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Making Sense of How to Evaluate Fetal Growth

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Making Sense of How to Evaluate Fetal Growth

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- Philips Ultrasound: Technology Consultant

Learning Objectives

After completing this presentation, the participant should be able to:

1. Describe the use and potential limitations of population-based weight reference ranges/standards for fetal size assessment
2. Discuss other approaches for fetal size assessment including customized growth curves and individualized growth assessment
3. Explain why accurate pregnancy dating is needed to assess fetal growth
4. Summarize major concepts about the prenatal diagnosis and clinical significance of fetal growth restriction and macrosomia.
1. General Overview

Fetal growth is a function of both seed and soil. It is dependent upon the growth potential of the fetus and the availability of intrauterine nutrition, in its broadest sense, to fulfill this potential. The result of these two factors is a wide distribution of birth size at any one gestational age, and a wide variation in the state of nutrition at birth.

Am J Obstet Gynecol 1966;94:951-963

Growth Abnormalities

Depends on how pathological growth processes are defined

Fetal Size Assessment  Neonatal Growth Outcome
ARTICLES
INTRAUTERINE GROWTH AS ESTIMATED FROM LIVEBORN BIRTH-WEIGHT DATA AT 24 TO 42 WEEKS OF GESTATION
Lulo O. Lubchenco, M.D., Charlotteman, M.D., Marin Drucker, M.D.,
and Patricia Rebell, M.D.
Pediatrics Infant Center, Department of Pediatrics, and Child Research Council,
University of Colorado Medical Center, Denver, Colorado

“Small for Gestational Age” = Infants with BW < 10th pct for Gestational Age

“Large for Gestational Age” = Infants with BW > 90th pct for Gestational Age

A standard of fetal growth for the United States of America

WILLIAM E. BRENNER, M.D.
DAVID A. EDELMAN, Ph.D.
CHARLES H. HENDRICKS, M.D.
Chapel Hill and Research Triangle Park, North Carolina

The appropriate interpretation of measured fetal growth throughout pregnancy in individual patients and populations is dependent upon the availability of adequate standards. There is no adequate standard of fetal weight throughout pregnancy that is suitable for patients in the U.S. To determine such a standard for infants delivered at birth and born live 26th, 28th, 30th, 32nd, and 36th week, and in the 10th, 50th, and 90th percentiles of birth weight for each maternal week of gestation were calculated from 430 fetuses of 8 to 20 maternal weeks' gestation aborted with postmortem autopsy from 35,772 liveborn infant delivered of patients at 21 to 44 maternal weeks' gestation. Abortion fetal cases were in normal weight and were delivered at 21 to 28 weeks' gestation. Fetal weights corrected factors for parity, race (American, Caucasian), and infant sex were calculated. The derived fetal growth curves are useful for clinical, public health, and investigational purposes. (Am J Obstet Gynecol 120: 569, 1975)
Birth weight (BW) is directly measured as an indicator of neonatal growth outcome.

Estimated fetal weight (EFW) is calculated using several size parameters for the assessment of fetal nutritional status.

26 different birth weight prediction models
3,705 sonographic EFW < 3 days delivery
For most models, estimates were within 15% of actual BW in more than 80% of cases.

Considerable variation among different models, although most showed good overall accuracy.

Models with 3-4 fetal biometric indices were better than models with only 1 or 2 indices (BW range 1000 - 4500 g)

Accuracy decreased at BW extremes, with overestimation in low-BW categories vs underestimation for BW > 4000 g

Model precision was lowest in the low-BW groups.
Once EFW is calculated, this result is compared to a population-based standard.

Radiology 1991; 181:129-133

Customised Birth Weight Standards

Weight for gestational age percentiles are individualized for maternal influences on fetal growth.

Stepwise Multiple Regression

- maternal height
- pre-pregnancy BMI
- ethnicity
- parity
- fetal gender

optimal 280 day BW predicted for each infant

Customised Birth Weight Standards

Since not all babies are born at 280 days, the target BW is extrapolated to the exact GA at birth using a Hadlock proportionality formula (1991)

Infant’s BW is compared to target BW

Any newborn with actual BW < 10th pct of assumed distribution around target weight is considered SGA


The case against customised birthweight standards

“However, their apparent benefits are more likely to have been derived from their incorporation of intrauterine-based (EFW) reference values at preterm ages than their adjustment for maternal characteristics.”

Paediatr Perinat Epidemiol. 2011;25:11-6

The case against customised birthweight standards

“Customised birthweight standards are widely recognised to improve the prediction of adverse perinatal outcomes compared with conventional birthweight-for-gestational-age charts.”

Paediatr Perinat Epidemiol. 2011;25:11-6
“Although maternal characteristics are able to explain population-level differences in birthweight, they are not strong enough predictors for individual-level prediction of birthweight.”

Paediatr Perinat Epidemiol. 2011;25:11-6

International standards for fetal growth based on serial ultrasound measurements: the Fetal Growth Longitudinal Study of the INTERGROWTH-21st Project


4,321 women - prospective longitudinal study
8 countries
Fetal biometry obtained q 5 weeks (14-42 weeks)

Comparison of the Hadlock and Intergrowth 21st formulas for calculating estimated fetal weight in a preterm population in France

578 normal singleton fetuses delivered with 2 days of scan

<table>
<thead>
<tr>
<th></th>
<th>Percent Diff ± 10% BW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hadlock EFW (HC, AC, FDL)</td>
<td>-0.7 ± 10.1%</td>
</tr>
<tr>
<td>Intergrowth EFW (HC, AC)</td>
<td>-3.5 ± 11.6%</td>
</tr>
</tbody>
</table>

Hadlock’s EFW formula was more accurate than INTERGROWTH’s formula for fetuses delivered between 22 and 34 weeks of gestation.

Monier I, et al. Am J Obstet Gynecol, accepted August 7, 2018

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**Racial/ethnic standards for fetal growth: the NICHD Fetal Growth Studies**

Catherine M. Buck Louis, PhD, MS; Ingriduworo Grodski, PhD, MPH; Paul S. Albers, PhD; Anthony Sciscione, DO; Deborah A. Way, MD; William A. Griswold, MD, MBA; Roger B. Newman, MD; Ronald Wagner, MD; Mary L. O’aho, MD; Daniel Skupski, MD; Michael F. Nugent, MD; Angela C. Rantin, MD; John Oruc, MD, MPH; Edward C. Chire, MD; Achiwui Canigo, MD; Mary L. Bedgear, MD; Sanghah Kim, PhD; Carlos Zhang, MD, MPH, PhD; Katherine L. Gerba, MD, MS

1,737 women - prospective longitudinal US study

Low risk singleton pregnancies

Fetal growth differences observed among 4 ethnic/racial groups


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**NICHD Fetal Growth Study**

1,387 women - prospective longitudinal US study (7 scans)

Low risk singleton pregnancies

Fetal growth variation observed among 10 countries

WHO Fetal Growth Study

WHO FETAL

LOCATION
18 Countries
Albania, Bangladesh, Democratic Republic of Congo, Ethiopia, Ghana, India, Kenya, Norway, and Thailand

RACE & ETHNIC
One overall growth chart
Fetal growth showed racial and ethnic variation, and the relationship between parameters varied among ethnic groups, with a highly skewed distribution.

INCLUSION/EXCLUSION
On a per-country basis,
Indicators for inclusion and exclusion were used to ensure the representativeness of the sample population.

ANALYTIC APPROACHES
Data transformation - biparabolic regression
Data transformation techniques were used to normalize the distribution of the data.

ESTIMATED FETAL WEIGHT
Data transformation - linear regression
Data transformation techniques were used to normalize the distribution of the data.

Individualized Growth Assessment

Rossavik Growth Model

\[ P = c (t) + k + s (t) \]

c growth regulation
k anatomic characteristic of size parameter
s growth controller specified by coefficient c
t duration of parameter growth
Individualized Growth Assessment

2nd TM growth velocities provide estimates of growth potential and predict 3rd TM size trajectories/birth characteristics

• Each fetus serves as its own control
• Biological variability is substantially reduced
• Fetal growth characterized by individual/composite anatomical parameters


iGAP Individualized Growth Assessment Program

igap.research.bcm.edu

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Free AJOG Special Edition

http://www.ajog.org/issue/S0002-9378(17)X0017-3
2. Sonographic Criteria for Dating Pregnancies

Accurate Dating is Crucial for Fetal Growth Assessment

- US measurement of embryo or fetus ≤ 13 6/7 weeks most accurate way to establish or confirm age
- Prioritize use of assisted reproductive technology (ART), if available, based on age of embryo and date of transfer

<table>
<thead>
<tr>
<th>Menstrual Age Range</th>
<th>Method of Measurement</th>
<th>Re-Dating Criteria US vs LMP Discrepancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>13 6/7 wk</td>
<td>CRL</td>
<td>&gt; 5 days</td>
</tr>
<tr>
<td>9 0/7 - 13 6/7 wk</td>
<td>BPD, HC, AC, FDL</td>
<td>&gt; 7 days</td>
</tr>
<tr>
<td>14 0/7 - 15 6/7 wk</td>
<td>BPD, HC, AC, FDL</td>
<td>&gt; 7 days</td>
</tr>
<tr>
<td>16 0/7 - 21 6/7 wk</td>
<td>BPD, HC, AC, FDL</td>
<td>&gt; 10 days</td>
</tr>
<tr>
<td>22 0/7 - 27 6/7 wk</td>
<td>BPD, HC, AC, FDL</td>
<td>&gt; 14 days</td>
</tr>
<tr>
<td>&gt; 28 0/8 weeks</td>
<td>BPD, HC, AC, FDL</td>
<td>&gt; 21 days</td>
</tr>
</tbody>
</table>

As soon as data from the last menstrual period (LMP), the first accurate ultrasound examination, or both are obtained, the gestational age and the EDD should be determined, discussed with the patient, and documented clearly in the medical record.

Subsequent changes to the EDD should be reserved for rare circumstances, discussed with the patient, and documented clearly in the medical record.
3. Fetal Macrosomia

**Fetal Macrosomia - Increased Risks**

- cesarean delivery
- shoulder dystocia
- clavicular fracture
- brachial plexus injury


**Fetal Macrosomia Incidence**

<table>
<thead>
<tr>
<th>Menstrual Age</th>
<th>50th Percentile</th>
<th>90th Percentile</th>
<th>95th Percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>37 weeks</td>
<td>3,117</td>
<td>3,956</td>
<td></td>
</tr>
<tr>
<td>38 weeks</td>
<td>3,263</td>
<td>4,027</td>
<td></td>
</tr>
<tr>
<td>39 weeks</td>
<td>3,400</td>
<td>4,107</td>
<td></td>
</tr>
<tr>
<td>40 weeks</td>
<td>3,495</td>
<td>4,185</td>
<td></td>
</tr>
<tr>
<td>41 weeks</td>
<td>3,527</td>
<td>4,217</td>
<td></td>
</tr>
<tr>
<td>42 weeks</td>
<td>3,522</td>
<td>4,213</td>
<td></td>
</tr>
</tbody>
</table>

Fetal Macrosomia Prediction

- 1717 women with singleton pregnancies
- EFW performed during preceding week
- clinical EFW before ruptured membranes


<table>
<thead>
<tr>
<th>EFW (grams)</th>
<th>Clinical EFW</th>
<th>US EFW</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All infants</td>
<td>-0.01 ± 10.4%</td>
<td>-1.4 ± 10.7%</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>&lt; 2500 (134)</td>
<td>10.0 ± 15.4%</td>
<td>6.8 ± 12.6%</td>
<td>&lt; 0.015</td>
</tr>
<tr>
<td>2500 - 4000 (1389)</td>
<td>0.2 ± 9.2%</td>
<td>-1.2 ± 10.3%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>&gt; 4000 (194)</td>
<td>-8.2 ± 6.9%</td>
<td>-8.3 ± 7.9%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Reviewed 63 accuracy studies (51 EFW, 12 AC)
- ROC curves for predicting EFW > 4,000 grams
- No differences between EFW or AC > 36 cm seen

"No difference in accuracy between ultrasonographically EFW and AC in the prediction of a macrosomic baby at birth. A positive test result is more accurate for ruling in macrosomia than a negative test result for ruling it out."


"The diagnosis of fetal macrosomia is imprecise. For suspected macrosomia, the EFW using ultrasound biometry is no better than obtained with clinical palpation." (Level A)

- suspected fetal macrosomia is not an indication for labor induction because induction does not improve maternal - fetal outcomes (Level B)
- labor and vaginal delivery are not contraindicated for women with EFW up to 5,000 g in the absence of maternal diabetes (Level B)
- with EFW > 4,500 grams, a prolonged 2nd stage of labor or arrest of descent in the second stage is an indication for delivery (Level B)
• consider cesarean delivery for suspected fetal macrosomia with EFW > 5,000 g in women without diabetes and > 4,500 g in women with diabetes

• suspected fetal macrosomia is not a contraindication to attempted vaginal birth after a previous cesarean delivery

4. Fetal Growth Restriction

1 in every 12 newborns in the United States are delivered with low birth weight (< 2,500 grams)

• perinatal death
• developmental delay
• learning disabilities
• cerebral palsy
• hearing loss
Fetal Growth Restriction

Fetal growth restriction, also known as intrauterine growth restriction, is a common complication of pregnancy that has been associated with a variety of adverse perinatal outcomes. There is a lack of consensus regarding normal age, ethnic, and diagnostic criteria for fetal growth restriction, with many controversies surrounding the optimal assessment and staging of the fetus for the growth restriction phase. The variable definitions of fetal growth restriction are subject to the criteria used and may be influenced by a variety of factors including maternal age, race, and socioeconomic status.

Birth Weight (g) for Gestational Age


Variable Definitions - FGR

- Denver (Lutchen et al., 1985)
- Liveborn Infants - White and Hispanic
- Cleveland and North Carolina (Hendricks, 1976)
- White & Black Liveborn Infants - Abortuses
- California (Williams, 1976)
- Birth Certificates - 4 Ethnic Groups
- St. Louis (Olt, 1993) - Postnatal Data
- US Reference (Alexander, 1966)

Which Population Cut-Off is Used?
12,317 singleton infants (1988-1996) ≥ 37 weeks gestation

<table>
<thead>
<tr>
<th>Birth Weight %</th>
<th>26th-75th</th>
<th>11-15th</th>
<th>8-10th</th>
<th>6-10th</th>
<th>4th-5th</th>
<th>3rd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Infants</td>
<td>3184</td>
<td>5400</td>
<td>5254</td>
<td>2065</td>
<td>3184</td>
<td>12,317</td>
</tr>
<tr>
<td>Apgar ≤ 3.5 min</td>
<td>7 (0.2)</td>
<td>6 (0.2)</td>
<td>7 (0.1)</td>
<td>9 (0.1)</td>
<td>9 (0.1)</td>
<td>5 (0.1)</td>
</tr>
<tr>
<td>UA Cord pH ≤ 7.0</td>
<td>12 (0.6)</td>
<td>9 (0.6)</td>
<td>8 (0.4)</td>
<td>27 (0.5)</td>
<td>12 (0.3)</td>
<td>212 (0.4)</td>
</tr>
<tr>
<td>Intubation Del Rm</td>
<td>11 (0.5)</td>
<td>20 (0.7)</td>
<td>19 (0.7)</td>
<td>27 (0.6)</td>
<td>317 (0.6)</td>
<td>70 (0.2)</td>
</tr>
<tr>
<td>Seizures (1st 24 hrs)</td>
<td>4 (0.2)</td>
<td>9 (0.2)</td>
<td>16 (0.1)</td>
<td>68 (0.1)</td>
<td>28 (0.3)</td>
<td>28 (0.3)</td>
</tr>
<tr>
<td>Sepsis (+ blood cult)</td>
<td>6 (0.3)</td>
<td>9 (0.3)</td>
<td>28 (0.3)</td>
<td>212 (0.4)</td>
<td>317 (0.4)</td>
<td>12 (0.1)</td>
</tr>
<tr>
<td>Death (1st 28 days)</td>
<td>9 (0.3)</td>
<td>2 (0.1)</td>
<td>3 (0.1)</td>
<td>18 (&lt;0.1)</td>
<td>2 (&lt;0.1)</td>
<td>9 (&lt;0.1)</td>
</tr>
</tbody>
</table>

*p < 0.05 refers to data compared to 26th-75th percentile

Adapted from Engl J Med 1999;340:1234-8

834 women singleton with small fetuses (81% SGA newborns)

Fetal Growth Restriction - Dx

Requires Accurate Gestational Dating Criteria
- certain LMP with regular menstrual cycles
- early pregnancy scan (e.g. 1st trimester)

Suspect FGR in the presence of US findings
- EFW < 10th percentile
- decreased amniotic fluid volume
- abnormal fetal Doppler study (UA, MCA, CPR)
Prevalence: ~ 3-5%

Mild placental disease:
- UA Doppler normal
- Low association preeclampsia
- Mild hypoxia + central CV adaptation
- Lower mortality (some late stillbirth)

Prevalence: ~ 1%

Severe placental disease:
- UA Doppler abnormal
- High association preeclampsia
- Severe hypoxic + systemic CV adaptation
- High mortality and morbidity

Early-Onset FGR (< 32 weeks)

- CHALLENGE: MANAGEMENT
- Prevalence: ~ 1%
- Severe placental disease:
  - UA Doppler abnormal
  - High association preeclampsia
- Severe hypoxic + systemic CV adaptation
- High mortality and morbidity

Late-Onset FGR (≥ 34 weeks)

- CHALLENGE: DIAGNOSIS
- Prevalence: ~ 3-5%
- Mild placental disease:
  - UA Doppler normal
  - Low association preeclampsia
- Mild hypoxia + central CV adaptation
- Lower mortality (some late stillbirth)


SGA Infant - Risk Factors

Maternal Risk Factors
- Short maternal stature
- Low maternal weight
- Indian or Asian ethnicity
- Nulliparity
- Mother was SGA
- Cigarette smoking
- Cocaine use

Maternal Disease
- Chronic hypertension
- Renal disease
- Anti-phospholipid syndrome
- Malaria


Growth Restricted Newborn

Obstetrical Factors

- heavy 1st TM bleeding
- placental abruption
- preeclampsia
- gestational hypertension

Short or Long Inter-Pregnancy Interval

Previous SGA infant

Prior Stillbirth


SGA Infant - Risk Factors

- intrauterine demise
- neonatal morbidity
  - hypoglycemia
  - hyperbilirubinemia
  - hypothermia
  - intraventricular hemorrhage
  - necrotizing enterocolitis
  - sepsis
  - respiratory distress syndrome
- neonatal death
- cognitive delays in childhood
- adult diseases


SGA Infant - Postnatal Sequelae

- hypoglycemia
- hyperbilirubinemia
- hypothermia
- intraventricular hemorrhage
- necrotizing enterocolitis
- sepsis
- respiratory distress syndrome
- neonatal death
- cognitive delays in childhood
- adult diseases

Long Term Outcomes - SGA Children at Age 10

“FGR influences cardiomyocyte development during critical windows of development, leading to a permanent deficiency in cardiomyocyte number and compensatory hypertrophy in a rodent model that recapitulates human development.”

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Universal 3rd trimester fetal biometry roughly tripled detection of SGA infants

Prospective Cohort Study (2008-2012)
- 4,512 nulliparous Woman
- fetal biometry at 20, 28, 36 weeks gestation
- gestational age adjusted z-scores
- AC growth velocity (differences in AC z-score between 36 and 20 week scan)


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Population Based Study - 14,100 live births (2010)
To assess the proportion of small for gestational age (SGA) and normal birthweight infants suspected of fetal growth restriction (FGR) during pregnancy

Investigate obstetric and neonatal outcomes by suspicion of FGR and SGA status at birth


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21.7% of SGA infants (n = 265) and 2.1% of non-SGA infants (n = 271) were suspected of FGR during pregnancy.

Antenatal suspicion of FGR among SGA infants was low and one-half of infants suspected of FGR were not SGA.

Neonatal outcomes were not better for SGA infants if FGR was suspected.


5. Case Examples

Case 1  CMV

23 y/o G3P2  two prior term vaginal deliveries
gestational diabetes

Anatomy Survey - 20.5 weeks
- good dating criteria
- BPD, HC, FDL < 5th percentile; AC @ 42nd percentile
- mean EFW @ 6th percentile
- hyperechoic bowel

Viral Studies
- CMV AB IGG High
- CMV AB IGM High
- CMV IGG Avidity Low

Hydrops
Case 1  CMV

Fetal Growth Restriction  Ascites/Hydrops

Case 2  Prior SGA Infant

19 y/o G4P1
Prior term 4 lb 11oz baby at 38 weeks

Anatomy Survey - 20.7 weeks
- good dating criteria
- mean EFW @ 13th
- no anomalies

normal UA Doppler

Case 3  Chronic Hypertension

35 y/o G2P1
Prior CSx at 39 weeks
2,637 g male (5 lb, 13 oz)
Chronic hypertension on labetalol
Aortic regurg from bicuspid aortic valve
BMI 40.8 kg/m2

20 week scan
- good dating criteria
- mean EFW @ 52nd%
- no anomalies

normal UA Doppler

2590 grams
36.3 weeks
Case 4 Chorioangioma

41 y/o G4P1  two prior early miscarriages
  one preterm C-Sx for sacral teratoma

Fetal Growth Scan - 37.9 weeks
  • good dating criteria
  • mean EFW @ 7th percentile
  • vascular placental mass
  • engorged neck vessels
  • normal amn fluid volume

Placental Vascular Mass

Engorged Neck Veins
Case 4  Chorioangioma

2,520 g female
5 lb, 9 oz  Apgars 9/9
16 hrs phototherapy
Discharged on Day 4

Conclusions

Fetal growth assessment requires accurate gestational dating criteria
- sure LMP with regular menstrual cycles
- early pregnancy scan (e.g. 1st trimester)

Not all small or large fetuses represent pathology

Suspect fetal macrosomia if EFW > 4,000 grams
or > 90th percentile for gestational age

Suspect fetal growth restriction for US findings
• EFW < 10th percentile
• decreased amniotic fluid volume
• abnormal fetal Doppler study (e.g. UA, MCA, CPR)

Key Steps:
- detect abnormal growth
distinguish “normal” vs “pathological”
integrate antenatal testing with delivery timing