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Sonographic Assessment of Fetal Growth Abnormalities

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Abbreviations: AC = abdominal circumference, BPD = biparietal diameter, CRL = crown-rump length, DFE = distal femoral epiphysis, EDD = estimated date of delivery, EFW = estimated fetal weight, FGR = fetal growth restriction, GA = gestational age, LMP = last menstrual period, MSD = mean sac diameter, PHE = proximal humeral epiphysis, PTE = proximal tibial epiphysis, TCD = transcerebellar diameter, UA = umbilical artery

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SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

- Accurately date a pregnancy in any trimester.
- List the terminology used to describe abnormal fetal growth.
- Describe the roles of Doppler US and other examinations of fetal well-being in the management of growth restriction.

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Fetal growth abnormalities have significant consequences for pregnancy management and maternal and fetal well-being. The accurate diagnosis of fetal growth abnormalities contributes to optimal antenatal management, which may minimize the sequelae of inadequate or excessive fetal growth. An accurate diagnosis of abnormal fetal growth depends on accurate pregnancy dating and serial growth measurements. The fetal size at any given stage of pregnancy is either appropriate or inappropriate for the given gestational age (GA). Pregnancy dating is most accurate in the first trimester, as biologic variability does not come into play until the second and third trimesters. The authors describe the determination of GA with use of standard US measurements and how additional parameters can be used to confirm dating. Once dates are established, serial measurements are used to identity abnormal growth patterns. The sometimes confusing definitions of *abnormal growth* are clarified, the differentiation of a constitutionally small but healthy fetus from a growth-restricted at-risk fetus is described, and the roles of Doppler US and other adjunctive examinations in the management of growth restriction are discussed. In addition, the definition of *selective growth restriction* in twin pregnancy is briefly discussed, as is the role of Doppler US in the classification of subtypes of selective growth restriction in monochorionic twinning. The criteria for diagnosing macrosomia and the management of affected pregnancies also are reviewed. The importance of correct pregnancy dating in the detection and surveillance of abnormal fetal growth and for prevention of perinatal maternal and fetal morbidity and mortality cannot be overstated.

The online slide presentation from the RSNA Annual Meeting is available for this article.

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Introduction

Confirmation of gestational dating and assessment of fetal growth are essential components of an obstetric US examination. Undetected fetal growth abnormalities may be associated with significant morbidity and mortality, and recognition of these problems is of paramount importance. Without correct gestational dating, fetal growth restriction (FGR) or excessive fetal growth is challenging to detect. Accurate diagnosis of fetal growth abnormalities contributes to optimal antenatal management, which may minimize the sequelae of inadequate or excessive fetal growth. As such, current guidelines in the United States recommend that every pregnant person undergo second-trimester US for anatomic evaluation and confirmation of dating at 18–22 weeks gestation (1). In this article, we review current standards for establishing gestational age (GA) and performing fetal growth evaluation. While we recognize that debate regarding how to mathematically define growth abnormalities (eg, by using percentiles

TEACHING POINTS

- Confirmation of gestational dating and assessment of fetal growth are essential components of an obstetric US examination.
- There is a critical difference between assessing size (a one-time measurement) and assessing growth (a serial assessment of size).
- Because constitutional and pathologic factors affect early embryonic growth the least, the accuracy of US for gestational dating is highest in early pregnancy and diminishes with advancing GA. Therefore, the dates established with first-trimester US should not be altered by future US examinations. However, review of the original images is preferable, whenever possible, for evaluating the measurement technique and ensuring accuracy.
- Fetal size, as defined on the basis of estimated fetal weight (EFW), is relevant only in the context of GA; size is either appropriate (within the 10th–90th percentiles) or inappropriate (small or large) for the given GA.
- A detailed sonographic assessment aids in the difficult task of separating fetuses with an EFW lower than the 10th percentile into those who are physiologically small but healthy and those who are pathologically growth restricted and therefore at risk for perinatal morbidity and mortality.

or standard deviations) continues, resolving this debate is beyond the scope of this review.

Epidemiologic studies tie fetal growth abnormalities to numerous short- and long-term sequelae. For instance, pathologic FGR (ie, with suboptimal delivery of oxygen and nutrients to the fetus, resulting in less than expected growth) may prompt cardiovascular remodeling and other developmental adaptations that protect the fetus in utero but increase the risks of neonatal morbidity and long-term health consequences (2,3). FGR is associated with stillbirth, prolonged neonatal hospitalization, feeding and respiratory difficulties, abnormal brain development, long-term cardiovascular disease, developmental delay, and early mortality (4).

On the other hand, fetal macrosomia may lead to maladaptive endocrinologic and cardiovascular responses. Large fetuses, especially those of diabetic mothers, have different body proportions, fat deposition, and metabolic profiles, resulting in increased risks of shoulder dystocia and neonatal hypoglycemia (5,6). In the long term, macrosomia or large-for-GA birth weight may confer increased risks of childhood obesity, insulin resistance, or overt diabetes, all of which contribute to poorer health (5,7).

The costs of abnormal fetal growth include financial and socioemotional costs to individuals, families, health care systems, and communities. Increased costs begin in the antenatal period and are compounded throughout neonatal life and beyond. FGR frequently results in preterm birth, with associated costs, as well as expenses related to readmissions and long-term health management (8,9). It is also important to note the social costs of lost productivity at home and work among the parents of infants with extensive medical needs (10).

While obstetric sonography itself cannot be used to alter or treat FGR or excessive fetal growth, an accurate diagnosis can help avoid unnecessary intervention and spur appropriate actions to avert further complications. An inaccurate diagnosis of FGR can lead to iatrogenic preterm delivery with the associated morbidities of preterm birth. However, failure to detect FGR could result in intrauterine demise of a potentially salvageable infant. Accurate diagnosis of abnormal fetal growth depends on accurate pregnancy dating and serial growth assessment because there is a critical difference between assessing size (a one-time measurement) and assessing growth (a serial assessment of size). In this article, we review the various definitions of *fetal growth abnormality*, the critical importance of accurate gestational dating, and the appropriate surveillance of suspected fetal growth abnormalities.

Gestational Dating: Why, When, How

Gestational dating provides a measurement of GA. Establishing the GA is a crucial task during the initial prenatal visit; accurate dates are necessary for genetic screening, timing the anatomic survey and US growth examinations, counseling regarding perinatal complications in the periviable period (22–25 weeks gestation), and timing the delivery. For instance, sonographic confirmation (or adjustment) of the estimated date of delivery (EDD) in the first trimester significantly reduces the number of postdate inductions (11). On the other hand, nondated or suboptimally dated pregnancies often prove to be challenging to manage.

Clinical Pregnancy Dating

The GA and EDD should be determined at the first prenatal visit, ideally in the first trimester, by using the last menstrual period (LMP) or assisted reproduction technology dating. In the absence of this information, US is used to establish the EDD. In vitro fertilization dates are based on a combination of blastocyst age and embryo transfer date. For example, the EDD for a 3-day-old embryo is 263 days from the embryo transfer date. In vitro fertilization–derived dates are nearly always confirmed by performing early US and should always be used clinically (12).

Gestational dating with use of the LMP requires *(a)* a known date of the LMP, *(b)* that the menstrual cycles occur regularly every 28

days, and *(c)* the absence of abnormalities (eg, abnormal bleeding, use of hormonal birth control) in the cycle immediately preceding conception. If these requirements are met, the due date is 280 days from the first day of the LMP. Even when these conditions are met, LMP dating introduces error because it assumes that ovulation invariably occurs on day 14 of a 28-day cycle (12). In addition, up to 50% of women do not know their LMP, and nearly half of all pregnancies in the U.S. are unplanned (13). In one randomized trial of US-based dating, 40% of women randomly assigned to undergo first-trimester US had altered dates owing to a discrepancy of greater than 5 days (14). When the LMP is unknown or does not fit the parameters noted above, first-trimester US should be used to corroborate or establish the gestational date (12).

Sonographic Dating in the First Trimester

Several studies (12,15–17) have demonstrated that first-trimester measurement of the crown-rump length (CRL) is highly accurate for pregnancy dating. In the first trimester, growth is most dependent on underlying embryologic events. As the fetus enters the second and especially the third trimesters of pregnancy, constitutional factors begin to influence the fetal growth trajectory (12). Simply stated, a fetus whose DNA is derived from parents of smaller stature will, by virtue of its genetic makeup, be smaller compared with the average population of fetuses of the same GA. A similar corollary exists for larger fetuses. In contrast, fetuses whose growth is compromised by aneuploidy, placental insufficiency, or overgrowth syndromes demonstrate a growth pattern that is not concordant with their anticipated or constitutional growth potential. Their abnormal size reflects the underlying anomaly.

Because constitutional and pathologic factors affect early embryonic growth the least, the accuracy of US for gestational dating is highest in early pregnancy and diminishes with advancing GA. Therefore, the dates established with first-trimester US should not be altered by future US examinations. However, review of the original images is preferable, whenever possible, for evaluating the measurement technique and ensuring accuracy. Commonly used US-based pregnancy dating criteria suggest that a discrepancy of greater than 5 days between the LMP- and US-derived dates is sufficient to change the EDD early in the first trimester. However, by 28 weeks, a discrepancy of greater than 21 days is required for this change (12).

Before the emergence of a visible embryo, the mean sac diameter (MSD) is used to estimate the GA. The MSD is the average of the orthogonal diameters of the gestational sac. The MSD lacks the accuracy of CRL measurements; therefore, many societies recommend deferring definitive dating until an embryo is visible (12,18). A gestational sac without any content represents a probable intrauterine pregnancy (IUP); a sac with a yolk sac or embryo, a definite IUP; and a sac with an embryo smaller than 7 mm without cardiac activity, a pregnancy of uncertain viability (19). For probable and definite IUP without an embryo, follow-up US is recommended to determine viability and definitively establish pregnancy dates (Fig 1) (20). Once an embryo is visible, the CRL is measured, and it alone (not a composite of CRL and MSD) is used to estimate the GA (Fig 2) (12,21). In cases of spontaneous twins (or other multifetal gestations), the CRL of the largest embryo or fetus should be used to establish dates in the first trimester (before 14 0/7 weeks [14 weeks, 0 of 7 days]) (22).

In addition to during scheduled first-trimester dating US, sonologists can encounter pregnancies in other settings such as in the evaluation of pelvic pain and bleeding. Emergency department visits can precede the first prenatal visit, and clinical or other pregnancy dates may not yet be established. At US scanning in these settings, the LMP and any size-date discrepancy should be documented to establish or corroborate pregnancy dates as early as possible.

Sonographic Dating in the Second Trimester

At 14 0/7 weeks (CRL, ~84 mm), the accuracy of the CRL for dating begins to decline owing to the technical challenges of visualizing the full length of the fetus and the increased possibility of measurement error due to fetal positioning (17). Given the increasing inaccuracy of US dating with advancing GA, a pregnancy in which US confirmation or GA revision occurs after 22 0/7 weeks should be considered suboptimally dated (12). Recommendations for adjusting gestational dating that take into consideration the standard deviation of biometric parameters at varying GAs can be found in American College of Obstetricians and Gynecologists Committee Opinion No 700: Methods for Estimating the Due Date (12). It is important to acknowledge that not all pregnant women present for care in the first trimester. For these women, many of whom have increased risk factors for poor obstetric outcomes, a systematic approach to corroborating or modifying the gestational dating at later points in the pregnancy has the potential to improve perinatal outcomes.

In the second trimester, GA assessment is based on standard biometric measurements of

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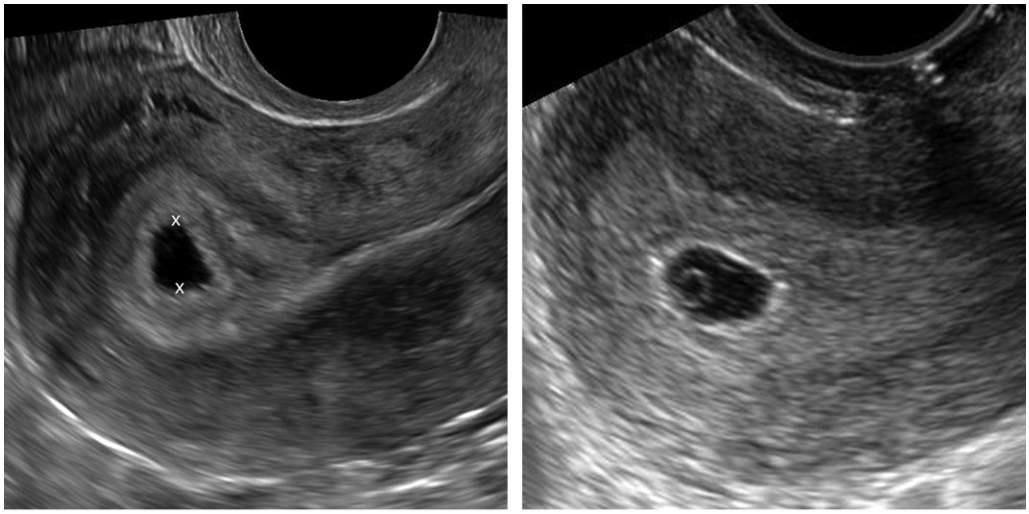


a. b.

Figure 1. Early first-trimester measurements and milestones. **(a)** US scan shows the MSD, which is the average of orthogonal diameters of the gestational sac measured from inner border to inner border. The MSD can be used to calculate the GA before an embryo is visible. An intrauterine sac–like structure without a yolk sac or embryo, as seen in this example, is described as a probable intrauterine pregnancy. Follow-up US is performed at 14 days, at which time a live embryo should be visible. **(b)** US scan shows an intrauterine sac–like structure with a yolk sac or embryo—that is, a definite intrauterine pregnancy. Follow-up US for assessment of a sac with only a yolk sac is performed at 11 days, at which time a live embryo should be visible. If an embryo with a CRL of less than 7 mm without cardiac activity is present, follow-up US is performed at approximately 7 days to ensure viability. Transvaginal US is preferred for accurate measurement.

head circumference, biparietal diameter (BPD), abdominal circumference (AC), and femoral diaphysis length (Figs 3–5) (18). In cases of multifetal gestation, the fetus with the larger head circumference should be used to establish the GA after 14 0/7 weeks (22). A number of formulas based on these standard parameters exist to estimate fetal weight and GA (23). Standard biometric measurements generally correlate well with clinical gestational dates and often are sufficient to confirm or adjust dating in many pregnancies. However, various circumstances can make standard fetal biometry less reliable. For instance, if a fetus has abnormalities such as ventriculomegaly or ascites, or if the mother presents late in pregnancy, standard biometry may yield a significantly overestimated or underestimated GA. In addition, if fetal growth abnormalities are suspected, additional anatomic parameters that corroborate the menstrual age are useful.

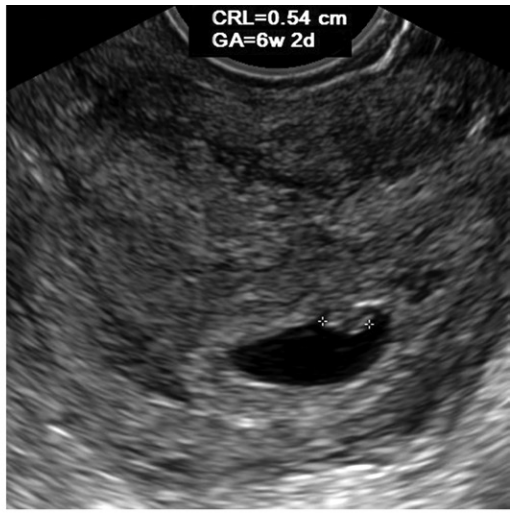
Adjuncts to Standard Biometry

Several fetal anatomic structures demonstrate consistent growth throughout the latter half of gestation, and measurements of these structures reliably correlate with GA. Of these measurements, transcerebellar diameter (TCD), foot length, renal length, and sacral length are among those for which there are published validated nomograms (24–27). In some instances, these structures maintain their relationship with GA even when growth abnormalities are present, making them particularly useful in those pregnancy cases in which growth abnormalities are suspected but the gestational dates are nonverified (Table 1) (28). Of note, TCD, renal length, and foot length nomograms are available at the open access website *www.perinatology.com*. Other sonographic markers such as epiphyseal ossification and fetal subcutaneous tissue measurement also may corroborate the GA. An important caveat is that adjunctive measures should be used only when the feature of interest is anatomically or structurally normal.

The TCD is easily measured in the axial oblique posterior fossa view that is used routinely during the anatomic survey (Fig 6). In euploid fetuses with a structurally normal cerebellum, the TCD has a log-linear correlation with GA and does not change with head shape. It is important to note that the GA-TCD correlation appears to be largely preserved in the settings of FGR and macrosomia (29,30). This finding is supported by human and nonhuman primate studies (31,32) that demonstrate the preservation of cerebellar blood flow in fetuses with growth restriction.

Fetal foot length is a commonly used sonographic and postnatal anatomic correlate to GA (Fig 7) (25,33). Although the fetal foot length is not exempt from the effects of global FGR, this measurement is particularly useful in the setting of other anomalies, such as anencephaly, ascites, and shortened long bones (eg, in skeletal dysplasia).

Renal size is another anatomic measurement that provides corroboration for gestational



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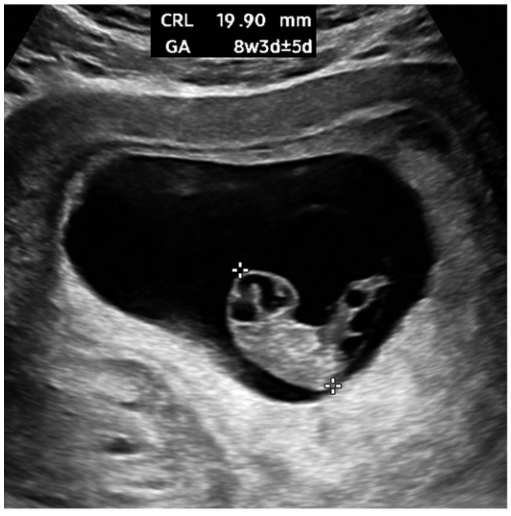

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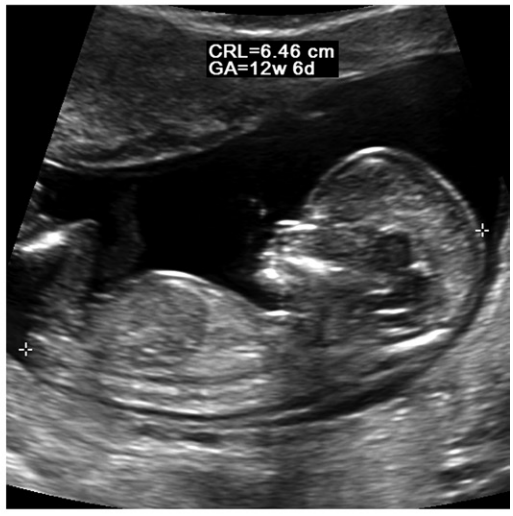

c.

Figure 2. CRL measurement. **(a)** US scan shows the CRL, which is the average of discrete fetal measurements from the tip of the head end to the tip of the rump end in the midsagittal plane of the embryo. The yolk sac is not included. **(b)** As the pregnancy advances, the embryo is easier to see, and accurate measurements can be obtained with transabdominal US. **(c)** US scan shows the fetus at the end of the first trimester, by which time the fetus has a recognizable human appearance. The maximal length in the craniocaudal direction is measured in a straight line (between the calipers), with the fetus in a neutral position, neither overly extended nor overly flexed, similar to the preferred positioning for nuchal translucency measurement.

dating. In the absence of renal anomalies or rare overgrowth syndromes such as Beckwith-Wiedemann syndrome, renal dimensions correlate well with GA (26,34). Renal length is measured in a longitudinal plane in the cephalocaudal direction and has a linear relationship with GA (Fig 8). Although the renal volume diminishes with FGR, the renal length remains relatively constant (34,35). Because of this constant relationship with GA, renal length, like TCD, can provide important adjunctive information regarding the GA, even in the setting of growth abnormalities. Renal length is easily measured in the third trimester, representing an important additional measurement at a point in pregnancy when the accuracy of standard fetal biometry decreases.

Sacral length also correlates linearly with gestational dates and appears to have a stable relationship with GA, even in the setting of growth abnormalities (27,36,37). This measurement is somewhat more technically challenging to perform than the other described measurements but is an important adjunct to standard biometry (Fig 9).

Ossification of the long bone epiphyses occurs in the third trimester. The staggered appearance of ossification centers provides insight into the likely ranges of GA. This is particularly useful in the setting of advanced gestation, when biometry is unreliable, and in cases of possible macrosomia or FGR, when there is concern for inaccurate dating (28). The DFE, PTE, and PHE have been studied most closely, with early work showing a close correlation between the appearance of ossification centers and the fetal lung maturity, as demonstrated at amniocentesis (38).

More recently, the appearance and even the measurement of the epiphyses have been correlated with GA. The DFE ossification center appears as a hyperechoic stippled or solid ovoid structure within the hypoechoic cartilaginous epiphysis of the distal femur at 32–33 weeks gestation (Fig 10). This ossification center is present

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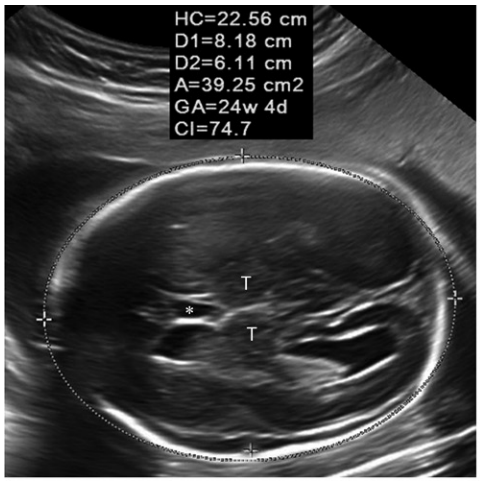

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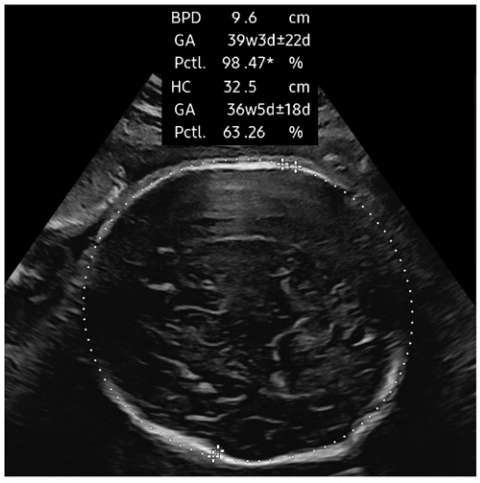

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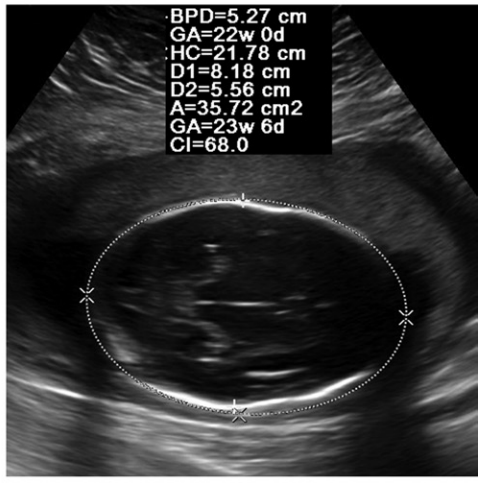


c.

Figure 3. Cranial biometry in three fetuses. *A* = area; *CI* = confidence interval; *D1* and *D2* = diameters 1 and 2, respectively; *HC* = head circumference. **(a)** US scan shows the BPD measured in the thalamic plane, with the cavum septi pellucidi (*) and thalami *(T)* in view. The cerebellum and orbits should not be visible, and the head circumference is oval. The BPD is measured with calipers on the outside of the superior bone edge and inside of the inferior bone edge, perpendicular to the falx cerebri and across the widest area, typically across the thalami. The head circumference is measured in the same plane, excluding the subcutaneous tissue (as opposed to the AC, which includes subcutaneous tissue). **(b, c)** Unlike the BPD, the head circumference is not greatly altered by brachycephaly (wide head, often with posterior flattening and increased BPD) **(b)** or dolichocephaly (boat-shaped cranium with decreased BPD) **(c)**. *Pctl.* = percentile.

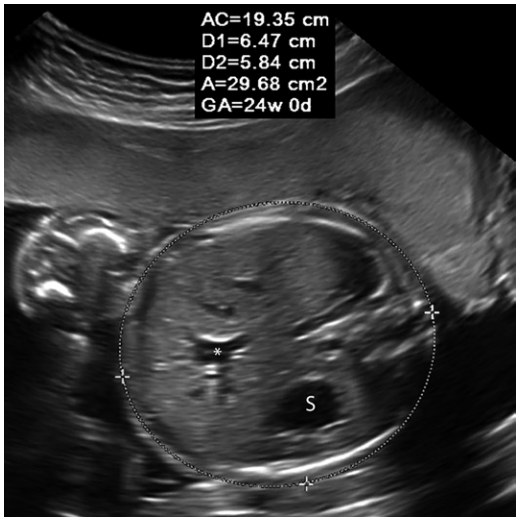


Figure 4. AC measurement. US scan shows the AC measured in a true transverse plane, with the vertebra and single ribs visible. When present, the stomach bubble *(S)* should be included on this image, as should the umbilical vein and portal sinus (*). Unlike the head circumference, the AC is measured at the skin edge (not the rib) to include the subcutaneous tissues. *A* = area; *D1* and *D2* = diameters 1 and 2, respectively.

in 94% of fetuses at 34 weeks (39); therefore, if it is not visualized, the fetal GA is almost certainly less than 34 weeks. Donne and colleagues (40) demonstrated that visualization of the DFE has a positive predictive value of 96% for predicting a GA of 32 weeks or older.

The PTE ossification center appears at approximately 35 weeks (Fig 11); it is not visualized before 34 weeks. It is present in approximately 80% of fetuses by 37 weeks, and its presence has a positive predictive value of 83% for predicting a GA of at least 37 weeks (40). The PHE is the last to appear and is absent before 38 weeks. It has a positive predictive value of 100% for predicting a GA of at least 38 weeks (Fig 12) (40). Thus, a fetus with visible ossification in all three epiphyses (DFE, PTE, and PHE) must have a GA of at least 38 weeks. If measured, the epiphyseal ossification centers should be visualized in an axial plane along the mediolateral surfaces of the epiphysis, and measurements should be taken from outer edge to outer edge. A combined measurement of the three ossification centers of 13 mm or greater has 100% specificity and a 100%

Table 1: Nonstandard Biometric Measurements Used to Corroborate GA and Fetal Size

Measurement	Relationship with GA	Pearls and Pitfalls
TCD	Log linear	Do not use in cases of Chiari malformation, or cerebellar anomalies or disruption
Foot length*	Linear	May be particularly useful in cases of skeletal dysplasia or diabetic embryopathy
Renal length	Linear	Do not use in cases of visceral overgrowth syndromes or abnormal kidneys
Sacral length	Linear	Do not use in cases of caudal regression sequence or open neural tube defects
DFE	Absence indicates <34 wk GA Presence has 96% PPV for predicting ≥32 wk GA	Most useful for designating a likely lower bound of GA Do not mistake intercondylar notch for DFE
PTE	Absence indicates <34 wk GA Presence has 83% PPV for predicting ≥37 wk GA	…
PHE	Presence has 100% PPV for predicting ≥38 wk GA	…

Note.—DFE = distal femoral epiphysis, PHE = proximal humeral epiphysis, PPV = positive predictive value, PTE = proximal tibial epiphysis.
*Foot length has poor reliability for corroboration of GA and fetal size in the setting of FGR and unknown reliability in the setting of macrosomia. All other listed measurements are reliable for these corroborations.

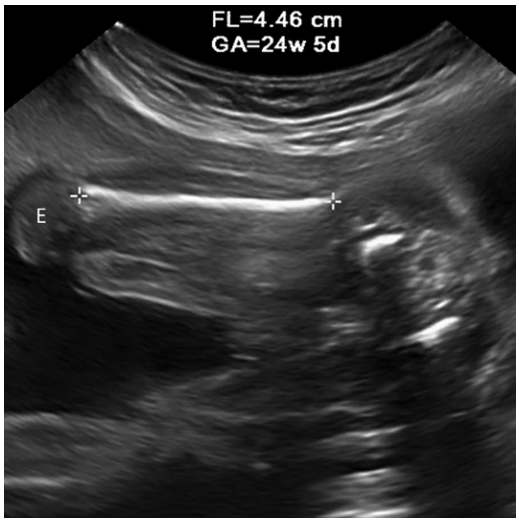


Figure 5. Femur length. US scan shows the femur length *(FL)*—that is, the length of the femoral diaphysis—measured on the long axis of the femur, perpendicular to the insonating beam. It is measured from end to end, excluding the distal epiphyses *(E)*.

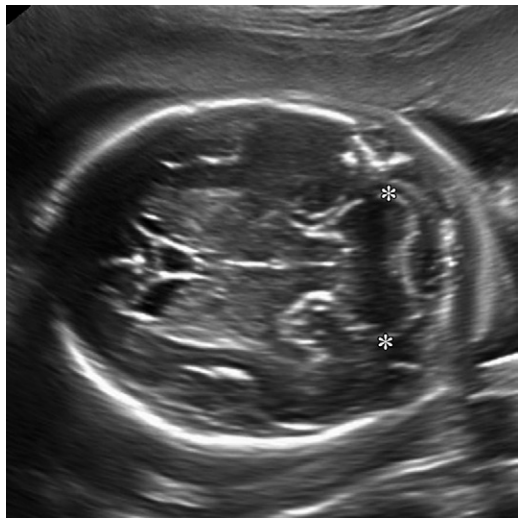
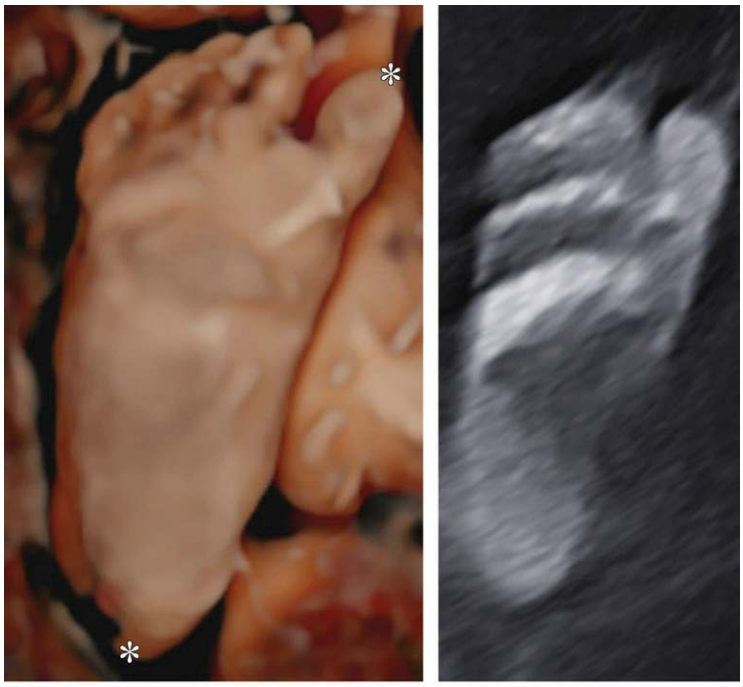


Figure 6. TCD measurement. On a standard transcerebellar (or posterior fossa view) US scan, the TCD is measured across the widest point of the cerebellum, with calipers (∗) placed on the lateral outer edges.

positive predictive value for determining a GA of greater than 37 weeks (40).

Finally, fetal subcutaneous tissue measurements may prove useful for validating the GA, assessing fetal metabolic reserve, and predicting the neonatal outcome of fetuses with growth abnormalities (Fig 13) (41–43). Published nomograms show that lateral abdominal wall thickness increases linearly, approximately 0.19 mm per week, with gestation (41). In the third trimester, low abdominal subcutaneous thickness has been associated with poor perinatal outcome and is predictive of pathologic FGR. Wu et al (43) suggest that lower abdominal wall thickness may correlate with the lack of metabolic reserve that characterizes pathologic FGR. Others have proposed the use of abdominal wall thickness in the evaluation of macrosomia (44,45). In one study involving women with pregestational diabetes, an abdominal wall thickness greater than 6.35 mm at 34 weeks gestation accurately predicted birth weight greater than the 90th percentile (46).



a. b.

Figure 7. Foot length in two fetuses. **(a)** Three-dimensional surface-rendered image of the foot of a 35-week-old fetus shows the footprint view used to measure foot length. The measurement is taken from the heel to the tip of the great toe (*). **(b)** Two-dimensional gray-scale US image shows the foot length in a 23-week-old fetus for comparison.

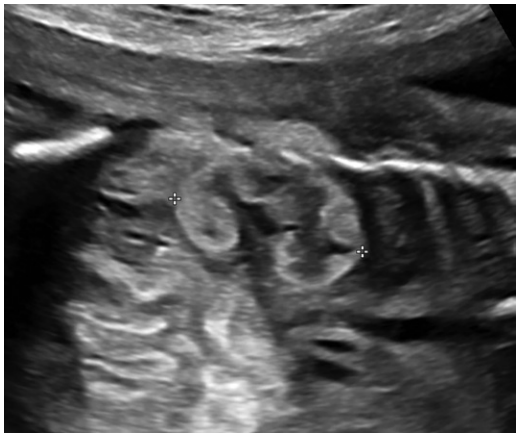


Figure 8. Renal length. Coronal gray-scale US image of the kidney at 23 weeks gestation shows the renal length, which is measured in a longitudinal plane (calipers) in the craniocaudal direction.

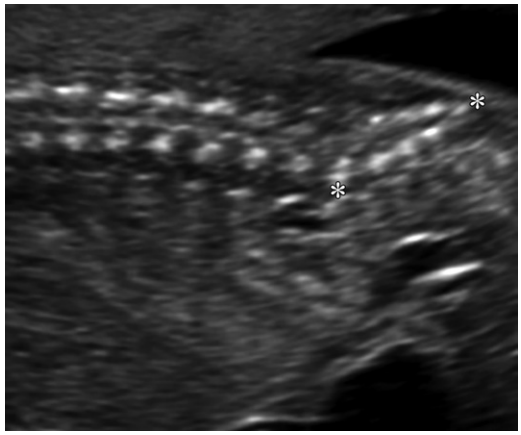


Figure 9. Sacral length measured on a sagittal gray-scale US image of the spine, including the distal tip and normal angulation between the 5th lumbar and first sacral vertebrae. The distance between the distal tip of the spine (S5) and anterior superior aspect of the first sacral vertebra (*) is measured in a straight line.

Defining Abnormal Fetal Growth

Fetal growth can be considered a measure of fetal well-being. Fetal size, as defined on the basis of estimated fetal weight (EFW), is relevant only in the context of GA; size is either appropriate (within the 10th–90th percentiles) or inappropriate (small or large) for the given GA. When the fetal size is inconsistent with the GA, it is imperative to take additional steps to determine whether the discrepancy represents a pathologic process. Serial fetal sonograms provide a growth trajectory, and adjunctive tests are used to differentiate among pathologic growth abnormalities, findings resulting from poor dating, and constitutional (normal) growth.

Of note, the initial diagnosis of inaccurate fetal size represents a particular challenge in cases of undated or suboptimally dated pregnancy. When a pregnant person has no sonographic confirmation or adjustment of dates before 22 0/7 weeks and the fetal size is more than 21 days different from the anticipated size based on the LMP, many experts recommend performing repeat US in 3–4 weeks to confirm that the fetal growth is following a normal trajectory, especially if the fetus is measuring smaller than expected (Fig 14).

Clinical practice and research efforts have been stymied by the lack of consensus regarding

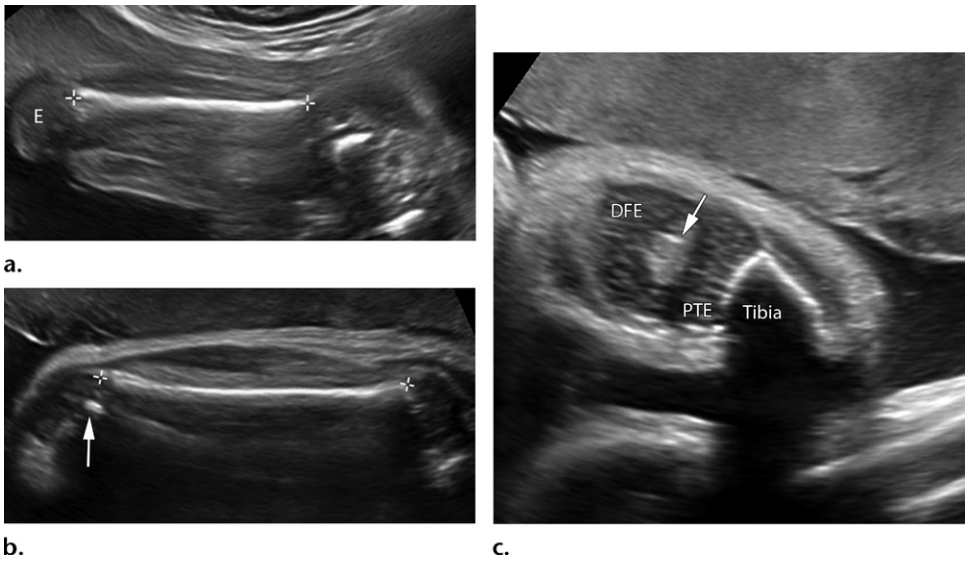


Figure 10. DFE measurement. **(a)** US scan shows femur length measurement in a fetus at 24 weeks gestation, with the epiphysis *(E)* seen as a homogeneous hypoechoic structure without internal calcification. **(b)** US scan shows femur length measurement in the same fetus at 34 weeks, with the epiphyseal ossification center (arrow) seen as a central echogenic focus within the epiphysis. The DFE is usually visible after 32 weeks gestation. **(c)** Coronal US image through the knee shows a potential pitfall in the assessment of DFE ossification. The echogenic region (arrow) is created by synovial folds in the intercondylar notch. The DFE and PTE are well seen, and neither is ossified.

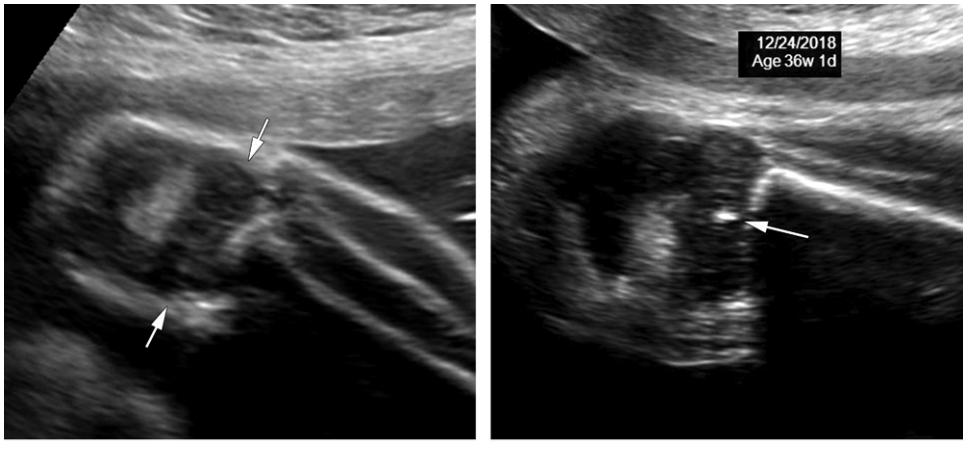


Figure 11. PTE in two fetuses. **(a)** Coronal US scan through the knee of a 30-week-old fetus shows the unossified PTE (arrows) as a homogeneous hypoechoic structure without internal calcification. **(b)** Coronal US scan through the knee of a 36-week-old fetus shows the epiphyseal ossification center (arrow) as a central echogenic focus within the epiphysis. The PTE is usually visible after 35 weeks gestation.

definitions and labels for inappropriate fetal size (Table 2) (47). The lack of consensus is due in part to varying standards for assessing fetal size, as well as varying capability of percentile thresholds for accurate identification of those fetuses at risk for complications. Although a full review of fetal growth standards is beyond the scope of this work, it is worth noting that numerous fetal growth curves exist, have proliferated rapidly in the past decade, and enable the identification of fetuses at risk for complications with varying degrees of success (23,48). Interested readers may find an additional relevant discussion in the special February 2018 issue of *American Journal of Obstetrics and Gynecology* (48), which is focused on fetal growth standards.

It is also important to note that each US software manufacturer chooses a fetal growth formula for its reporting package; therefore, formulas for determining fetal weight percentages vary across platforms. It would behoove sonologists to become familiar with the formula used for their reporting package and the associated limitations.

To briefly review, early fetal growth standards (eg, those of Brenner and Williams) were derived on the basis of birth weights of both live and stillborn

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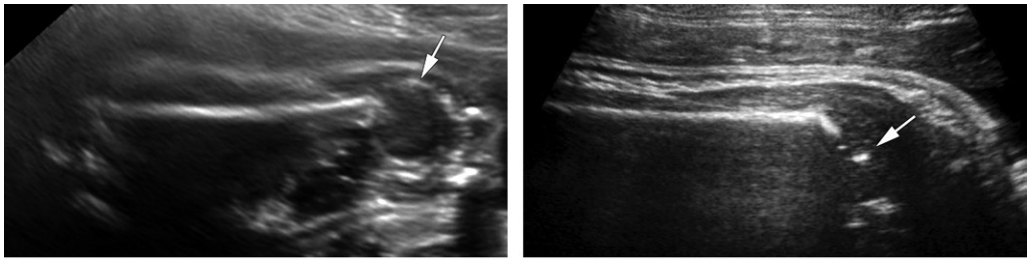
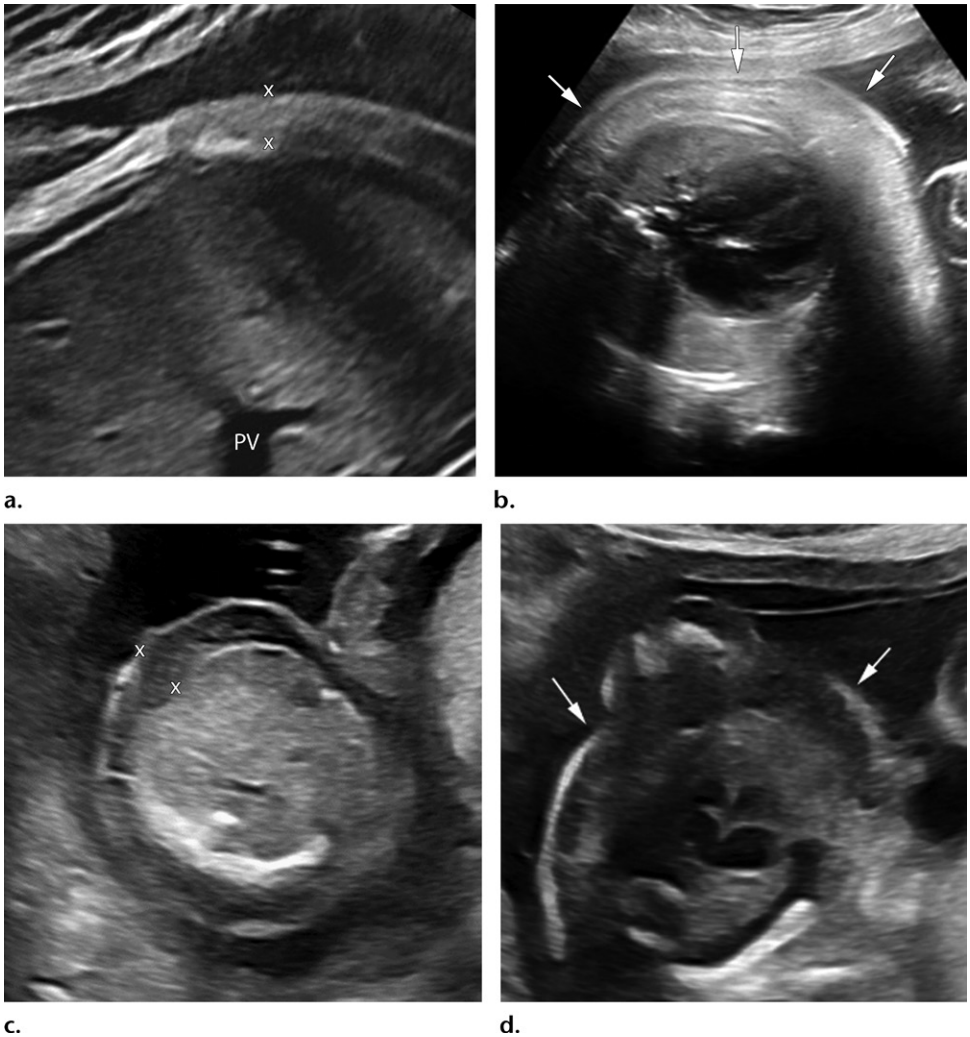


a. b.

Figure 12. PHE in two fetuses. **(a)** Coronal US scan through the shoulder of a 33-week-old fetus shows the unossified PHE as a homogeneous hypoechoic structure (arrow) without internal calcification. **(b)** Coronal US scan through the shoulder of a 41-week-old fetus shows the epiphyseal ossification center (arrow) as a central echogenic focus within the epiphysis. The PHE is usually visible after 38 weeks gestation.



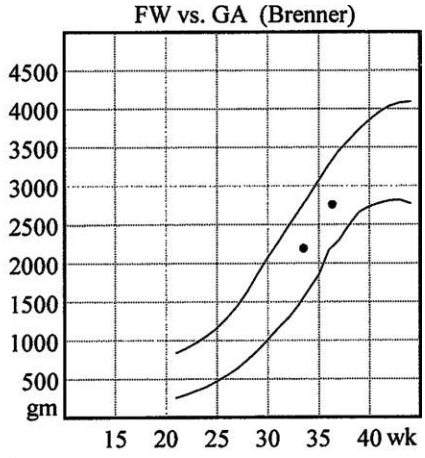
a. b.

c. d.

Figure 13. Lateral abdominal wall fat thickness. **(a)** US scan shows lateral abdominal wall thickness, which is measured in the same plane as the AC, perpendicular to the ultrasound beam, excluding the rib and any hypoechoic muscle, at the thickest area in the near field. In this example, the abdominal wall fat thickness is 5.3 mm at 37 weeks, between the 75th and 95th percentiles. Fat thickness of less than 3 mm at 36 weeks gestation predicts growth restriction and low birth weight, whereas increased abdominal wall fat thickness is associated with an increased rate of cesarean section, especially in the setting of maternal diabetes. *PV* = portal vein for orientation on this magnified image of the fetal abdominal wall at the level of the AC. **(b)** US scan shows fetal macrosomia, which tends to be associated with fat accumulation in other body areas (eg, thigh, cheek, upper thorax), as shown in this fetus of a diabetic mother, with marked subcutaneous fat deposition in the chest wall (arrows). The infant was macrosomic at birth. **(c)** For comparison, a case of fetal hydrops with skin edema is shown. Transabdominal US scan axial to the fetal abdomen shows skin edema (*x* to *x*), which is hypoechoic, unlike subcutaneous fat, which is echogenic. **(d)** Transabdominal US scan axial to the fetal chest at the level of four-chamber heart view in the fetus in **c** confirms the presence of hypoechoic skin edema (arrows) and shows pleural effusion.

	Measurement	GA
BPD	8.5 cm	34w 2d
HC	30.6 cm	34w 0d
AC	29.0 cm	33w 0d
FL	6.6 cm	33w 6d

a.



b.

Figure 14. EFW trajectory in a sonographically redated third-trimester pregnancy. Chart **(a)** and graph **(b)** show fetal measurements **(a)** and appropriate interval growth **(b)** after sonographic redating to 33 weeks gestation in a patient who had limited prenatal care and was referred owing to suspected FGR. At presentation, her gestational dates were off by 23 days, ossification was present in the DFE only, and the renal and cerebellar sizes suggested a GA of 33 weeks. Amniotic fluid volume and cord Doppler US findings were normal, and the fetus was active. The LMP-based GA was changed to a US-based GA, and a 3-week follow-up study confirmed appropriate interval growth **(b)**. Data on the horizontal axis in **b** are GAs. The patient delivered a healthy infant at term. Correct dating avoided induction of labor and iatrogenic preterm delivery resulting from an incorrect diagnosis of growth restriction. *FL* = fetal length, *FW* = fetal weight (vertical axis in **b**), *HC* = head circumference.

Table 2: Commonly Used Definitions for Fetal Growth Abnormalities

Growth Abnormality Term	Definition
FGR	EFW lower than 10th percentile for GA (ACOG)*
	EFW or AC lower than 10th percentile for GA (SOGC, SMFM)
	Severe if EFW lower than 5th percentile or lower than 3rd percentile for GA, depending on source
Small for GA	Birth weight lower than 10th percentile for GA*
	EFW or AC lower than 10th percentile for GA (RCOG)
Large for GA	EFW greater than 90th percentile for GA or birth weight greater than 90th percentile for GA
Macrosomia	Birth weight ≥4000 g* versus birth weight ≥4500 g, depending on source

Note.—ACOG = American College of Obstetricians and Gynecologists, RCOG = Royal College of Obstetricians and Gynaecologists, SMFM = Society for Maternal-Fetal Medicine, SOGC = Society of Obstetricians and Gynaecologists of Canada.
*Definition used at the authors' institution.

infants of varying GAs (49,50). One limitation of growth curves developed according to birth weights is that the weights of infants born at early GAs often are, on average, lower than the weights of fetuses in ongoing pregnancies. In other words, the population of fetuses delivered at 29 weeks owing to a combination of stillbirth, maternal complications (such as preeclampsia with severe features), and obstetric complications (such as chronic abruption or bleeding previa) includes many more fetuses with impaired growth than does the population of fetuses in ongoing pregnancies at 29 weeks.

The higher proportion of smaller fetuses in the delivered population shifts the mean fetal weight downward. Consequently, using these standards to assess all ongoing pregnancies will result in fewer fetuses being assigned to a low–fetal-weight percentile (eg, <10th percentile). Some argue that these curves may fail to include some pathologically small fetuses. Other growth standards (eg, Hadlock, INTERGROWTH-21, World Health Organization) are based on US measurements of presumably healthy fetuses of various GAs (51–53). In addition, more recent standards based on large amounts of data may provide customized curves that account for maternal weight, age, race, and fetal sex (54). However, it appears that the performance of these curves in identifying fetuses

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at risk for complications may not surpass that of the noncustomized Hadlock curve (48).

Fetal Growth Restriction

Ideally, FGR would refer to those fetuses that have not achieved their full growth potential owing to some restrictive (eg, placental, chromosomal, or infectious) process. However, the ability to reliably determine which small fetuses will go on to have neonatal consequences of pathologic growth restriction is limited (55). An EFW lower than the 10th percentile, though not a perfect measure of FGR, is implicated in 20%–45% of nonanomalous stillbirths and contributes to a significant proportion of potentially preventable stillbirths (56,57). The stillbirth rate for fetuses with an EFW below the 10th percentile is 1.5%, twice that of fetuses with a normal EFW (58). In addition, this EFW is associated with neonatal intensive care unit admission and severe acidosis at birth (59).

In the United States, many practitioners use the term *fetal growth restriction* to define sonographic EFW lower than the 10th percentile for GA (58). However, in May 2020, the U.S.-based Society for Maternal-Fetal Medicine updated its recommendations regarding the diagnosis of FGR to include EFW lower than the 10th percentile *or* AC lower than the 10th percentile (59). The Society of Obstetricians and Gynaecologists of Canada (SOGC) and the Royal College of Obstetricians and Gynaecologists (RCOG) of the United Kingdom use EFW lower than the 10th percentile or AC lower than the 10th percentile to diagnose abnormal growth (60,61). The inclusion of AC lower than the 10th percentile as a criterion for FGR is based on the findings in several studies (62,63) that have shown this parameter alone, as compared with EFW lower than the 10th percentile, to have a similar performance in predicting neonatal morbidity. The SOGC uses the diagnostic term *fetal growth restriction,* but the RCOG uses the term *small for gestational age*. These different definitions and diagnostic terms are a source of confusion when comparing data from studies from different countries (47).

The diagnosis of FGR based on percentiles is independent of the growth curve used to make the diagnosis. Most ultrasound software uses Hadlock curves to report individual biometric percentiles (eg, AC), even if the EFW percentiles are calculated by using a different curve (eg, Williams). The term *severe fetal growth restriction* is reserved for the smallest fetuses; however, again, definitions are inconsistent. Some studies use EFW lower than the 5th percentile, while others use EFW lower than the 3rd percentile to define severe FGR. However inconsistent, these definitions are a starting point from which to further refine the determination of which fetuses are most at risk for adverse perinatal consequences.

Small for GA

We choose to follow the dictum that small for GA is a clinical diagnosis based on the birth weight. If the birth weight is lower than the 10th percentile for GA, the infant is described as being small for GA, regardless of the sonographic EFW. This approach differentiates between the estimated weight based on mathematic calculations derived by using measurements that are susceptible to error and the indisputable direct measurement of birth weight. As with EFW curves, there are several curves for neonatal weight percentiles, and they all are based on the weights of delivered infants. Therefore, these curves are skewed toward lighter infants, especially those born prematurely, as discussed earlier.

Large for GA

According to American College of Obstetricians and Gynecologists guidelines, large for GA describes fetuses and neonates with weight higher than the 90th percentile for GA (64). Like fetuses who have FGR or are small for their GA, a portion of fetuses and neonates deemed to be large for their GA have some form of pathologic overgrowth (eg, secondary to maternal diabetes), while others are constitutionally large but otherwise healthy.

Macrosomia

A consensus definition of macrosomia has proven to be difficult to reach (64). Macrosomia implies a clinical diagnosis of birth weight higher than an absolute limit, either 4000 g or 4500 g, regardless of the GA. A birth weight of more than 4000 g is in the 90th percentile for 39 weeks gestation, while 4500 g is greater than the 95th percentile for all term gestations between 37 and 42 weeks (64). Macrosomia is an important diagnosis, as studies have associated it with shoulder dystocia and other adverse neonatal consequences (5). Note that, as with our preferred definition of small for GA, a diagnosis of macrosomia is factual and based on direct measurement of the birth weight.

Given the lack of consensus terminology for large fetal size, we recommend establishing a standardized method of reporting studies in which there is concern that the fetus is possibly large for GA. We prefer to describe the risk for macrosomia in this fashion: "The EFW is greater than the 90th percentile for GA. This places the fetus at risk for macrosomia." Ideally, the reports should also contain a statement regarding the reliability of the GA determination. An EFW higher than the 90th percentile is far more concerning in a maternal

patient whose menstrual dating was verified at US in the first trimester than it is in a maternal patient who received late care and has uncertain dates. In the latter setting, use of some of the nonstandard biometric parameters and assessment of epiphyseal ossification centers may help to narrow the range of possible GAs. Careful attention to stigmata of overgrowth syndromes is important, as these may preclude the use of some biometric adjuncts. For instance, syndromic renal enlargement in Beckwith-Wiedemann syndrome precludes the use of renal length for GA corroboration.

Managing Pregnancies Affected by Abnormal Fetal Growth

FGR: Initial Diagnosis

Typically, FGR is diagnosed no earlier than the middle of the second trimester, around the time of the fetal anatomic survey. An EFW lower than the 10th percentile for GA should prompt additional investigation, and ascertaining the accuracy of the gestational dating is first and foremost in this process. Subsequently, a detailed sonographic assessment aids in the difficult task of separating fetuses with an EFW lower than the 10th percentile into those who are physiologically small but healthy and those who are pathologically growth restricted and therefore at risk for perinatal morbidity and mortality.

The assessment should focus on sonographic findings that are consistent with the three main causative diseases in FGR: aneuploidy, infection, and placental insufficiency. Aneuploidy tends to cause FGR early in gestation and may account for as many as 20% of cases of FGR diagnosed before 26 weeks; triploidy and trisomy 18 are the most common diagnoses (58,61,65). Triploidy is suspected when there is a significant discrepancy between the head size and body size, with body size lagging considerably. Careful attention to anatomic structures and relative biometric features is crucial for identifying constellations of findings associated with common aneuploidies and syndromes. Assessment of amniotic fluid volume is an integral part of evaluation. The amniotic fluid volume is typically quantified by measuring the maximal vertical pocket (MVP) before 28 weeks gestation. The amniotic fluid index—that is, the sum of the four deepest pockets free of fetal parts or umbilical cord—is measured after 28 weeks, when a larger fetal size allows reproducible four-quadrant measurements. MVP depths are used to define oligohydramnios (MVP <2 cm) and polyhydramnios (MVP >8 cm) throughout the second and third trimesters. The amniotic fluid volume is frequently normal with aneuploidy, but it is reduced in the setting of placental insufficiency. When FGR is identified, genetic information may be obtained by using noninvasive screening tests such as cell-free fetal DNA testing, or, preferably, diagnostic amniocentesis. Viral studies of the amniotic fluid also may be performed if clinically indicated.

Maternal infections, including TORCH (*t*oxoplasmosis, *o*ther infections [parvovirus, syphilis, human immunodeficiency virus, etc], *r*ubella, *c*ytomegalovirus, and *h*erpes), also can contribute to FGR. Of these, cytomegalovirus is the most common (58,61). In addition to maternal clinical symptoms, US findings may include calcifications in the brain, abdominal organs, and placenta; hepatosplenomegaly; and brain lesions such as parenchymal cysts, ventriculomegaly, and cerebral migrational disorders. Maternal serum testing with immunoglobulin G and immunoglobulin M titers may help to establish the chronicity of maternal cytomegalovirus infection. Positive immunoglobulin G and immunoglobulin M levels with low immunoglobulin G avidity are concerning for acute cytomegalovirus infection (66). A review of the indications for and interpretation of maternal testing for infection is beyond the scope of this article. However, interested readers can refer to the special May 2006 issue of *Reproductive Toxicology* (66). A review by Crino and Driggers (67) provides an overview of specific sonographic findings that raise suspicion for certain viral infections.

Placental insufficiency tends to result in FGR in the third trimester, but severe cases can manifest earlier (61,68). US findings are less specific but can include diminished amniotic fluid volume and decreased placental volume with increased placental echogenicity or calcification. Placental insufficiency frequently results in brain-sparing growth restriction, in which the AC and EFW lag while the head size measured by using the BPD and head circumference remains normal (69). Placental insufficiency may also correlate with maternal disease, most commonly antiphospholipid antibody syndrome and preeclampsia with severe features (70). Maternal well-being should be closely tracked, especially when severe FGR is identified.

The timing of the diagnosis of FGR may provide clues to the cause. Previously, the terms *asymmetric fetal growth restriction* and *symmetric fetal growth restriction* were used to describe ostensibly distinct causes, but these have largely been abandoned in favor of early- and late-onset FGR, with most authors defining late-onset growth restriction as growth restriction diagnosed after 32 weeks gestation (Table 3) (71–73).

FGR: Follow-up and Surveillance

During pregnancies complicated by FGR, surveillance is warranted to allow intervention that may

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Table 3: Early versus Late FGR

Parameter(s)	Early FGR	Late FGR
Consensus definition	1. AC or EFW <3rd percentile *or* UA AEDF ***or*** 2. AC or EFW <10th percentile ***with*** a. UA-PI >95th percentile ***and/or*** b. UA-PI >95th percentile	1. AC or EFW <3rd percentile ***or*** 2. At least two of the following: a. AC or EFW <10th percentile b. AC or EFW crossing centiles >2 quartiles c. Cerebroplacental ratio <5th percentile or UA-PI >95th percentile
Prevalence and proportions	1%–2% prevalence 20%–30% of all growth-restricted fetuses	8%–10% prevalence 70%–80% of all growth-restricted fetuses
Common causes	Aneuploidy or genetic syndrome Infection Severe placental insufficiency	Placental insufficiency (mild or moderate) Maternal malnutrition …
Clinical pearls	UA Doppler abnormalities (70%) UA Doppler deterioration over time is common 60% preeclampsia	UA Doppler abnormalities (<10%) UA Doppler deterioration pattern not common 10%–15% preeclampsia
Clinical challenges	Delivery timing	Detection
Postnatal affect	High mortality and morbidity	Low mortality and moderate morbidity but larger population effect

Sources.—References 71–73.
Note.—AEDF = absence of end-diastolic flow, UA = umbilical artery, UA-PI = UA pulsatility index.

prevent or reduce morbidity and mortality. Thus, surveillance should begin only when the fetus reaches a size and GA at which intervention is likely to be successful. Neonatal resuscitation success and limitations vary among hospitals. Although the lower limits of resuscitation have decreased across the United States, few institutions routinely offer neonatal resuscitation at less than 23 0/7 weeks gestation. Neonatal survival, neurologically intact survival in particular, is still relatively rare for neonates in the 23rd gestational week or who weigh less than 500 g (74). Ideally, discussions regarding life-saving interventions in the setting of severe FGR should occur in a patient-centered multidisciplinary fashion, with input from maternal-fetal medicine and neonatology colleagues.

Mothers whose fetuses have an EFW lower than the 10th percentile for GA should undergo serial growth US in 3–4-week intervals after the diagnosis. Owing to the margin of error in sonographic biometry, the EFW should not be routinely measured more frequently than every 3 weeks (18,75). Serial measurements provide a growth trajectory, allowing the managing clinician to continuously reevaluate viability, perinatal risk, and delivery timing. Although investigators in several studies have attempted to identify trajectory models that might aid in identifying at-risk fetuses, as yet the data are insufficient to promote statistical trajectory modeling as a clinical tool (76). That said, fetal growth that has halted or fallen across multiple percentiles (eg, decreasing from 10th to 5th percentile to less than 1st percentile) should be cause for alarm (Fig 15). On the other hand, fetuses with suspected growth restriction who are constitutionally small tend to follow their growth curve over time without crossing percentiles (Fig 16).

FGR: Doppler US Studies for Risk Stratification

The application of Doppler waveforms to identify high-risk FGR has evolved considerably from its earliest use. Doppler indices and ratios involving multiple fetal and maternal vessels have been assessed for their utility in the management of FGR. However, the usefulness of these measurements in predicting perinatal morbidity and mortality in the setting of FGR beyond that of standard umbilical artery (UA) Doppler US is limited (58).

***UA Doppler US.*—**UA Doppler US provides a window into the health of the fetoplacental unit. The fetoplacental circuit is normally a low-resistance system in which the fetus obtains nutrients and eliminates metabolic waste with little cardiac effort. Under normal circumstances, blood flow from the fetal descending aorta into the UAs and toward the placenta should occur during both systole and diastole, a testament to the low resistance in the placental bed (Fig 17) (59). Placental insufficiency represents the clinical end point of various mechanisms that alter placental vascular compliance by way of changes in the small muscular

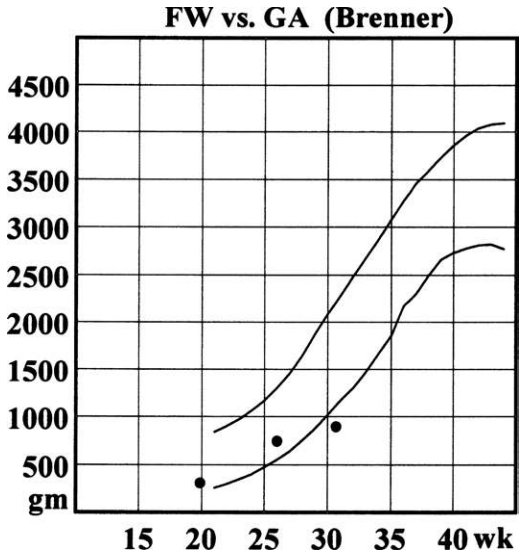

Figure 15. EFW trajectory in the setting of FGR. Graph demonstrates a progressive decline in fetal weight *(FW)* (vertical axis), a concerning pattern that indicates the need for detailed sonographic assessment and increased prenatal surveillance. In this case, at 30 weeks 5 days gestation (horizontal axis), all biometric parameters were lower than the 5th percentile for GA according to the LMP with confirmatory first-trimester US. Nonstress testing was nonreactive, the biophysical profile score was 2/8, there was a single fluid pocket 1.8 cm in depth, and cord Doppler US revealed absent end-diastolic flow with runs of reversed end-diastolic flow. The maternal patient was a multigravida with a history of one term stillbirth, three preterm growth-restricted infants, and HELLP (*h*emolysis, *e*levated *l*iver enzymes, and *l*ow *p*latelet count) syndrome. She was immediately transferred for repeat cesarean section delivery. The infant weighed 780 g and spent 57 days in the neonatal intensive care unit. The placenta weighed 132 g (<3rd percentile), and pathologic assessment revealed massive perivillous fibrinoid deposition, a known and recurrent cause of FGR.

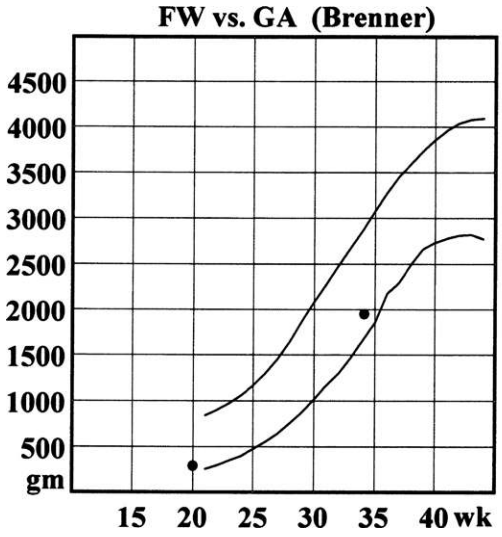

Figure 16. EFW trajectory in a constitutionally small but healthy fetus. Graph demonstrates an appropriate interval growth (vertical axis) in a fetus whose size was in the lower range of normal. The infant was small for GA (horizontal axis) at birth, weighing 2550 g, which is less than the 5th percentile for 39 weeks gestation. She is currently healthy, growing normally, and meeting developmental milestones. This case is an example of constitutional small size. *FW* = fetal weight.

arteries of the tertiary villi. Increased placental vascular resistance decreases UA flow to the placenta (so-called forward flow) during diastole (Fig 17). As resistance increases, the diastolic flow velocity may drop to zero, resulting in absent end-diastolic flow, or in cases of very high resistance, the flow in the UAs may actually be reversed because the fetal diastolic pressure is no longer sufficient to combat the pressure in the placental bed (Fig 17). As might be expected, reversed end-diastolic flow in the UA belies advanced placental disease and is estimated to represent obliteration of more than 60%–70% of the placental function (77).

UA Doppler US should be performed when the fetus is not overly active, if possible. For reproducibility of serial measurements and in multifetal gestations, a segment of cord close to the fetal abdominal cord insertion is recommended. In the setting of a high-quality waveform, multiple measurements are not indicated. Any measurements should be obtained on the highest-quality waveform(s) rather than averaged over several waveforms.

Doppler US indices include the resistance index, pulsatility index, and systolic-diastolic ratio. Of these, the systolic-diastolic ratio is the most commonly used for assessment of UA flow. Nomograms based on GA for the systolic-diastolic ratio are available at *www.perinatology.com*. Systolic-diastolic ratios greater than the 95th percentile for GA are considered abnormal. Absent or reversed end-diastolic flow does not require quantification and is always abnormal. The use of UA Doppler US in the management of suspected FGR is associated with a 29% relative reduction in perinatal mortality as well as a decrease in induced labors and cesarean deliveries (78). The absence of UA Doppler abnormalities portends a good perinatal outcome and can help guide clinicians in appropriately prolonging the pregnancy to the 38th week (59).

There are no established guidelines for the timing of UA Doppler US studies; however, most recommend performing Doppler US evaluations in 1–2-week intervals (59). If consecutive UA Doppler US assessments yield normal results, the interval between assessments can be reasonably increased (59). Systolic-diastolic ratios greater than the 95th percentile prompt more frequent evaluation, and the development of absent or reversed diastolic flow prompts careful consideration of delivery, with the risks of early delivery weighed against the risks of iatrogenic

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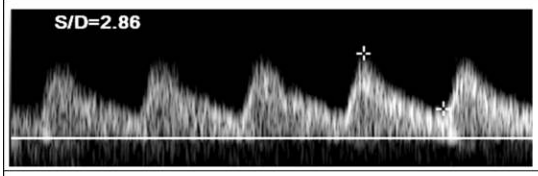
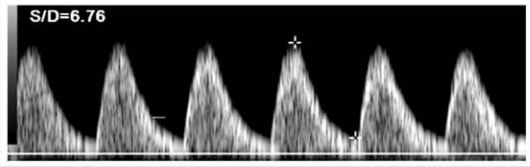
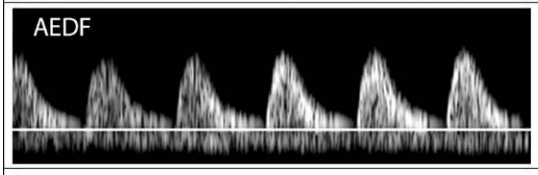
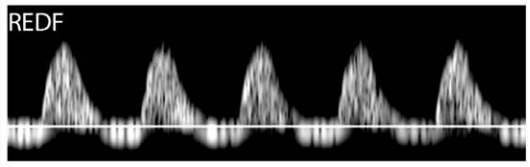
Doppler Tracing	Description	Management Recommendation
	Normal, low resistance flow in the umbilical artery in the 3rd trimester with continuous antegrade diastolic flow and systolic-to-diastolic (SD) ratio of 2.86.	In FGR with an EFW ≥ 3rd percentile, this waveform portends a good prognosis, and the goal is for delivery at 38–39 weeks. Of note, delivery timing for suspected **severe** FGR (EFW < 3rd percentile) is 37 weeks with normal UA Doppler waveform.
	Increased placental vascular resistance results in decreased diastolic flow and an abnormally elevated SD ratio of 6.76.	With elevated SD ratio, the frequency of antenatal testing is increased and the goal for delivery is 37 weeks.
	Absence of end-diastolic flow (AEDF) is always abnormal. The continuous flow below the baseline is umbilical vein flow and should not be mistaken for reversed flow in the UA.	With AEDF, antenatal testing is increased, corticosteroids are administered, and the goal for delivery is 33–34 weeks.
	Reversed end-diastolic flow (REDF) is an ominous finding. Placental resistance is so high that UA flow is reversed (dips below the baseline) in diastole.	With REDF, antenatal testing is increased, corticosteroids are administered, and the goal for delivery is 30–32 weeks. This result should be communicated directly and urgently to the managing obstetrician.

Figure 17. UA Doppler waveforms. Top row: Normal low-resistance flow in the UA in the third trimester, with continuous antegrade diastolic flow and a systolic-diastolic ratio of 2.86. Second row from top: Elevated UA resistance, with increased placental resistance manifesting as decreased diastolic flow and an abnormal systolic-diastolic ratio (6.76). Third row from top: Absence of end-diastolic flow, which is always abnormal. Bottom row: Decrease in UA flow to below the baseline at diastole, indicating reversed end-diastolic flow, which is an ominous finding. The cited delivery date goals are those recommended in the clinical guidelines of the Society for Maternal-Fetal Medicine (59) and should be interpreted in the full clinical context, including other maternal or fetal findings that may dictate delivery earlier than the stated GA.

prematurity. Thus, UA Doppler US is generally not performed until there is a reasonable expectation of successful neonatal resuscitative efforts (usually at >23 weeks gestation).

In rare circumstances, such as previable severe FGR with a suspected placental cause, reversed or absent end-diastolic flow may corroborate the placental cause of the disease and predict impending fetal death. This information may help to appropriately prepare the maternal patient for a poor obstetric outcome; however, it should not be used as a definitive diagnostic tool.

Ductus Venosus Doppler US.—The ductus venosus is the first of three physiologic shunts in the fetal circulation that preferentially guide oxygenated blood toward the fetal brain and heart. In the setting of a normal physiologic profile, the fetal venous circulation demonstrates persistent forward flow. Increased placental vascular resistance can lead to poor cardiac contractility; when this occurs, forward flow in the ductus venosus is impeded and the waveform becomes abnormal.

The clinical use of ductus venosus Doppler US is controversial, as it has not been shown to routinely improve perinatal outcomes. Obstetric societies in the United States caution that there are insufficient data supporting improved outcomes to recommend the routine clinical use of ductus venosus Doppler US (59).

Middle Cerebral Artery Doppler US.—Fetal hypoxia results in preferential redistribution of oxygenated blood toward the brain, the so-called brain-sparing effect (69). Middle cerebral artery (MCA) Doppler US can be easily performed, and under normal circumstances, the MCA shows a higher resistance waveform than does the UA, which should have a lower systolic-diastolic ratio or pulsatility index than the MCA at all times during pregnancy (69,79).

The clinical use of MCA systolic-diastolic ratios or pulsatility indexes for assessment of FGR is controversial. The cerebroplacental ratio (CPR), the ratio between cerebral blood flow (as measured with MCA Doppler US) and placental blood flow (as measured with UA Doppler US), also has been proposed as a measure of fetal well-being in the setting of FGR. In a meta-analysis (69), the CPR, as compared with standard UA Doppler US measurement, demonstrated superior value for the prediction of composite neonatal

morbidity and risk of emergency cesarean section but no benefit for the prediction of perinatal mortality or other assessed outcomes. MCA Doppler US alone did not perform better than UA Doppler US in the prediction of any assessed outcomes. Therefore, obstetric societies in the United States caution that the additional information obtained from MCA Doppler US and CPR measurements is insufficient to recommend their routine use for guiding clinical care (59).

FGR: Clinical Assessments and Interventions to Optimize Delivery Timing and Outcome

Sonographic evaluation of the growth-restricted fetus provides crucial information for guiding additional clinical assessments. Foremost among these assessments are the nonstress test and modified biophysical profile, which is a combination of the nonstress test and amniotic fluid volume assessment. In cases of suspected placental insufficiency, a reassuring nonstress test has a 95% negative predictive value for stillbirth in the subsequent week. There is no consensus on the frequencies at which to perform nonstress tests and modified biophysical profiles, and management varies by institution and perceived severity of growth restriction phenotype.

In preterm fetuses with severe growth restriction and UA Doppler US abnormalities, daily or even continuous electronic fetal heart rate monitoring may be recommended as a means of prolonging the pregnancy for as long as possible. In fetuses with a less severe phenotype and/or normal UA Doppler results, less frequent testing may be indicated. At many institutions, nonstress testing is performed once or twice weekly to coincide with the frequency of UA Doppler US assessments; testing and US frequency are then adjusted according to the findings (58,59).

Other routine obstetric interventions aimed at reducing risks associated with prematurity should be performed in the setting of FGR when preterm delivery is anticipated. Before 34 weeks gestation, antenatal corticosteroids are administered, ideally 48 hours before delivery, to improve lung maturity and reduce respiratory and other perinatal morbidities. In addition, at between 34 0/7 and 36 6/7 weeks gestation, if delivery within the next 7 days is anticipated and steroids have not been administered previously, a course of antenatal steroids should be considered. However, if the fetal status warrants immediate delivery at or after 34 weeks gestation, the delivery should not be delayed in order to administer antenatal corticosteroids. Magnesium sulfate is given before 32 weeks gestation for fetal neural protection (58,59,80).

FGR: Special Case in Twin Gestations

Fetal growth abnormalities also occur in cases of multiple gestations. When only one twin fails to fulfill its growth potential, this is referred to as selective FGR (Fig 18). This is of particular concern in monochorionic pregnancies because the demise of the growth-restricted twin has potentially catastrophic consequences for the normally growing twin owing to complex vascular anastomoses in the shared placenta (81). As with singleton pregnancies, with twin pregnancies, inconsistent nomenclature has impeded the development of evidence-based management protocols for selective FGR. To address this issue, an international panel of experts used a Delphi process to reach a consensus on the definition of selective FGR, as described in Table 4 (82).

UA Doppler US findings in the smaller twin in a monochorionic pair are used to determine the severity of the selective FGR phenotype (83). With type I selective FGR, there is persistent end-diastolic flow in the UA. With type II selective FGR, there is persistently absent or reversed end-diastolic flow. With type III, end-diastolic flow cycles range between present (even if abnormal) end-diastolic flow and intermittently absent or reversed flow. A type III pattern is also called cyclical flow. Prognoses vary by selective FGR subtype, with the worst outcomes occurring in cases of type II gestation with absent or reversed end-diastolic flow in the growth-restricted twin. However, cyclical type III flow indicates large intertwin vascular connections, creating an unstable situation in which the demise of one twin can occur with little warning. Type I selective FGR can be managed expectantly, but there is a potential role for fetal intervention in type II and type III cases (84).

Fetal Macrosomia and Large for GA: Initial Diagnosis

Fetuses that are large for their GA can be identified in a number of ways. Typically, the diagnosis is made in the third trimester during routine evaluation for maternal risk factors (eg, diabetes) or when the clinical measurement of the symphysis-fundal height is abnormal (Fig 19). More rarely, syndromic overgrowth may be diagnosed at the time of the fetal anatomic survey.

It is worth noting that the accuracy of US for correct prediction of macrosomia is suboptimal. The suboptimal prediction performance is related to the later GA at which large-for-GA fetuses are diagnosed and the poorer performance of EFW formulas at the upper extremes of weight. Meta-analyses (64) demonstrate that US has 56% sensitivity and 93% specificity for predicting neonatal birth weight greater than 4000 g and decreases in accuracy with increasing weight. Only 33%–44%

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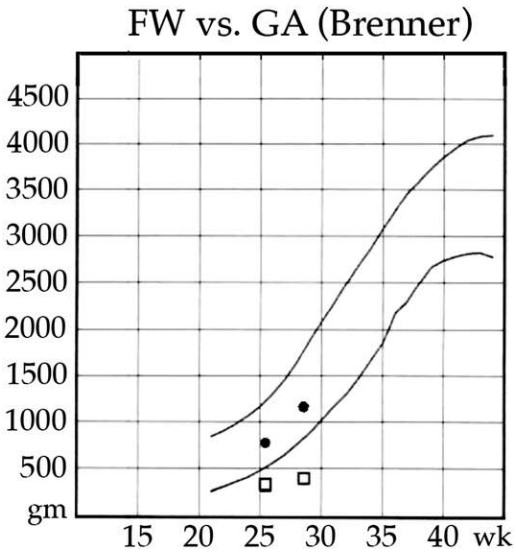

Figure 18. EFW trajectory demonstrating selective growth restriction in dichorionic twins. Graph shows a progressive decline in the EFW of twin A (□) but normal growth of twin B (○). Twin A died in utero at 30 weeks gestation. The maternal patient developed preeclampsia with severe features at 35 weeks and was delivered by cesarean section. This is an example of the maternal effects of an abnormal pregnancy. The surviving infant initially required intensive care unit treatment but was healthy at the time of discharge.

of fetuses with a birth weight of greater than 4500 g can be accurately identified with US (64.) Given these data, the additional US measurements described previously, such as fetal subcutaneous tissue thickness, may add additional context to the determination of macrosomia.

Additional assessments after the diagnosis of a large-for-GA fetus should include clinical evaluation for maternal risk factors and US evaluation of the fetus. Like FGR, the large-for-GA condition can be constitutional, but it may also represent a pathologic entity. Most commonly, maternal pathophysiologic conditions such as diabetes, dyslipidemia, obesity, and abnormal glucose tolerance play a role (64). The relationship between maternal metabolic factors and fetal growth is complex and varies by maternal age, race, and body composition. However, approximately 30% of women with gestational diabetes and nearly 40% of women with pregestational diabetes will have a fetus that is large for its GA (64).

US assessment should include careful evaluation for findings that suggest an overgrowth syndrome. An exhaustive review of such entities is beyond the scope of this review; however, it is worth noting that, unlike FGR, an isolated finding of large for GA in the third trimester typically does not warrant genetic evaluation. Other sonographic measurements, such as polyhydramnios in the setting of maternal diabetes, may provide further evidence of the underlying cause of EFW greater than the 90th percentile.

Fetal Macrosomia: Follow-up and Surveillance

Following the diagnosis of a fetus with an EFW greater than the 90th percentile, follow-up is dictated by the presence of any maternal disorders and the GA at which the diagnosis was made. Although the consequences of fetal macrosomia include maternal and fetal morbidities, the surveillance of these fetuses is not well defined.

The maternal complications and consequences of macrosomia generally stem from a difficult delivery, regardless of whether it is vaginal or by cesarean. The uterine distention caused by fetal macrosomia, as well as the potential for more protracted labor, increases the possibility of postpartum hemorrhage. There are also associated increased risks for third- and fourth-degree vaginal lacerations and cesarean delivery, which in itself increases the risk for severe maternal morbidity (eg, transfusion, hysterectomy, and intensive care unit admission) (64).

Fetal complications can result from birth trauma, especially shoulder dystocia, and metabolic abnormalities, which may occur regardless of maternal diabetes status. Although many cases of shoulder dystocia resolve without significant neonatal trauma, the speed with which a shoulder dystocia is reduced and the infant is delivered dictates the likelihood of severe injury. These injuries may include clavicular fracture or brachial plexus injury, which may result in Erb palsy. In severe cases, infants may die or have severe neurodevelopmental delay due to hypoxic brain injury (5,64). Metabolic complications include neonatal hypoglycemia, which may require admission to the neonatal intensive care unit, and longer-term metabolic disorders (5,64).

Unless another indication such as maternal diabetes exists, antenatal surveillance using nonstress tests or modified biophysical profiles is not warranted for isolated cases of a fetus large for GA (64). Furthermore, scheduled induction at earlier GAs has not been consistently shown to reduce neonatal or maternal morbidity in cases of suspected macrosomia. A Cochrane Library database review of expectant management versus induction at 38 weeks for suspected macrosomia did not reveal improved rates of shoulder dystocia or cesarean delivery (85). In addition, the safest method of delivery when macrosomia is suspected is not well elucidated, given that the relationship between fetal size, maternal pelvimetric features, and likelihood of vaginal delivery cannot be reliably predicted. Accordingly, the American College of Obstetricians and Gynecologists recommends

Table 4: Criteria for Diagnosis of Selective FGR

Pregnancy Type	EFW Percentile	ΔEFW	AC Percentile	UA-PI Percentile	No. of Criteria Needed
MC	<10th	≥25%	<10th	>95th	Three of four
DC	<10th	≥25%	…	>95th	Two of three

Source.—Reference 82.
Note.—An EFW lower than the 3rd percentile in one twin is sufficient to diagnose selective FGR. Otherwise, the listed criteria are used in combination. DC = dichorionic, ΔEFW = difference in EFW between the twins, MC = monochorionic, UA-PI = UA pulsatility index.

that consideration of primary cesarean delivery for macrosomia be limited to cases of suspected EFW higher than 4500 g at term in mothers with diabetes or to cases of suspected EFW higher than 5000 g at term in mothers without diabetes (86). The decision to offer cesarean delivery should be left up to the managing obstetrician on the basis of American College of Obstetricians and Gynecologists guidelines and clinical circumstances.

Conclusion

Fetal growth abnormalities have a profound effect on pregnancy management, delivery timing, and perinatal outcome for the mother and infant. Fetal size is assessed in relation to what is expected at any given GA. Therefore, correct pregnancy dating is critical for the detection and surveillance of abnormal fetal growth and the prevention of perinatal maternal and fetal morbidity and mortality.

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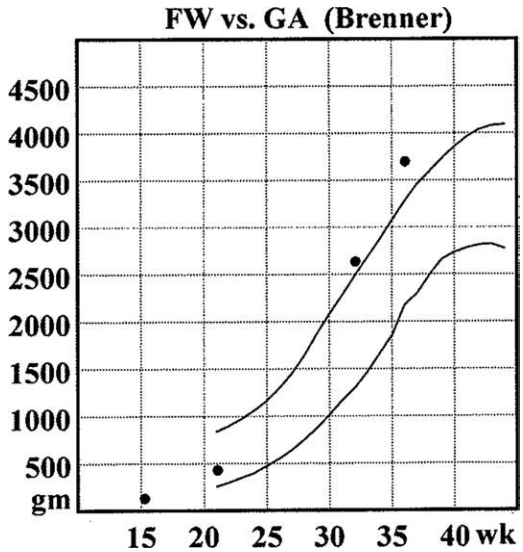

Figure 19. EFW trajectory demonstrating increased risk for macrosomia. Graph shows a progressive increase in the EFW (vertical axis) with advancing GA (horizontal axis). The EFW was greater than the 90th percentile at 32 and 36 weeks GA, whereas earlier US results (at 15 and 21 weeks) were concordant with menstruation dates. The infant was not actually macrosomic at birth, weighing 3829 g, but delivery was complicated by shoulder dystocia and the infant spent several days in the neonatal intensive care unit owing to episodes of hypoglycemia. He also had extensive bruising of the left shoulder and torso.

References

1. Committee on Practice Bulletins—Obstetrics and the American Institute of Ultrasound in Medicine. Practice Bulletin No. 175: Ultrasound in Pregnancy. Obstet Gynecol 2016;128(6):e241–e256.
2. Barker DJ. Adult consequences of fetal growth restriction. Clin Obstet Gynecol 2006;49(2):270–283.
3. Colella M, Frérot A, Novais ARB, Baud O. Neonatal and Long-Term Consequences of Fetal Growth Restriction. Curr Pediatr Rev 2018;14(4):212–218.
4. Crispi F, Miranda J, Gratacós E. Long-term cardiovascular consequences of fetal growth restriction: biology, clinical implications, and opportunities for prevention of adult disease. Am J Obstet Gynecol 2018;218(2S):S869–S879.
5. Henriksen T. The macrosomic fetus: a challenge in current obstetrics. Acta Obstet Gynecol Scand 2008;87(2):134–145.
6. Bamberg C, Hinkson L, Henrich W. Prenatal detection and consequences of fetal macrosomia. Fetal Diagn Ther 2013;33(3):143–148.
7. Gu S, An X, Fang L, et al. Risk factors and long-term health consequences of macrosomia: a prospective study in Jiangsu Province, China. J Biomed Res 2012;26(4):235–240.
8. Russell RB, Green NS, Steiner CA, et al. Cost of hospitalization for preterm and low birth weight infants in the United States. Pediatrics 2007;120(1):e1–e9.
9. Marzouk A, Filipovic-Pierucci A, Baud O, et al. Prenatal and post-natal cost of small for gestational age infants: a national study. BMC Health Serv Res 2017;17(1):221.
10. Hodek JM, von der Schulenburg JM, Mittendorf T. Measuring economic consequences of preterm birth: m ethodological recommendations for the evaluation of personal burden on children and their caregivers. Health Econ Rev 2011;1(1):6.
11. Whitworth M, Bricker L, Mullan C. Ultrasound for fetal assessment in early pregnancy. Cochrane Database Syst Rev 2015;2015(7):CD007058.

12. Committee on Obstetric Practice, the American Institute of Ultrasound in Medicine, and the Society for Maternal-Fetal Medicine. Committee Opinion No 700: Methods for Estimating the Due Date. Obstet Gynecol 2017;129(5):e150–e154.
13. Wegienka G, Baird DD. A comparison of recalled date of last menstrual period with prospectively recorded dates. J Womens Health (Larchmt) 2005;14(3):248–252.
14. Bennett KA, Crane JMG, O'shea P, Lacelle J, Hutchens D, Copel JA. First trimester ultrasound screening is effective in reducing postterm labor induction rates: a randomized controlled trial. Am J Obstet Gynecol 2004;190(4):1077–1081.
15. Robinson HP, Fleming JE. A critical evaluation of sonar "crown-rump length" measurements. Br J Obstet Gynaecol 1975;82(9):702–710.
16. Verburg BO, Steegers EA, De Ridder M, et al. New charts for ultrasound dating of pregnancy and assessment of fetal growth: longitudinal data from a population-based cohort study. Ultrasound Obstet Gynecol 2008;31(4):388–396.
17. Hadlock FP, Shah YP, Kanon DJ, Lindsey JV. Fetal crown-rump length: reevaluation of relation to menstrual age (5-18 weeks) with high-resolution real-time US. Radiology 1992;182(2):501–505.
18. AIUM-ACR-ACOG-SMFM-SRU Practice Parameter for the Performance of Standard Diagnostic Obstetric Ultrasound Examinations. J Ultrasound Med 2018;37(11):E13–E24.
19. Barnhart K, van Mello NM, Bourne T, et al. Pregnancy of unknown location: a consensus statement of nomenclature, definitions, and outcome. Fertil Steril 2011;95(3):857–866.
20. Doubilet PM, Benson CB, Bourne T, et al. Diagnostic criteria for nonviable pregnancy early in the first trimester. N Engl J Med 2013;369(15):1443–1451.
21. Reddy UM, Abuhamad AZ, Levine D, Saade GR; Fetal Imaging Workshop Invited Participants. Fetal imaging: executive summary of a joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Institute of Ultrasound in Medicine, American College of Obstetricians and Gynecologists, American College of Radiology, Society for Pediatric Radiology, and Society of Radiologists in Ultrasound Fetal Imaging Workshop. J Ultrasound Med 2014;33(5):745–757.
22. Khalil A, Rodgers M, Baschat A, et al. ISUOG Practice Guidelines: role of ultrasound in twin pregnancy. Ultrasound Obstet Gynecol 2016;47(2):247–263.
23. Romero R, Tarca AL. Fetal size standards to diagnose a small- or a large-for-gestational-age fetus. Am J Obstet Gynecol 2018;218(2S):S605–S607.
24. Chavez MR, Ananth CV, Smulian JC, Yeo L, Oyelese Y, Vintzileos AM. Fetal transcerebellar diameter measurement with particular emphasis in the third trimester: a reliable predictor of gestational age. Am J Obstet Gynecol 2004;191(3):979–984.
25. Mercer BM, Sklar S, Shariatmadar A, Gillieson MS, D'Alton ME. Fetal foot length as a predictor of gestational age. Am J Obstet Gynecol 1987;156(2):350–355.
26. Chitty LS, Altman DG. Charts of fetal size: kidney and renal pelvis measurements. Prenat Diagn 2003;23(11):891–897.
27. Sherer DM, Abramowicz JS, Plessinger MA, Woods JR Jr. Fetal sacral length in the ultrasonographic assessment of gestational age. Am J Obstet Gynecol 1993;168(2):626–633.
28. Gottlieb AG, Galan HL. Nontraditional sonographic pearls in estimating gestational age. Semin Perinatol 2008;32(3):154–160.
29. Chavez MR, Ananth CV, Smulian JC, Vintzileos AM. Fetal transcerebellar diameter measurement for prediction of gestational age at the extremes of fetal growth. J Ultrasound Med 2007;26(9):1167–1171; quiz 1173–1174.
30. Snijders RJM, De Courcy-Wheeler RH, Nicolaides KH. Intrauterine growth retardation and fetal transverse cerebellar diameter. Prenat Diagn 1994;14(12):1101–1105.
31. Behrman RE, Lees MH, Peterson EN, De Lannoy CW, Seeds AE. Distribution of the circulation in the normal and asphyxiated fetal primate. Am J Obstet Gynecol 1970;108(6):956–969.
32. Hernandez-Andrade E, Figueroa-Diesel H, Jansson T, Rangel-Nava H, Gratacos E. Changes in regional fetal cerebral blood flow perfusion in relation to hemodynamic deterioration in severely growth-restricted fetuses. Ultrasound Obstet Gynecol 2008;32(1):71–76.
33. Meirowitz NB, Ananth CV, Smulian JC, McLean DA, Guzman ER, Vintzileos AM. Foot length in fetuses with abnormal growth. J Ultrasound Med 2000;19(3):201–205.
34. Konje JC, Okaro CI, Bell SC, de Chazal R, Taylor DJ. A cross-sectional study of changes in fetal renal size with gestation in appropriate- and small-for-gestational-age fetuses. Ultrasound Obstet Gynecol 1997;10(1):22–26.
35. Silver LE, Decamps PJ, Korst LM, Platt LD, Castro L. Intrauterine growth restriction is accompanied by decreased renal volume in the human fetus. Am J Obstet Gynecol 2003;188(5):1320–1325.
36. Karabulut AK, Köylüoğlu B, Uysal I. Human foetal sacral length measurement for the assessment of foetal growth and development by ultrasonography and dissection. Anat Histol Embryol 2001;30(3):141–146.
37. Ozat M, Kanat-Pektas M, Gungor T, Gurlek B, Caglar M. The significance of fetal sacral length in the ultrasonographic assessment of gestational age. Arch Gynecol Obstet 2011;283(5):999–1004.
38. Mahony BS, Bowie JD, Killam AP, Kay HH, Cooper C. Epiphyseal ossification centers in the assessment of fetal maturity: sonographic correlation with the amniocentesis lung profile. Radiology 1986;159(2):521–524.
39. Mahony BS, Callen PW, Filly RA. The distal femoral epiphyseal ossification center in the assessment of third-trimester menstrual age: sonographic identification and measurement. Radiology 1985;155(1):201–204.
40. Donne HD Jr, Faúndes A, Tristão EG, de Sousa MH, Urbanetz AA. Sonographic identification and measurement of the epiphyseal ossification centers as markers of fetal gestational age. J Clin Ultrasound 2005;33(8):394–400.
41. Dubinsky TJ, O'Regan J, Sonneborn R, Hippe DS, Dighe M, Moshiri M. A Nomogram of Lateral Abdominal Wall Fat Thickness in Normal Third Trimester Fetuses. Ultrasound Q 2019;35(1):30–34.
42. Warska A, Maliszewska A, Wnuk A, Szyszka B, Sawicki W, Cendrowski K. Current knowledge on the use of ultrasound measurements of fetal soft tissues for the assessment of pregnancy development. J Ultrason 2018;18(72):50–55.
43. Wu L, Richardson ML, Dubinsky T. Predicting Adverse Neonatal Outcome Especially When Gestational Age Is Uncertain: Utility of Sonographic Measurement of Fetal Abdominal Wall Thickness. Ultrasound Q 2017;33(3):208–212.
44. Rigano S, Ferrazzi E, Radaelli T, Cetin ET, Pardi G. Sonographic measurements of subcutaneous fetal fat in pregnancies complicated by gestational diabetes and in normal pregnancies. Croat Med J 2000;41(3):240–244.
45. Maruotti GM, Saccone G, Martinelli P. Third trimester ultrasound soft-tissue measurements accurately predicts macrosomia. J Matern Fetal Neonatal Med 2017;30(8):972–976.
46. Garabedian C, Vambergue A, Salleron J, Deruelle P. Prediction of macrosomia by serial sonographic measurements of fetal soft-tissues and the liver in women with pregestational diabetes. Diabetes Metab 2013;39(6):511–518.
47. Gordijn SJ, Beune IM, Ganzevoort W. Building consensus and standards in fetal growth restriction studies. Best Pract Res Clin Obstet Gynaecol 2018;49:117–126.
48. Blue NR, Beddow ME, Savabi M, Katukuri VR, Chao CR. Comparing the Hadlock fetal growth standard to the Eunice Kennedy Shriver National Institute of Child Health and Human Development racial/ethnic standard for the prediction of neonatal morbidity and small for gestational age. Am J Obstet Gynecol 2018;219(5):474.e1–474.e12.
49. Brenner WE, Edelman DA, Hendricks CH. A standard of fetal growth for the United States of America. Am J Obstet Gynecol 1976;126(5):555–564.
50. Williams RL, Creasy RK, Cunningham GC, Hawes WE, Norris FD, Tashiro M. Fetal growth and perinatal viability in California. Obstet Gynecol 1982;59(5):624–632.

51. Hadlock FP, Harrist RB, Sharman RS, Deter RL, Park SK. Estimation of fetal weight with the use of head, body, and femur measurements--a prospective study. Am J Obstet Gynecol 1985;151(3):333–337.
52. Papageorghiou AT, Ohuma EO, Altman DG, et al. International standards for fetal growth based on serial ultrasound measurements: the Fetal Growth Longitudinal Study of the INTERGROWTH-21st Project. Lancet 2014;384(9946):869–879.
53. Kiserud T, Piaggio G, Carroli G, et al. The World Health Organization Fetal Growth Charts: A Multinational Longitudinal Study of Ultrasound Biometric Measurements and Estimated Fetal Weight. PLoS Med 2017;14(1):e1002220. [Published correction appears in PLoS Med 2017;14(3):e1002284.]
54. Gardosi J, Francis A, Turner S, Williams M. Customized growth charts: rationale, validation and clinical benefits. Am J Obstet Gynecol 2018;218(2S):S609–S618.
55. Blue NR, Grobman WA, Larkin JC, et al. Customized versus Population Growth Standards for Morbidity and Mortality Risk Stratification Using Ultrasonographic Fetal Growth Assessment at 22 to 29 Weeks' Gestation. Am J Perinatol 2020. 10.1055/s-0040-1705114. Published online March 20, 2020.
56. McCowan L, Horgan RP. Risk factors for small for gestational age infants. Best Pract Res Clin Obstet Gynaecol 2009;23(6):779–793.
57. Page JM, Thorsten V, Reddy UM, et al. Potentially Preventable Stillbirth in a Diverse U.S. Cohort. Obstet Gynecol 2018;131(2):336–343.
58. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics and the Society forMaternal-Fetal Medicin. ACOG Practice Bulletin No. 204: Fetal Growth Restriction. Obstet Gynecol 2019;133(2):e97–e109.
59. Martins JG, Biggio JR, Abuhamad A. Society for Maternal-Fetal Medicine Consult Series #52: diagnosis and management of fetal growth restriction (replaces clinical guideline number 3, April 2012). Am J Obstet Gynecol 2020;223(4):B2–B17.
60. Lausman A, Kingdom J; Maternal Fetal Medicine Committee. Intrauterine growth restriction: screening, diagnosis, and management. J Obstet Gynaecol Can 2013;35(8):741–748.
61. Royal College of Obstetricians and Gynecologists. The Investigation and Management of the Small-for-Gestational-Age Fetus: Green-top Guideline No. 31. London, England: Royal College of Obstetricians and Gynecologists, 2013.
62. Caradeux J, Martinez-Portilla RJ, Peguero A, Sotiriadis A, Figueras F. Diagnostic performance of third-trimester ultrasound for the prediction of late-onset fetal growth restriction: a systematic review and meta-analysis. Am J Obstet Gynecol 2019;220(5):449–459.e19.
63. Blue NR, Yordan JMP, Holbrook BD, Nirgudkar PA, Mozurkewich EL. Abdominal Circumference Alone versus Estimated Fetal Weight after 24 Weeks to Predict Small or Large for Gestational Age at Birth: A Meta-Analysis. Am J Perinatol 2017;34(11):1115–1124.
64. Committee on Practice Bulletins—Obstetrics. Macrosomia: ACOG Practice Bulletin, Number 216. Obstet Gynecol 2020;135(1):e18–e35.
65. Monk D, Moore GE. Intrauterine growth restriction: genetic causes and consequences. Semin Fetal Neonatal Med 2004;9(5):371–378.
66. Mendelson E, Aboudy Y, Smetana Z, Tepperberg M, Grossman Z. Laboratory assessment and diagnosis of congenital viral infections: rubella, cytomegalovirus (CMV), varicella-zoster virus (VZV), herpes simplex virus (HSV), parvovirus B19 and human immunodeficiency virus (HIV). Reprod Toxicol 2006;21(4):350–382.
67. Crino JP, Driggers RW. Ultrasound Findings Associated With Antepartum Viral Infection. Clin Obstet Gynecol 2018;61(1):106–121.
68. Resnik R. Intrauterine growth restriction. Obstet Gynecol 2002;99(3):490–496.
69. Morris RK, Say R, Robson SC, Kleijnen J, Khan KS. Systematic review and meta-analysis of middle cerebral artery Doppler to predict perinatal wellbeing. Eur J Obstet Gynecol Reprod Biol 2012;165(2):141–155.
70. Burton GJ, Jauniaux E. Pathophysiology of placental-derived fetal growth restriction. Am J Obstet Gynecol 2018;218(2S):S745–S761.
71. Figueras F, Caradeux J, Crispi F, Eixarch E, Peguero A, Gratacos E. Diagnosis and surveillance of late-onset fetal growth restriction. Am J Obstet Gynecol 2018;218(2S):S790–S802.e1.
72. Gordijn SJ, Beune IM, Thilaganathan B, et al. Consensus definition of fetal growth restriction: a Delphi procedure. Ultrasound Obstet Gynecol 2016;48(3):333–339.
73. Savchev S, Figueras F, Sanz-Cortes M, et al. Evaluation of an Optimal Gestational Age Cut-Off for the Definition of Early- and Late-Onset Fetal Growth Restriction. Fetal Diagnosis and Therapy. 2014;36(2):99-105.
74. Stensvold HJ, Klingenberg C, Stoen R, et al. Neonatal Morbidity and 1-Year Survival of Extremely Preterm Infants. Pediatrics 2017;139(3):e20161821.
75. Mongelli M, Ek S, Tambyrajia R. Screening for fetal growth restriction: a mathematical model of the effect of time interval and ultrasound error. Obstet Gynecol 1998;92(6):908–912.
76. Hiersch L, Melamed N. Fetal growth velocity and body proportion in the assessment of growth. Am J Obstet Gynecol 2018;218(2S):S700–S711.e1.
77. Kingdom JCP, Burrell SJ, Kaufmann P. Pathology and clinical implications of abnormal umbilical artery Doppler waveforms. Ultrasound Obstet Gynecol 1997;9(4):271–286.
78. Alfirevic Z, Stampalija T, Dowswell T. Fetal and umbilical Doppler ultrasound in high risk pregnancies. Cochrane Database Syst Rev 2017;6(6):CD007529. https://doi.org/10.1002/14651858.CD007529.pub4.
79. Kennedy AM, Woodward PJ. A radiologist's guide to the performance and interpretation of obstetric Doppler US. RadioGraphics 2019;39(3):893–910.
80. Ting JY, Kingdom JC, Shah PS. Antenatal glucocorticoids, magnesium sulfate, and mode of birth in preterm fetal small for gestational age. Am J Obstet Gynecol 2018;218(2S):S818–S828.
81. Jha P, Morgan TA, Kennedy A. US Evaluation of Twin Pregnancies: Importance of Chorionicity and Amnionicity. RadioGraphics 2019;39(7):2146–2166.
82. Khalil A, Beune I, Hecher K, et al. Consensus definition and essential reporting parameters of selective fetal growth restriction in twin pregnancy: a Delphi procedure. Ultrasound Obstet Gynecol 2019;53(1):47–54.
83. Gratacós E, Lewi L, Muñoz B, et al. A classification system for selective intrauterine growth restriction in monochorionic pregnancies according to umbilical artery Doppler flow in the smaller twin. Ultrasound Obstet Gynecol 2007;30(1):28–34.
84. Townsend R, D'Antonio F, Sileo FG, Kumbay H, Thilaganathan B, Khalil A. Perinatal outcome of monochorionic twin pregnancy complicated by selective fetal growth restriction according to management: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2019;53(1):36–46.
85. Boulvain M, Irion O, Dowswell T, Thornton JG. Induction of labour at or near term for suspected fetal macrosomia. Cochrane Database Syst Rev 2016;2016(5):CD000938.
86. American College of Obstetricians and Gynecologists (College); Society for Maternal-Fetal Medicine; Caughey AB, Cahill AG, Guise JM, Rouse DJ. Safe prevention of the primary cesarean delivery. Am J Obstet Gynecol 2014;210(3):179–193.