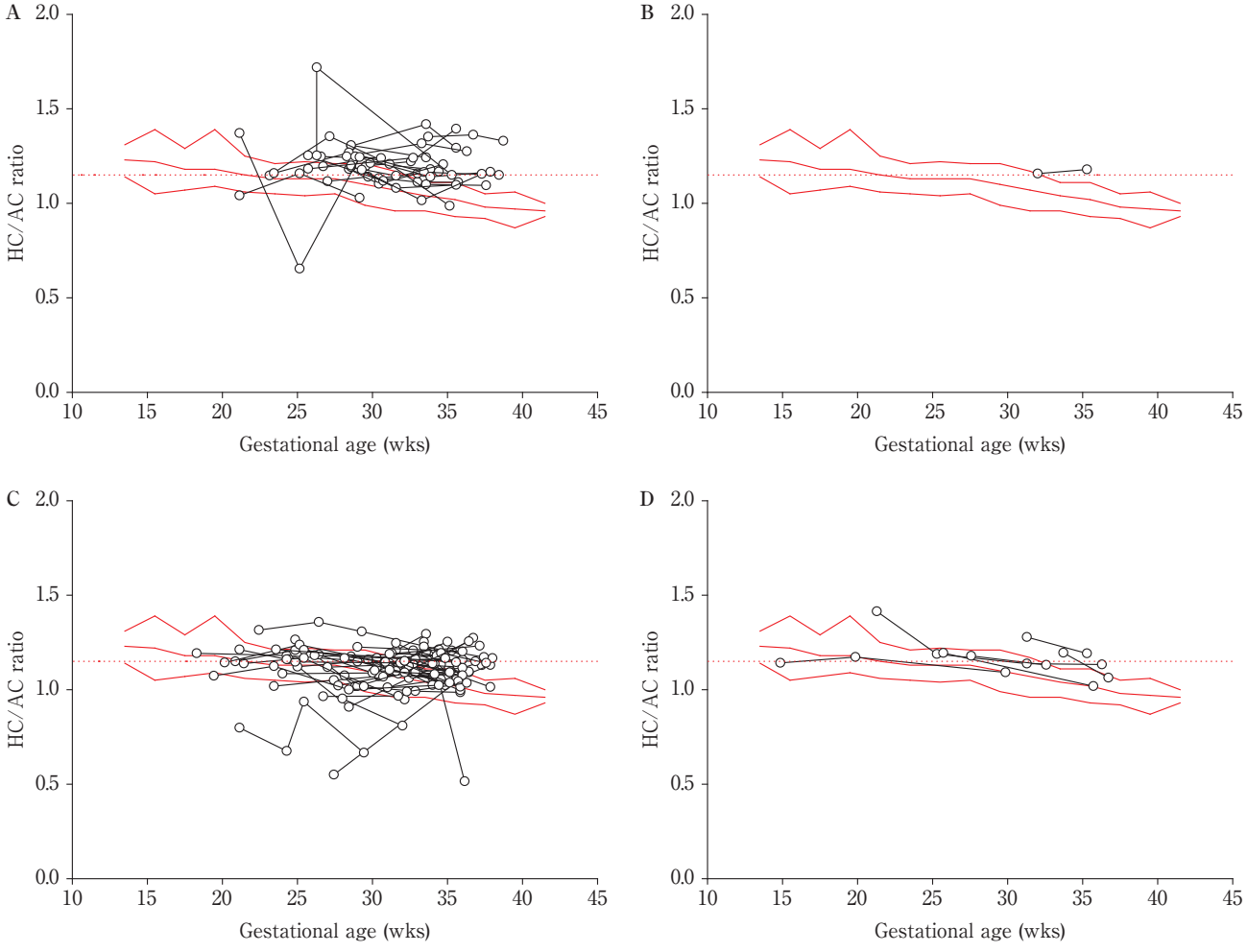

Fig. 5 Head-to-abdominal circumference ratio (HC/AC ratio) in neonates who underwent multiple prenatal ultrasound examinations: **(A)** small-for-gestational-age (SGA) neonates with disease (red), **(B)** SGA neonates without disease (green), **(C)** appropriate-for-gestational-age neonates with disease (black), and **(D)** normal neonates (blue). Red lines represent mean HC/AC ratios with 5th and 95th percentile confidence limits, as reported by Campbell et al.[9]
The red dotted line represents an HC/AC ratio of 1.15.

HC/AC ratio was associated with increased risk of poor growth at birth. To confirm our findings, future prospective studies should assess long-term postnatal outcomes and fetuses without abnormalities at primary screening.

In conclusion, an elevated HC/AC ratio was associated with increased risk of SGA at birth, and an HC/AC ratio

greater than 1.15 was a predictor of SGA, regardless of gestational age at the time of ultrasonography.

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Conflicts of interest: The authors declare no conflicts of interest.

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