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INDIVIDUALIZED NEONATAL GROWTH ASSESSMENT: DOES PRENATAL GROWTH CESSATION AFFECT THE PREDICTION OF BIRTH CHARACTERISTICS?

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Abstract

Objective—To investigate growth cessation at term and birth characteristic predictions in a large sample using Individualized Growth Assessment.

Methods—A prospective longitudinal study of 119 pregnancies with normal growth outcomes was carried out from 18 weeks, MA, to delivery. Measurements of head circumference (HC), abdominal circumference (AC), femur diaphysis length (FDL), mid-thigh circumference (ThC), head profile cube (Hcube), abdominal profile cube (Acube) and mid-arm circumference (ArmC) were obtained using 3D ultrasonography at 3–4 week intervals. Rossavik growth models were determined from these data using sample-specific and previously published procedures. These models were used to predict birth characteristics at different ages. Predicted and measured birth characteristics were compared and Percent Differences (% Diff) calculated. Growth cessation age [GCA] was defined by the absence of systematic change in % Diff values [derived from predictions at GCA's] in those fetuses delivering after the GCA. Systematic (mean % Diff) and random (% Diff 95% range) prediction errors were compared to published data and when using different assumptions about growth cessation. New Growth Potential Realization Index [GPRI] reference ranges were established.

Results—Growth cessation ages were 38 weeks for HC, AC, THC, WT and ArmC [CHL: 38.5 weeks]. Assuming growth-to-delivery gave positive slopes [4/6 different from zero] and non-random distributions for % Differences after the 38 weeks. Systematic and random prediction errors, based on predictions at the GCA's, were similar to those published previously except for WT [based on Hcube and Acube]. However, predicted weights derived from BPD, AC and TVol

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had prediction errors of −4.1+/−8.3%. After correction for non-zero systematic prediction errors [AC, ThC, ArmC, WT], mean GPRI values were close to 100, with normal ranges similar [WT larger] than those obtained previously.

Conclusions—Growth cessation at term occurred for all six birth characteristics studied. Prediction errors and GPRI normal ranges in this large sample were similar to those obtained previously in much smaller samples. A simple weight estimation procedure utilizing three anatomical parameters (BPD, AC, TVol) gave the most precise WT predictions. Our results provide the methods and standards required to individualize the assessment of neonatal growth outcome.

Keywords

fetal growth; individualized growth assessment; growth cessation; Rossavik model; estimated fetal weight

INTRODUCTION

Although anatomical parameters such as the head circumference and crown-heel length are routinely measured, the primary means for evaluating neonatal growth status currently is to compare birth weights to age-specific weight standards (1). Based on this comparison, the neonate is classified as Small-for-Gestational-Age [SGA] if the weight is below the 10th percentile, Appropriate-for-Gestational-Age [AGA] if between the 10th and 90th percentile or Large-for-Gestational-Age [LGA] if above the 90th percentile (2). This system was originally designed to correct for age at delivery, but does not correct for other confounding variables such as differences in growth potential, growth cessation before delivery or the way growth abnormalities manifest themselves in different individuals (3). These factors are likely to cause misclassification, creating subgroups that contain neonates with normal and abnormal growth, while those neonates whose growth abnormality is not manifest in weight cannot be detected (4,5,6). Up to 20% of neonates in pregnancies at risk for growth abnormalities have been found in this latter category (6).

An alternative approach to the traditional birth weight classification system was proposed by Deter and Harrist using a Neonatal Growth Profile (7). This Profile consists of five anatomical parameters {head circumference [HC], abdominal circumference [AC], thigh circumference [ThC], crown-heel length [CHL], weight [WT]} measured within 24–48 hours of delivery. These measurements are not compared to population standards but rather to individual predicted values obtained from parameter-specific, Rossavik growth models. These models are derived from 2nd trimester growth velocities [direct indicators of growth potential] determined during a time when aberrant growth is usually absent (3), However, this individualized approach depends on identifying a growth cessation age [GCA], after which no interval fetal growth is detected prior to delivery (3). For each anatomical parameter, a Growth Potential Realization Index [GPRI] is calculated using the following equation: $\mathrm{GPRI}=\{[\mathrm{actual\ measurement}/\mathrm{predicted\ measurements}]\}\times 100$. Sets of GPRI values have revealed different patterns of abnormal growth in both IUGR and Macrosomic neonates (6) These sets can also be used to form a composite parameter called the Neonatal Growth Assessment Score [NGAS], which has effectively separated IUGR, Normal and

Macrosomic neonates even when growth abnormalities manifest themselves in different ways in different individuals (6).

This investigation examines the process of prenatal growth cessation and the prediction of birth characteristics, using a large sample of fetuses with normal neonatal growth outcomes. The sample is 4–6 fold larger than those used in prior investigations and six anatomical parameters were studied. Our results were compared to those obtained in previously published longitudinal studies using Rossavik growth models.

METHODS

The sample and methods used in this investigation have been previously described in detail (8). The prospective longitudinal study was carried out using a protocol approved by the Human Investigation Committee at William Beaumont Hospital [Royal Oak, MI] and the Institutional Review Board at the National Institute of Child Health and Human Development [Bethesda, MD].

Population Sample

A sample of 119 pregnancies, from a longitudinal study of fetal growth and neonatal outcome carried out at William Beaumont Hospital, Royal Oak, MI, was selected based on normal neonatal growth outcomes. These outcomes were identified using a specific form of the five member [HC, AC, ThC, CHL, WT] modified Neonatal Growth Assessment Score [m_3NGAS_{51}] using a sample-specific, 95% reference range [177–218%]. Comprehensive prenatal evaluation of growth using Individualized Growth Assessment [IGA] indicated that the fetuses grew normally (8).

Ultrasound Studies

Fetal ages were determined primarily from 1st trimester CRL measurements or LMP's, confirmed by 2nd trimester ultrasound studies (8). Serial ultrasound examinations were carried out beginning at 18 weeks, MA, [first scan: 18.6 ± 0.7 S.D. weeks] and ending at approximately 37 weeks, MA [last scan: 37.4±1.5 SD weeks]. The number of scans per fetus was 6.8± 0.8 SD. The last-scan-to-delivery interval was 1.7±1.2 SD weeks. Three-dimensional ultrasonography with hybrid mechanical and curved array abdominal transducers [Voluson systems 730,730 Expert, E8, GE Healthcare, Milwaukee, WI] was used to acquire volume data sets at each examination. With these data sets, measurements of HC, AC, ThC, femur diaphysis length [FDL], upper arm circumference [ArmC], head cube [Hcube] and abdominal cube [Acube] were obtained as previously described (8). These measurements were used to specify 2nd trimester Rossavik Growth models (8). Using these growth models, predicted values for HC, AC, ThC, CHL and WT at birth were obtained as described in the Data Analysis section.

Neonatal Evaluation

Within 48 hours of delivery, 5 basic anatomical measurements [WT, CHL, HC, AC, ThC, ArmC] were obtained from each fetus as previously described (9,10). These measurements were used in the evaluation of neonatal growth status (6,9).

Data Analysis

Second trimester model specification—Rossavik growth models [$P = c\,(t)^{k+st}$] can be specified in the 2nd trimester if the time variable t is properly defined and coefficient [c, k, s] estimates can be obtained. To correct for the use of menstrual age and differences in embryological development, t was defined as the menstrual age minus the appropriate Start Point [SP] (3). Start Points for each anatomical parameter in individual fetuses were obtained from measurements before 28 weeks using linear regression as previously described (11). Estimates of Coefficients k [representing anatomical characteristics] for different parameters were obtained by regression analysis and were subsequently fixed at their mean values (8). Individual Coefficients c [related to growth potential] values were estimated from the slopes of the 2nd trimester growth curves and functions relating slope to c(8). Similarly, individual Coefficient s [unknown control system] estimates were obtained using the Coefficient c estimates and functions relating s to c (8). For the purpose of these analyses, the procedures established using the sample of 119 (8), are designated sample-specific Rossavik growth model specification procedures. Similar data obtained with other samples (10,12,13,14,) are called previously published Rossavik growth model specification procedures. Both types of procedures were used to obtain sets of predicted birth characteristics.

Prediction of birth characteristics—With the 2nd trimester Rossavik growth models specified as described above, birth characteristics [HC, AC, ThC, FDL, Hcube, Acube, ArmC] were predicted at different time points. Birth characteristics were predicted at the actual birth age for those fetuses delivering at 38 weeks, MA, or before (9). For those delivering after 38 weeks, MA, predictions were made at 38 weeks. In the case of the CHL, predictions at several ages had to be made in order to find the correct Growth Cessation Age. In all these studies, predicted values for FDL were converted to predicted CHL values using the optimal function determined previously for singletons (15). Predicted WT values were obtained from the predicted Hcube and Acube values using the function described by Deter et al (16). Predicted WT's were also obtained using the same type of function but with variable estimates derived from a subsample of the fetuses being studied longitudinally. These estimates were obtained using 50 fetuses that had scans within 1 week of delivery. Birth weight was the dependent variable and the measured Hcube and Acube values the independent variables. Weighting factor, ratio and difference estimates (see Reference # 16) that are part of this new weight estimation function were obtained using Maximum Likelihood estimation (17). In another weight estimation procedure, predicted BPD, AC and TVol values converted to weight estimates using the function described by Lee and colleagues (18):

$$\mathrm{Log}_e\,\mathrm{WT} = -0.8297 + 4.0344\,(\log_e \mathrm{BPD}) - 0.782\,(\log_e \mathrm{BPD})^2 + 0.7853\,(\log_e \mathrm{AC}) + 0.0528\,(\log_e \mathrm{TVol})^2$$

Detection of growth cessation age (GCA)—In a subset of fetuses delivering after 38 weeks, MA, Percent Differences [% Diff] were calculated using the following equation (9):

$$\%\,\mathrm{Diff} = \{[\mathrm{predicted\ measurement} - \mathrm{birth\ measurement}]/\mathrm{birth\ measurement}]\} \times 100$$

Predicted measurements were those predicted at the assumed GCA's {38 weeks [HC, AC, ThC, WT, ArmC], 38.5 weeks [FDL], actual birth age [HC, AC, FDL, ThC, WT, ArmC]}. Linear equations were fit to the Percent Differences as a function of birth age. The slopes of these equations were compared to zero using the t-test. A negative, non-zero slope indicated further growth after the assumed GCA. A positive, non-negative slope indicated growth cessation before the assumed GCA. A zero slope indicated that the correct GCA had been chosen. In latter cases, % Diff values exhibited a random distribution beyond the GCA.

Systematic and random prediction errors—Predicted birth measurements were compared to actual birth measurements and the Percent Differences determined. Linear regression was used to determine if there was a relationship between % Differences and birth age. The slopes of the linear functions were compared to zero using the t-test. Means and SD's of the Percent Differences were calculated for each anatomical parameter and the means compared to zero using the t-test. Means that deviated significantly from zero were taken as indicative of systematic prediction errors and used to specify correction factors for these systematic errors [see Supplementary File for a description of the correction factor procedure] (9). Random prediction errors were defined as the range containing 95% of the Percent Differences. To facilitate comparisons, these ranges are presented in a zero-mean based form by subtracting mean values from the upper and lower limits of the original ranges.

A possible interaction between the methods for predicting Hcube and Acube values at the Growth Cessation Age and functions used in converting predicted Hcube and Acube values to weight estimations were evaluated. Predicted Hcube and Acube values at 38 weeks were obtained using procedures previous published (12). These values were used to calculate predicted WT values using previously published weight estimation functions (16) and the sample-specific weight estimation functions described above. Predicted WT values were compared to actual birth weights and systematic and random prediction errors were determined for four possible combinations using the procedures described in the previous paragraph. The systematic and random prediction errors obtained with the method of Lee et al (18) were also included in this analysis. The systematic prediction errors were evaluated by ANOVA and Tukey's pair wise multiple comparison test. Random prediction errors were evaluated using the pair wise Correlated Variance test (19)

Growth Potential Realization Index—Using actual and predicted birth measurements, Growth Potential Index [GPRI] values for 6 anatomical parameters [WT, CHL, HC, AC, ThC, ArmC] were calculated with one of two equations (9):

$$\mathrm{GPRI}=[\text{actual measurement}/\text{predicted measurement}]\times 100 \quad (1)$$

$$\mathrm{GPRI}=[\text{actual measurement}/\{\text{predicted measurement}\times\text{correction factor}\}]\times 100 \quad (2)$$

Means and standard deviations were calculated and the mean values compared to 100 using the t-test. Ranges containing 95% of the GPRI values were determined for all six anatomical parameters. For WT, GPRI data derived from the five evaluated sequences are presented.

In all statistical tests, a p-value <0.05 was considered to indicate a statistically significant difference.

RESULTS

Growth Cessation

In the subsample delivering after 38 weeks, MA. 68% had spontaneous labor, 13% induced labor and 19% no labor. Delivery was vaginal in 72% and by cesarean section in 28%. Since growth cessation has been demonstrated at 38 weeks, MA, in most previous investigations (9, 10, 13, 14, 20, 21, 22), we assumed Growth Cessation Age [GCA] of 38 weeks for our initial studies. All slopes of the linear functions relating Percent Difference [% Diff] to Birth Age [BA] were not different from zero, except CHL [Table 1], indicating a random distribution of Percent Differences after 38 weeks. For CHL, the slope of the linear function was negative and significantly different from zero, indicating that the GCA had not been reached. As shown in Table 1a, use of a GCA value of 38.5 weeks resulted in a slope that was not significantly different from zero. Using the predictions at these GCA's, the mean Percent Differences did not differ from zero for the two skeletal parameters [HC, CHL] but showed systematic over-estimations for the four soft tissue parameters [AC, ThC, ArmC, WT].

Table 1b summarizes our Growth Cessation study limited the period after the growth cessation ages [38 weeks, MA for all parameters except CHL {38.5 weeks}]. Either growth cessation or growth to delivery was assumed for each parameter. For the former, all slopes of the % Diff vs. Birth Age functions were negative and not different from zero; the distributions of % Diff's appeared to be random [Figure 1].. For the latter, all slopes were positive and significantly greater than zero; the distributions of % Diff's were not random [Figure 1]. The mean % Diff values in the latter group were significantly higher [paired t-test] than the means obtained assuming a GCA of 38 weeks [CHL: 38.5 weeks].

Prediction of Birth Characteristics Assuming Growth Cessation

As seen in Table 2, systematic prediction errors [mean % Diff] were greater [exception: AC] in the larger sample compared to those from the smaller samples when sample-specific Rossavik growth model specification procedures [sMSP] were used with the current sample. No major changes in systematic errors were seen when previously published Rossavik growth model specification procedures [pMSP] were used with this sample, although all mean values were significantly different [paired t-test] from those obtained with sMSP. Comparisons of sMSP means to zero (t-test) indicated that there were significant systematic errors for AC, ThC and ArmC, leading to Correction Factors of 0.897, 0.883, and 0.843, respectively.

Table 2 also shows that the sMSP random prediction errors were similar to pMSP random prediction errors, as well as with the previously published random prediction errors, for HC, AC, and CHL. Those for ThC were considerably larger. As expected, random prediction errors were larger for soft tissue parameters [ThC, ArmC] than for skeletal parameters [HC, CHL].

The sample-specific weight estimation function derived from the subsample of 50 had the following form:

$$\mathrm{EWT}=0.543\,[3.2183\,(\mathrm{MA}-\mathrm{SP}_{\mathrm{Hcube}})^{(-0.0014+0.0008\,(\mathrm{MA}-\mathrm{SP}_{\mathrm{Hcube}}))}]\,\mathrm{Hcube}+0.457\,[2.7174\,(\mathrm{MA}-\mathrm{SP}_{\mathrm{Acube}})^{(-0.2+0.0033(\mathrm{MA}-\mathrm{SP}_{\mathrm{Acube}}))}]\,A$$

where MA (menstrual age) is the fetal age at the time of the scan, and SP is the parameter specific Start Point. The mean Percent Difference for the subsample was 0.22% with a SD of ± 10.4%.

Table 3 presents the results for the more complex procedure needed to predict birth weight [WT]. Since WT cannot be predicted directly as can other parameters, specific anatomical parameters [Hcube, Acube, BPD, AC and TVol] must first be predicted then converted to a predicted WT using appropriate weight estimation functions, This process has been designated a Sequence. As can be seen in Table 3, there is an interaction between the anatomical prediction procedure and the weight estimation function in those cases where Hcube and Acube were used. If both aspects of the WT prediction process are developed in the same population, systematic prediction errors are smaller and not statistically different. Random prediction errors were similar but the difference was statistically significant. Mixed sequences had significantly higher systematic and random prediction errors, the former being significantly different from each other but not the latter. For Sequence 5 [BPD, AC, TVol (18)], the systematic prediction error was significantly different from those of other sequences except Sequence 2. The random prediction error for this sequence was significantly smaller than those of the other four sequences. However, none of the combinations studied gave results similar to those found previously using Sequence 1 in a sample of 25 (23). As the systematic prediction error for Sequence 1 and 2 [Table 3] were not significantly different from zero (t-test), no correction factors are needed. However, correction factors of 0.927, 1.103 and 1.041 were required for Sequences 3, 4 and 5 since significant systematic prediction errors were found.

Growth Potential Realization Index Reference Ranges

Tables 4a and 4b present GPRI values obtained in this sample with sample-specific growth model specification procedures and their associated correction factors. Mean values were close to 100% for all parameters but differences from 100% were statistically significant [t-test] for AC, ThC, ArmC and WT [Sequences 3, 4, 5]. The 95% ranges were very similar to those obtained in smaller samples except for WT [ranges considerably larger for all 5 sequences]. The range for Sequence 5 was the smallest while that for Sequence 4 was the largest.

DISCUSSION

Growth Cessation in Late Pregnancy

Human growth is often considered to be a continuous process although frequent, serial pediatric measurements have documented periods of discontinuous or pulsatile growth in most normal infants up to 21 months of age (24,25). These observations support a two-stage hypothesis describing short time duration events [saltations] that are associated with longer

refractory periods [stasis] (26). In the fetus, Bernstein et al. (27) have described prolonged periods (≥ 2 weeks) without measurable growth for BPD, AC, FDL and HDL when measurements were made at 2.7 day intervals between 25 and 36 weeks, MA.

Our results indicate that a similar period of fetal growth stasis occurs during late pregnancy. This observation should be considered in determining optimal methods for predicting neonatal birth characteristics. The application of this fundamental concept to a three-parameter weight estimation function (BPD, AC, TVol) resulted in the lowest random prediction errors [2 SD: 16.5%] even for weight predictions made approximately 14 weeks before delivery. This special case of growth stasis [‘fetal growth cessation’] was originally proposed for weight by Rossavik et al in 1988 (28). Deter and colleagues (9,15) subsequently extended this concept to other fetal growth parameters (HC, AC, ThC and CHL). As described above, Growth Cessation Age [GCA] is defined as the prediction age when the linear slope of Percent Difference versus Birth Age curve is not significantly different from zero. If premature selection of GCA is made, actual measurements become larger due to continued growth while predicted measurements at the premature GCA remain the same, producing % Difference values that are increasingly negative. Conversely, after the true GCA the actual measurements do not increase but the predicted values become larger if predicted at a later GCA since Rossavik model predictions have no upper limit. This results in % Difference values that become increasingly positive. Only selection of an appropriate GCA gives a zero slope and a random distribution of % Difference values for fetuses delivering after the true GCA..

Previous studies by Deter and colleagues (9,15) indicated that the GCA for HC, AC, ThC, CHL and WT was 38 weeks, MA. GCA values of 39.5 weeks, MA, for HC, CHL and WT were found in a Dutch population by Kurniawan et al (20,21,22) In this large sample of normally growing fetuses, growth cessation was identified in all six parameters measured at birth, the GCA being 38 weeks except for the CHL [38.5 weeks]. If one focuses on the period between 38 weeks and delivery [Figure 1], the differences in Percent Difference distributions associated with assuming growth cessation at the GCA or Growth-To-Delivery [GTD] are clearly demonstrated. With the former assumption, the Percent Differences are randomly distributed around the regression line and no systematic change of Percent Differences with Birth Age is seen. With the latter assumption, Percent Differences increase with Birth Age. As postulated by Rossavik et al (28), this period of limited growth may be required to permit energy diversion to support other changes [e.g. terminal cell differentiation (29)] needed for postnatal life. If growth cessation does not occur, macrosomia can result even in normally growing fetuses (30).

Prediction of Birth Characteristics

Establishment of Growth Cessation Age permits reliable predictions of birth characteristics. Those obtained with IGA are corrected for differences in growth potential and age at delivery, as well as growth cessation and systematic prediction errors. As can be seen in Table 2, the results obtained are very similar for HC, AC, and CHL regardless of differences in population, sample size and model specification procedures. Model specification differences do not affect predictions of ThC but the increase in sample size did increase the

random prediction error [the previous ThC sample is part of the current sample], suggesting that the smaller sample was not representative.

Differences in population, sample size and model specification procedures did affect the WT predictions. WT is the only parameter not directly predicted but estimated using a complex function involving the predicted anatomical parameters [Hcube, Acube, BPD, AC, TVol]. The original weight estimation function using Hcube and Acube was derived from Houston and Oslo, Norway samples (16) and may not be optimal for the Detroit area sample. Better results were obtained using previously published anatomical prediction procedures and weight estimation function [Sequence 1, Table 3] compared to sample specific model specification procedures and previously published weight estimation function [Sequence 3, Table 3]. This suggests a link between prediction procedures and the weight estimation functions. Use of sample-specific procedures for both anatomical prediction and weight estimation [Sequence 2, Table 3] gave improved weight estimates. Previously published prediction procedures combined with the sample-specific weight estimation procedure [Sequence 4, Table 3] gave worse weight estimates. With the exception of 4 subjects, the results indicate that a relationship between anatomical prediction methods and weight estimation functions exists if based on Hcube and Acube. However, use of sample-specific methods for both aspects of weight prediction [Sequence 2, Table 3] did not produce the best predicted weight estimates. This is surprising since previous work with polynomial weight estimation functions have shown that sample-specific coefficients significantly improves weight estimates (18). In comparing the characteristics of the two Hcube-Acube functions for weight estimation used in this investigation, two important differences were found. The Houston method gives more importance to the Acube and its component estimates were obtained by iterative regression analysis using both cross-sectional and longitudinal data sets. The sample-specific method gives more importance to the Hcube and the component estimates were obtained simultaneously using Maximum Likelihood analysis. These differences may be responsible for the results obtained in the current investigation. However, it is unlikely that differences in sample characteristics are the cause since the Houston methods have given weight estimates with similar accuracy in a Dutch population (22).

The best results for predicting birth weight were obtained using sample specific model specification procedures for BPD, AC and TVol, together with the polynomial function of Lee et at (18). This function was developed for the same population as that studied longitudinally in this investigation although a cross-sectional sample was used. In a cross-sectional sample, the most accurate weight estimations had a systematic error of 0.1% and a 2 SD random error of 13.2%. These values are comparable to the weight prediction errors reported previously using 2nd trimester Rossavik models for Hcube and Acube (23). The cross-sectional sample was much larger [138 versus 25 subjects] and the interval from prediction to delivery much shorter [within 4 days versus approximately 14 weeks]. These two factors, affecting the prediction process in opposite directions, may have canceled each other's effect. In the current longitudinal study, the larger sample would be expected to increase birth weight prediction variability, as seen in Table 3. In any case, it is clear that Sequence 5 (BPD, AC, TVol) was the optimal procedure for obtaining birth weight predictions.

Relatively few previous publications describe data on the prediction of birth characteristics remote from term. No publications for AC, ThC and ArmC are currently available and only one for HC (21) and CHL (20). The HC and CHL studies used IGA methods similar to those in this study and were carried out on a sample of 50 Dutch fetuses/neonates. For HC, the systematic prediction errors [mean: −0.2% vs. −0.01%] were similar but random prediction errors [2 SD: +/−3.8% vs. +/− 8.0%] were lower than in the current study, probably due to sample differences. The values for CHL were 0.9% vs. 0.6% and +/−6.6% vs. +/− 7.6% for the systematic and random prediction errors, respectively.

For WT, there are 8 published investigations, two using IGA procedures (22, 23), two using the scan-to-delivery interval as an independent variable in the weight estimation function (31,32) and four using methods that assume constant growth along cross-sectional size percentile lines in the 3rd trimester (33,34,35,36). The two previous IGA studies, using measurements obtained before 28 weeks, MA and correcting for growth potential, age at delivery and growth cessation, gave similar systematic [mean: 2.3%, 1.7% vs. − 4.1%] and random errors [2 SD: 18.6%, 12.0% vs. 16.5%] prediction errors. The samples in these studies were smaller [50, 25] and came from different populations [Holland, Houston]. The two scan-to-delivery interval studies, predicting only from around 35 weeks, gave similar systematic [mean: −4.2%, −3.6% vs. −4.1%] but larger random [2 SD: 20.2%, 21.4% vs. 16.5%] prediction errors. The four investigations based on the assumption of constant percentile growth from 33–37 weeks to delivery found systematic prediction errors ranging from −0.1% to 8.5% and random prediction errors ranging from 16% to 30%. Similar results were obtained by Santonja-Lucas (34) for predictions made before 30 weeks, MA, in smaller samples. The differences between studies made direct comparisons difficult.

Growth Potential Realization Indices

The Growth Potential Realization Index (GPRI) is the most meaningful measure of size at birth because it is independent of the two principal confounding variables, namely differences in growth potential and birth age. It also corrects for systematic prediction errors and growth cessation. GPRI's can be determined for any anatomical parameter that is measured prenatally and postnatally [HC, AC, ThC, ArmC] or estimated from other prenatal measurements [CHL, WT]. As seen in Table 3, the mean GPRI values for all anatomical parameters were very close to 100% and the ranges were reasonably symmetrical around 100%. This would be expected in a group of neonates with normal growth outcomes where good agreement between actual and predicted birth characteristics is likely. Despite the many differences between the current study and those done previously (13,15,37), the GPRI means and ranges were quite similar for HC, ThC and CHL. The range for AC is more symmetric in the current study, suggesting that the sample studied previously (37) was not representative. For WT, a substantial increase in range was seen in the larger sample regardless of Sequence studied. The ranges were smaller and the mean values closer to 100 when there was consistency between the anatomical prediction procedure and the weight estimation function [Sequences 1, 2, 5]. However, the narrowest range was obtained with Sequence 5 so it is recommended for WT prediction.

CONCLUSIONS

Fetal growth cessation prior to delivery was clearly demonstrated for all anatomical parameters studied in newborns with normal growth outcome. This concept should be taken into consideration whenever remote predictions of neonatal birth characteristics are being carried out. Predictions of birth characteristics were similar [HC, AC, CHL] or showed greater variability [ThC, WT] to those obtained with smaller samples. The optimal prediction of WT was obtained with the less complicated method of Lee et al (18). GPRI standards were essentially the same [HC, ThC, CHL] or better [AC], except for WT, in this large sample. These results, obtained on a sample 4 – 6 fold larger than those used previously, provide more reliable standards for the evaluation of neonatal size parameters on an individualized basis..

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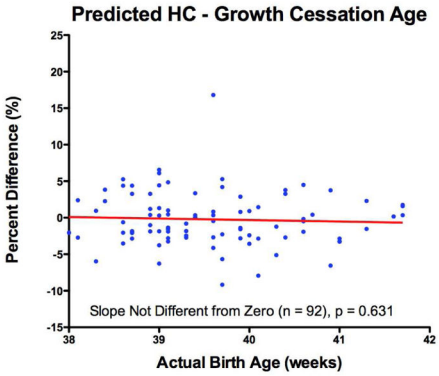

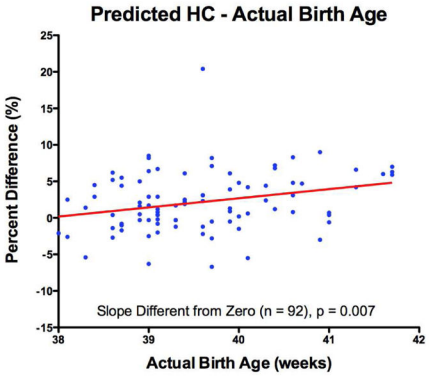

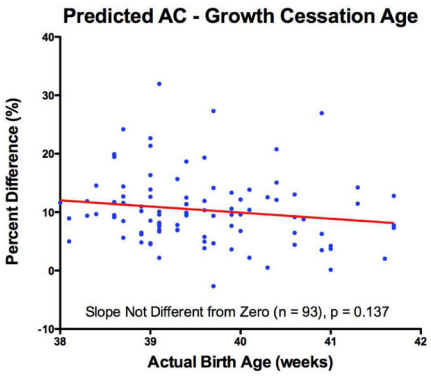

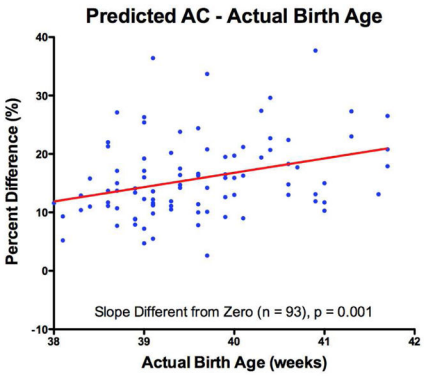

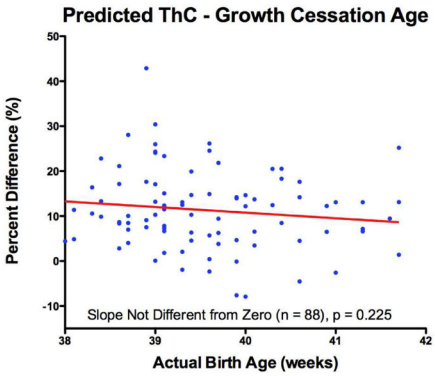

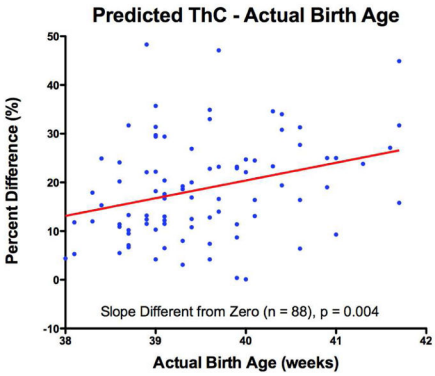

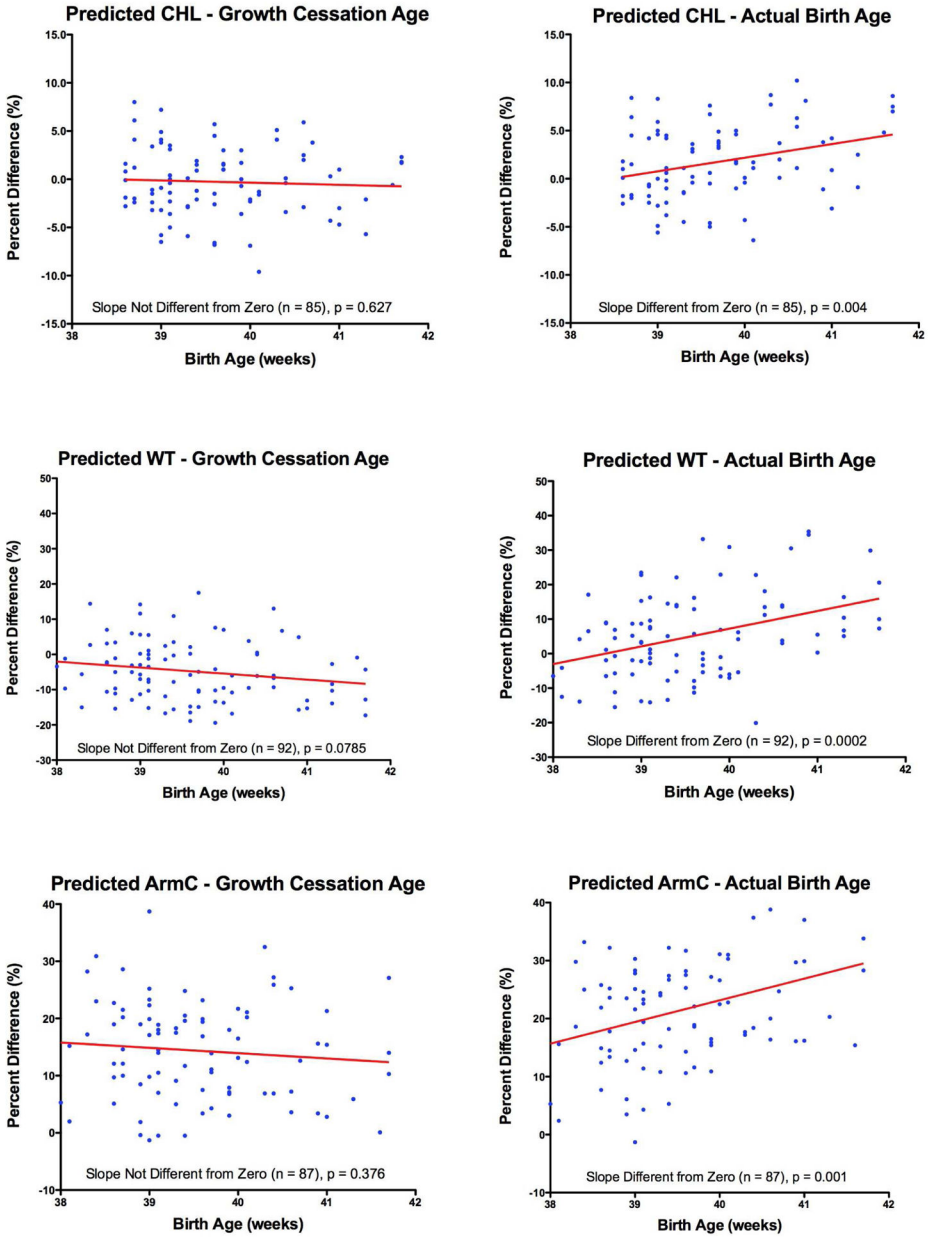

Figure 1.

Percent Difference versus Birth Age Assuming Growth Cessation or Growth to Delivery. Percent Differences [{{predicted − actual}/actual} × 100] for six birth characteristics, assuming either growth cessation at 38 weeks, MA [CHL: 38.5 weeks]{left panel}, or growth to delivery {right panel). The period studied is from the growth cessation age to the maximum delivery age. The number of observations and the comparison of the linear slope to zero are given at the bottom of each subfigure. Sequence 5 was used for WT. (HC = head circumference; AC = abdominal circumference; ThC = mid-thigh circumference; CHL = crown-heel length; WT = weight; ArmC = mid-arm circumference).

Table 1a

GROWTH CESSATION AGE

Parameter.	N.	Linear Regression.		Percent Differences[1].		
		Slope	P-value[1]	Mean	P-value[2]	SD
		%Diff/wk		%		%
HC-38[3]	117	−0.45	ns	0.0	ns	4.0
AC-38	118	−0.41	ns	10.3	0.0001	5.7
ThC-38	113	−0.71	ns	11.7	0.0001	8.6
CHL-38	117	−0.60	0.009	−0.6	ns	3.5
-38.5		−0.38	ns	0.08	ns	3.4
WT-38	117	−0.94	ns	7.3	0.0001	11.8
ArmC-38	112	−0.02	ns	15.0	0.0001	8.7

[1] Percent Differences [%Diff]: %Diff = {{predicted. − actual)/actual] × 100

[2] comparison of slope or mean with zero; ns: p-value > 0.05

[3] number indicates the growth cessation age used, in menstrual weeks

Table 1b

GROWTH CESSATION AT 38 WEEKS versus AT DELIVERY

Parameter	N	Growth Cessation at 38 Weeks[1]				Growth Cessation at Delivery			
		Slope	P-Value[2]	% Diff		Slope	P-Value[2]	% Diff	
				M	SD			M	SD
		%Diff/wk		%	%	%Diff/wk		%	%
HC	92	−0.48	ns	−0.2	3.7	1.25	0.007	2.1	4.0
AC	93	−1.20	ns	10.4	6.1	2.45	0.001	15.8	6.8
ThC	89	−1.25	ns	11.3	8.8	3.64	0.003	18.6	10.3
CHL	85	−0.23	ns	0.3	3.6	1.42	0.004	1.7	3.9
WT	92	−2.24	ns	6.7	11.9	8.23	0.001	21.5	16.2
ArmC	87	−0.93	ns	14.4	8.6	3.73	0.001	21.5	9.6

[1] growth cessation was at 38.5 weeks for CHL

[2] comparison of slope or mean with zero; ns: p-value greater than 0.05

Table 2

SYSTEMATIC AND RANDOM BIRTH CHARACTERISTIC PREDICTION ERRORS

Parameter.	N.	sModel Specification[1].		pModel Specification[1]		N.	pModel Specification	
		Systematic	Random	Systematic	Random		p Systematic	pRandom
		%	%	%	%		%	%
HC	117	0.0	−6.3 to 6.3	0.5	−6.6 to 6.4	20	1.1	−4.9 to 4.8
AC	118	10.3	−8.3 to 13.9	10.7	−12.5 to 13.3	20	17.3	−11.2 to 6.2
ThC	113	11.7	−14.3 to 16.4	10.1	−16.8 to 16.8	30	8.9	−9.5 to 9.5
CHL	117	0.1	−6.8 to 6.8	3.8	−7.6 to 7.6	20	−0.1	−6.0 to 6.0
ArmC	113	15.7	−17.4 to 17.4	15.1	−19.0 to 19.0	--	--	----

s – sample-specific for Detroit area sample: p - previously published [References # 10,13,15,37]

[1]The same Detroit area sample was used for first 2 model specification procedures

Systematic: mean of Percent Differences

Random: zero-mean based 95% Percent Difference range [2 SD range following subtraction of the mean prediction error from both the upper and lower limits of the original 2 SD range]

Table 3

EFFECTS OF ANATOMICAL PARAMETER PREDICTION PROCEDURES AND WEIGHT ESTIMATION FUNCTIONS ON BIRTH WEIGHT PREDICTION

Sequence[1]	N	Anatomical Measure Prediction Procedure	Weight Estimation Function	Systematic Error[2]	Random Error[2]
				%	%
1	117	previously published[3]	previously published[4]	−0.2	−19.7 to 19.7
2.	117	sample specific	sample specific	−2.1	−21.7 to 21.7
3	117	sample specific	previously published[4]	7.3	−23.5 to 23.5
4	117	previously published[3]	sample specific	−10.3	−20.8 to 20.8
5	117	sample specific	previously published[5]	−4.1	− 16.5 to 16.5
previously published[6]	25	previously published[3]	previously published[4]	−1.7	−9.6 to 13.6

[1] Sequence refers to the 2-step process of anatomical parameter prediction followed by weight estimation

[2] See footnote of Table 2 for definition;

[3] Reference #12;

[4] Reference #16;

[5] Reference #18;

[6] Reference #23 ANOVA and Tukey's Pairwise Comparison tests showed that all systematic errors were significantly different from each other with 2 exceptions: Sequence 1 vs. Sequence 2 and Sequence 2 vs. Sequence 5. The Correlated Variance tests indicated that the Random Error for Sequence 5 was significantly different from those for the other four Sequences. The Random Error for Sequence 1 differed from those for Sequences 2 and 3.

Table 4a

GROWTH POTENTIAL REALIZATION INDEX VALUES

Parameter.	N.	GPRI.		N.	pGPRI[1].	
		Mean	95% Range		Mean	95% Range
		%	%		%	%
HC	117	100	94 – 107	20	99	95 – 105
AC	118	101	90 – 110	20	103	97 – 109
ThC	113	102	87 – 117	30	102	88 – 118
CHL	117	100	94 – 106	20	100	94 – 106
ArmC	112	103	87 – 119	--	---	----

[1] References #10,13,15,37

Table 4b

GROWTH POTENTIAL REALIZATION INDEX VALUES FOR WEIGHT

Sequence[1]	N	GPRI.		N.	GPRI[2].	
		Mean	95% Range		Mean	95% Range
		%	%		%	%
1	117	101	81 – 121	20	100	92 – 108
2	117	101	80 – 120	--	---	----
3	117	102	82 – 126	--	---	----
4	117	102	78 – 126	--	---	----
5	117	101	84 – 118	--	---	----

[1] See Table 3 for definition of Sequences;

[2] Reference #37