Detection and Management of Intrauterine Growth Restriction.

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Conflicts of Interest

• I have no financial disclosures
My Clinical Experience

• The Newton Wellesley experience
  ✦ Patients identified with IUGR and sent to BWH
  ✦ Patients sent back as no problem identified on BWH growth charts
  ✦ NWH changed their growth charts to those used at BWH to prevent this

• BWH clinical macrosomia
  ✦ BPD 95, AD 120, FL 77
  ✦ 4142 gms
  ✦ 96th % at 39 weeks.
Aims

• To give insight into the lack of science in fetal weight assessment
• To realize the limitations of our current practice
• To show we can optimize the management of the small baby with current technology
Why Measure Fetal Size?

• To prevent stillbirth

• To avoid the problems of macrosomia
Importance: Stillbirth

Gordon C S Smith,
Ruth C Fretts Lancet.
2007 Nov 17;
370:1715-25

Figure 1: Causes of stillbirth with modified version of Wigglesworth classification for all singleton births in Scotland, 1992-2001
Data from 2635 antepartum stillbirths, from a total of 563719 births (rate 4.7 per 1000). Over the same period, there were 320 intrapartum stillbirths in 561,084 singletons alive at the onset of labour. 75% of these stillbirths were anoxic, 17% were classified as caused by congenital abnormality, and the remaining 8% had diverse other causes. SGA = small for gestational age (smallest decile of birthweight for sex and week of gestation). AGA = appropriate for gestational age (rest of population). The data sources are as described in reference 13. Smith GCS, unpublished data.
Morbidity and Mortality in 1560 SGA Fetuses

Risk factors for NE

- Abnormal placental appearance: 2.07
- Emergency cesarean: 2.17
- Instrumental delivery: 2.23
- Family history of seizure: 2.55
- Family history of neurological disorders: 2.73
- Viral illness: 2.97
- Moderate/severe antepartum bleeding: 3.57
- Intrapartum fever: 3.82
- Occiput posterior presentation: 4.29
- IUGR 3rd-9th percentile: 4.37
- Infertility treatment: 4.43
- Acute intrapartum event: 4.44
- Severe preeclampsia: 6.3
- Maternal thyroid disease: 9.7
- IUGR <3rd percentile: 38.23

How Do You Measure Fetal Size?
Identify Patients at Risk for Placental Insufficiency

- Hypertension
- Pre-eclampsia
- Antiphospholipid antibody syndrome
- Renal disease
- Diabetes
- Vascular disease
- Cyanotic heart disease
- Recurrent antepartum hemorrhage
- Hemoglobinopathies
- Thrombophilia
- Smoking
- Multiple gestation
- Pulmonary disease
Diagnosis of IUGR

- **Fundal Height**
  - Variable sensitivity (28-86%), improved with consistent provider
  - Discordance $\geq 3$ cm
  - Not sensitive enough to screen pregnancies at risk for growth restriction

- **Ultrasound**
  - Sonographic EFW best morphometric test to screen for IUGR
Definition?

• No internationally agreed upon definition
• World Health Organization: Infants <2500 gms
• Estimated birthweight <10%
  ✦ 70-80% constitutional
  ✦ 20-30% pathologic
  ✦ SGA – newborn with birthweight <10% (ACOG)
• EFW <3%
  ✦ Clinically the most useful for differentiating fetuses at highest risk of morbidity and mortality
• AC <10% (RCOG)
• Customized growth potential (recommended by RCOG)
Biometry

• Measurements
  ✦ BPD, AC, & FL
  ✦ Specific measurements
  ✦ Ratios

• Estimated fetal weight (formula to derive weight and method to derive percentile)
  ✦ Alexander
  ✦ Hadlock
  ✦ Shepard
  ✦ Warsof
  ✦ Williams
  ✦ Customized formulae

• Variation inter method and even intra method between years of publication and GA + %
Norms

- Which population?
- Who is included?
- Who is excluded?
- Intuitively, how should your population compare?
- Beyond norms, how do you prove abnormality vs normality (interval growth, amniotic fluid volume, and Dopplers)
Norms

- Population
- Ultrasound
- Customized
Population Norms

• Alexander / Doubilet
  ✦ Normal population of birth weight distribution taken from actual weight in a large cohort of babies born at BWH
  ✦ However babies born earlier tend to do so because something is abnormal
    • PET, abruption, extreme IUGR etc.
  ✦ They tend to be smaller (making the comparisons look relatively larger)
Population Norms

Alexander GR Obstet Gynecol 1996:87;163

Diagram showing birth weight in grams against gestational age in weeks.
Ultrasound Norms

- Ultrasound norms are taken from a database of measurements of fetuses from a cohort of mothers who are “the ideal” therefore having the most normal pregnancies.
- Hadlock
  - Texan, healthy women, abnormal pregnancies excluded
    - Intergrowth study
- The tend to be a narrow range (and often make comparisons look small)
Ultrasound Norms

Hadlock FP et al. Radiology 1991; 181:129
Population vs Ultrasound Norms

![Graph showing birth weight or estimated fetal weight (g) vs gestational age (weeks).]
### Birth Weight

#### Table 2. Smoothed Percentiles of Birth Weight (g) for Gestational Age: U.S. 1991 Single Live Births to Resident Mothers

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### Estimated Fetal Weight

#### In Utero Fetal Weight Standards at US

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Pctl = percentile.
Customized Norms

• Have patient specific data for appropriate comparison: the concept of standard normal curves not appreciating genetic difference
  ✦ Maternal height
  ✦ BMI
  ✦ Race
  ✦ Abnormal pregnancy history
  ✦ Smoking
  ✦ Socioeconomic group
  ✦ Education
  ✦ Serum analytes
Customized Norms

Which Norm to Use?

- Depends on what you want to find, how aggressive you want to be, and how cynical you are
- It depends on what you see as being practical and what your goals are
  - Using ultrasound norms will increase your scanning rate (and Doppler usage)
  - Using customized norms will increase observation even more
- For how much difference in outcome?
Customized Fetal Growth Potential and Pregnancy Outcome

• Retrospective analysis of FASTER population to compare pregnancy complications of SGA_{POP} vs. SGA_{CUST}

• Threatened PTL, antepartum hemorrhage, PIH, pre-eclampsia, stillbirth, early neonatal death

• Subgroup that was small by customized, but not standard curves was associated with complications

• Subgroup small by standard, but not customized not associated with adverse outcome

✨ Gardosi and Francis AJOG 2009;201:28.e1-8
Identification of Pathologically Small Fetuses Using Customized, Ultrasound and Population-Based Norms.

Nicole Smith, Radek Bukowski, Ann Thomas, Julian Robinson

Ultrasound Obstet Gynecol 5th February 2014 (Epub ahead of print)
Background

• Hypothesis

- Stillborn fetuses are more likely to be SGA or LGA than are liveborn fetuses

• Study Aims

- To evaluate whether the growth potential formula is better able to identify extremes of growth than are standardized or birthweight-based norms
Methods

- **Cases**: all singleton stillbirths from 1/1/2001 - 12/31/2010
- **Controls**: random 4:1 selection of liveborn fetuses from 85,968 singletons born in the same time period
- **Inclusion criteria**
  - Ultrasound evaluation of a live fetus at >24 weeks gestation, within one month of delivery
- **Exclusion criteria**
  - Major congenital anomaly
  - Demise related to PPROM, acute maternal illness or trauma
Methods

• Growth centile at ultrasound was calculated using 3 formulas:
  • Standardized population ultrasound norm (Hadlock)
  • Customized (growth potential) formula
  • Hospital-specific, birthweight based curve (Doubilet)

• Sensitivity and specificity for diagnosis of extremes of growth were compared
Indications for Ultrasound

- Breech
- Fluid
- NRNST
- Fetal
- Decreased FM
- Cervix, placenta
- Postdates
- AMA
- Other maternal med dz
- Diabetes
- HTN
- Growth
- Preterm labor
- Unknown

% of total

- Stillbirth
- Livebirth
Distribution of Growth: Livebirths

Graph showing the distribution of growth centiles for livebirths. The graph compares three methods: GP, Hadlock, and Doubilet.

- % of total livebirths
- Growth centile
Distribution of Growth: Stillbirths

![Bar chart showing the distribution of growth centiles for stillbirths, with data points for GP, Hadlock, and Doubilet methods.](chart.png)
## Sensitivity & Specificity: SGA

Growth < 10% ile only

<table>
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<tr>
<th>Formula</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>ROC AUC</th>
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<td>86.3 (80.5-90.6)</td>
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<td>28.6 (17.0-43.5)</td>
<td>90.4 (85.1-93.9)</td>
<td>57.5 (47.3-67.6)</td>
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<tr>
<td>Doubilet</td>
<td>12.0 (5.1-25.5)</td>
<td>97.0 (93.2-98.8)</td>
<td>50.9 (41.5-60.3)</td>
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Sensitivity & Specificity: SGA or LGA

Growth >90%ile or < 10%ile

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<td>Doubilet</td>
<td>24.5 (13.8-39.2)</td>
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Conclusions

• Ultrasound-based growth curves performed better than a birthweight-based curve in identifying fetuses with extremes of growth at risk for stillbirth

• Sensitivity for extremes of fetal growth was greater with growth potential than with Hadlock (but not statistically different).

• Specificity was lowest for growth potential.
In Practice

• For at least a decade BWH used a population growth curve and underestimated IUGR

• If we use Growth Potential we will detect more IUGR at the cost of a greater amount of scans, and for (in our experience) no difference in stillbirth

• We use Hadlock (which one?)
MFMU Network

• The association of CP with SGA birthweight in preterm neonates by individualized and population based percentiles

• An individualized SGA growth standard does not improve the association with, or prediction of, CP or death by 2 years
Warning of Asphyxia

Kick Chart

Cardiotocogram

Biophysical Profile

Doppler
Dopplers

- Maternal uterine artery
- Umbilical artery
- Ductus venosus
- Middle cerebral artery
- Inferior vena cava
- Umbilical vein
UA Doppler Velocimetry
Umbilical Artery
Venous Dopplers
Ductus Venosus
MCA
Pathologic Findings

Normal IUFD
The Fetal Prayer

I am a fetus in the womb,
I fear that it may become my tomb,
I hope my obstetrician hears me shout.
When it is time to get me out!
Temporal Sequence of Changes in IUGR Fetuses

- Increased umbilical artery S/D ratio
- Decreased impedance of middle cerebral artery (brain sparing)
- Absent EDF in UA
- Venous doppler changes
- Abnormal BPP / CTG
  - Umbilical vein pulsation, spontaneous late decelerations are signs of central nervous system hypoxia and cardiovascular collapse
Management

- Initial assessment
  1. GA
  2. Biometry q ≥ 2 weeks
  3. Monitor interval growth
  4. AFI
  5. Doppler of uterine and umbilical arteries
  6. HX of viral infection + TORCH
Practical Management of Near-term IUGR (34-36 weeks)

• **UA doppler normal, no risk factors:**
  • Once weekly dopplers and AFI
  • Serial growth q 2 weeks
  • Manage to term as long as appropriate interval growth

• **UA doppler diminished flow:**
  • Twice weekly dopplers / fetal testing
  • Serial growth q 2 weeks
  • Deliver if 36 weeks, inadequate interval growth, diminished / absent EDF, oligohydramnios, HTN, BPP ≤ 6/10
Practical Management of Preterm IUGR

- **32-34 weeks:** Admission / steroids / daily testing if absent EDF

- **<32 weeks**
  - Normal UA dopplers: same as near-term
  - Diminished or absent EDF: MCA and venous dopplers
  - Deliver if reverse UA EDF, non-reassuring CTG/BPP
Interventions to improve outcome?

• Insufficient evidence for maternal nutrient supplementation, plasma volume expansion, hospital bedrest, or oxygen therapy

• RCT did not support treatment with low-dose aspirin

Recurrence of IUGR

1\textsuperscript{st} pregnancy
- SGA
- AGA

2\textsuperscript{nd} pregnancy
- 29\% SGA
- 9\% SGA
Summary

• There are many different systems for estimating fetal weight
• Once identified as small for gestational age, how to identify pathological from constitutional?
  ✦ Interval growth
  ✦ Umbilical artery
  ✦ Ductus venosus
  ✦ Many other Dopplers (cardiac, venous, & MCA), more academic than practical
    • Move to BPP / CTG instead