Fetal growth velocity and body proportion in the assessment of growth

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Fetal growth restriction implies failure of a fetus to meet its growth potential and is associated with increased perinatal mortality and morbidity. Therefore, antenatal detection of fetal growth restriction is of major importance in an attempt to deliver improved clinical outcomes. The most commonly used approach towards screening for fetal growth restriction is by means of sonographic fetal weight estimation, to detect fetuses small for gestational age, defined by an estimated fetal weight <10th percentile for gestational age. However, the predictive accuracy of this approach is limited both by suboptimal detection rate (as it may overlook non-small-for-gestational-age growth-restricted fetuses) and by a high false-positive rate (as most small-for-gestational-age fetuses are not growth restricted). Here, we review 2 strategies that may improve the diagnostic accuracy of sonographic fetal biometry for fetal growth restriction. The first strategy involves serial ultrasound evaluations of fetal biometry. The information obtained through these serial assessments can be interpreted using several different approaches including fetal growth velocity, conditional percentiles, projection-based methods, and individualized growth assessment that can be viewed as mathematical techniques to quantify any decrease in estimated fetal weight percentile, a phenomenon that many care providers assess and monitor routinely in a qualitative manner. This strategy appears promising in high-risk pregnancies where it seems to improve the detection of growth-restricted fetuses at increased risk of adverse perinatal outcomes and, at the same time, decrease the risk of falsely diagnosing healthy constitutionally small-for-gestational-age fetuses as growth restricted. Further studies are needed to determine the utility of this strategy in low-risk pregnancies as well as to optimize its performance by determining the optimal timing and interval between exams. The second strategy refers to the use of fetal body proportions to classify fetuses as either symmetric or asymmetric using 1 of several ratios; these include the head circumference to abdominal circumference ratio, transverse cerebellar diameter to abdominal circumference ratio, and femur length to abdominal circumference ratio. Although these ratios are associated with small for gestational age at birth and with adverse perinatal outcomes, their predictive accuracy is too low for clinical practice. Furthermore, these associations become questionable when other, potentially more specific measures such as umbilical artery Doppler are being used. Furthermore, these ratios are of limited use in determining the etiology underlying fetal smallness. It is possible that the use of the 2 gestational-age-independent ratios (transverse cerebellar diameter to abdominal circumference and femur length to abdominal circumference) may have a role in the detection of mild-moderate fetal growth restriction in pregnancies without adequate dating. In addition, despite their limited predictive accuracy, these ratios may become abnormal early in the course of fetal growth restriction and may therefore identify pregnancies that may benefit from closer monitoring of fetal growth.

Key words: conditional percentiles, growth, individualized growth, serial, velocity

Background

The term "fetal growth restriction" (FGR) implies failure of a fetus to meet its growth potential. However, given the difficulty in determining the growth potential of the individual fetus, the definition of FGR is challenging and is often based on a combination of measures of fetal size and abnormal Doppler studies.[1-5]

FGR is associated with excess perinatal mortality and morbidity.[6-11] Accordingly, improved detection of FGR has been identified as 1 of the top-10 interventions needed to reduce the global burden of stillbirth.[12] Although various tools are available to screen for FGR, including maternal obstetric history[13,14] and serum markers,[15-21] the most commonly screening approach is through sonographic fetal weight estimation to detect fetuses that are small for gestational age (SGA), defined empirically as an estimated fetal weight (EFW) <10th percentile for gestational age.[22-26] This approach, however, has a high false-positive rate for FGR, as the majority of SGA fetuses are healthy constitutionally small fetuses rather than growth restricted.[25] Furthermore,

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the detection rate of this approach is also limited given that it may overlook those fetuses with impaired growth even though EFW still remains >10th percentile.[27] Thus, additional measures, mindful of the need to identify failure to achieve individual growth potential, are needed to establish effective screening for FGR.

In the current article we will review 2 strategies that may improve the diagnostic accuracy of sonographic fetal biometry for FGR: (1) use of serial ultrasound evaluations to assess fetal growth; and (2) assessment of fetal body proportions.

The use of serial ultrasound evaluations to assess fetal growth

One strategy to improve the diagnosis of FGR is through the use of serial ultrasound evaluations. This approach is intuitive and emphasizes the idea that FGR should be viewed as a process rather than a point event. Indeed, the validity of this concept has already been established in infants, where it was shown that growth velocity is more predictive of size later in life than any single cross-sectional measurement of infant size.[28] However, the optimal approach to interpret the information obtained from serial measurements of the same fetus remains unclear.

Interpretation of serial sonographic assessments of fetal biometry

Several approaches are available for the interpretation of serial measurements of fetal biometry including fetal growth velocity, conditional percentiles, projection-based methods, and individualized growth assessment (IGA).

Fetal growth velocity. Fetal growth velocity is defined as the change in fetal size between 2 time points during gestation.[29,30] This approach can be applied to the change in either a specific fetal biometric index (eg, abdominal circumference [AC] or biparietal diameter [BPD]) or in EFW, and is usually expressed as change in absolute value of the biometric index per time unit (eg, mm/wk or g/d) or as a change in z-score (ie, the value of the biometric index normalized for gestational age) per time unit (known as z-velocity) (Figure 1, A).[31]

Several standards for fetal growth velocity have been published.[29,32-36] The methodology used to generate growth velocity standards differs considerably between studies, and can be grossly divided into 2 types. The first and most commonly used methodology, often referred to as "average growth velocity," is based on direct measurement of fetal size on ≥2 time points along gestation. The average growth velocity is calculated by dividing the difference in fetal size by the time interval between the 2 time points. In the case of >2 sets of measurements, the average growth velocity can be calculated using linear regression. Obviously, this approach is based on the assumption that fetal growth is linear throughout the time interval being studied. For example, Guihard-Costa et al[34] used a set of cross-sectional and longitudinal data to calculate the growth velocity rate of 3 biometric indices within individual 3-week intervals between 7-40 weeks. Subsequently, Bertino et al[36] used 2-stage linear model to generate growth velocity standards for 5 biometric indices based on 6- or 10-week intervals. Owen et al,[29] in a longitudinal study of 274 low-risk women, calculated the mean growth velocity for several biometric indices and EFW across 4-week intervals, and used a quadratic equation to model the mean and SD of the growth velocity of the various indices and EFW across these intervals. Others used cross-sectional data to generate growth velocity standards based on the difference between birthweight and the median EFW at 20 weeks,[32] and between sonographic AC at 36-20 weeks of gestation.[33]

The second methodological approach for the calculation of fetal growth velocity is known as "instantaneous growth velocity" and was used by Deter and Harrist[35] in a longitudinal study of 20 fetuses. In that study, the authors generated growth velocity standards for BPD, head circumference (HC), AC, and femur length (FL) based on the Rossavik growth model, which describes the change of the individual biometric index as a function of gestational age using the following function: $I = c(t)^{k+s(t)}$ (where I represents the individual biometric index; t represents gestational age; and c, k, and s are the model coefficients). The instantaneous growth velocity was calculated using the first derivative of the Rossavik growth model by gestational age (dI/dt), which provides the instantaneous growth velocity at gestational age t. This approach may be more accurate for the generation of growth velocity standards since, in contrast to the average growth velocity approach, it is not limited by the assumption that fetal growth is linear within a given time interval.

Conditional percentiles. An alternative approach towards the interpretation of serial measurements of fetal biometry is through the calculation of conditional percentiles.[37-42] The underlying concept is that the calculation of EFW percentile takes into account (or is conditioned on) previous weight estimation of the same fetus earlier in pregnancy. Thus, the first weight estimation (or the conditioning scan) is used to adjust the standard growth curve to the expected growth trajectory of the individual fetus, and the EFW percentile at the time of the subsequent exam is determined based on this new adjusted curve, which is narrower and shifted toward the initial percentile compared with the original standard growth curve (Figure 1, B). This approach is based on multilevel modeling that takes into account the variability in growth within and between fetuses.[37,39]

Projection-based methods. Projection-based methods use linear mixed-effects models to predict EFW at a later point in gestation based on ≥2 observations of EFW and are a way to combine size and velocity information (since both the start value as well as rate of growth over time are factored into the projection).[43,44] A projected EFW below a fixed cut-off (eg, 5th or 10th percentile for gestational age) can then