Ultrasound Evaluation for Fetal Growth Restriction

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Objectives

- Why screen
- Who to screen
- When to screen/when to test
- What test(s) to use
- Where are we going

Disclosures

- None

Definitions

- Fetal growth restriction – Failure of a fetus to reach its growth potential
- Small for gestational age newborns – EFW < 10th% or AC < 10th%
- Severe SGA - < 3rd%
- LBW - < 2500 gms

WHY?

- Risk of fetal death
  - 1.5% with EFW < 10th%
  - 2.5% with EFW < 5th%
- Morbidity – Neonatal: hypoglycemia, hyperbilirubinemia, hypothermia, IVH, NEC, seizures, sepsis, RDS .... neonatal death
- Morbidity – Childhood: congnitive delay and Adulthood: higher risk for chronic disease (Barker hypothesis)

Morbidity and mortality in 1560 small for gestational age fetuses.

Maternal and fetal risk factors for stillbirth: population based study

<table>
<thead>
<tr>
<th>Fetal growth restriction:</th>
<th>n=38,953</th>
<th>n=386</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>79,596 (98.7)</td>
<td>108 (48.7)</td>
</tr>
<tr>
<td>Yes</td>
<td>381 (4.1)</td>
<td>35 (9.2)</td>
</tr>
</tbody>
</table>

*Place of birth combined if either subgroup < 1000 women. Birth weight < 10th percentile related to maternal weight centile.

Overall stillbirth rate of 4.2/1000 but 2.4/1000 without FGR.

Population-Based Estimates of In-Unit Survival for Very Preterm Infants - female

Population-Based Estimates of In-Unit Survival for Very Preterm Infants - male

Balance of risks/benefits of early delivery

Barker hypothesis
Barker hypothesis

**TABLE 1.** Hazard Ratios (95% Confidence Intervals) for Death From CHD According to Weight at Birth and at Age 1 y in 10,636 Men in Hertfordshire

<table>
<thead>
<tr>
<th>Weight (lb)</th>
<th>&lt; 5.5</th>
<th>5.5-6.5</th>
<th>6.6-7.5</th>
<th>&gt; 7.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before 65 y</td>
<td>1.30 (0.98-1.73)</td>
<td>1.27 (0.99-1.61)</td>
<td>1.19 (0.91-1.60)</td>
<td>1.00 (0.75-1.35)</td>
</tr>
<tr>
<td>All Ages</td>
<td>1.37 (1.00-1.90)</td>
<td>1.29 (1.00-1.66)</td>
<td>1.14 (0.91-1.44)</td>
<td>1.00 (0.75-1.35)</td>
</tr>
</tbody>
</table>

**WHO?**
- Maternal risk factors
  - History of FGR
  - Diabetes, hypertension, autoimmune disorders, renal disease
  - Tobacco or other substance use
  - Low prepregnancy birth weight
  - High altitude
- Pregnancy course
  - Poor weight gain
  - Preeclampsia
  - Short fundal height

**Etiologies**

**TABLE 2.** Percentage of Men Aged 64 y with Impaired Glucose Tolerance or Diabetes According to Weight at Birth in 370 Men in Hertfordshire

<table>
<thead>
<tr>
<th>Weight (lb)</th>
<th>&lt; 5.5</th>
<th>5.5-6.5</th>
<th>6.6-7.5</th>
<th>&gt; 7.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Men with 2-hr Glucose (95% Confidence Intervals)*</td>
<td>40 (6.1-52)</td>
<td>34 (5.4-49)</td>
<td>31 (4.6-45)</td>
<td>22 (4.5-39)</td>
</tr>
<tr>
<td>Odds Ratio</td>
<td>6.6 (1.5-28)</td>
<td>4.8 (1.3-17)</td>
<td>4.6 (1.4-16)</td>
<td>2.6 (0.8-8.9)</td>
</tr>
<tr>
<td>P for trend</td>
<td>&lt; 0.001</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for current BMI.

References:
- Barker hypothesis
- WHO?
- Etiologies
- Correlation for birth weight
Maternal constraint
- Small breed embryo transplanted to large breed uterus will growth larger than a small breed embryo remaining in a small breed uterus
- Multiple gestation in humans

Maternal nutrition
- Starvation effect most pronounced in third trimester (Holland example)
- Starvation in the first trimester with normal birthweight daughters but small granddaughters – epigenetic effects

Fetus
- Genetic potential

Placenta
- Placental growth (mass) in first half of pregnancy with remodeling (terminal villi) in later half of pregnancy
- Fetal growth in second half of pregnancy
Placental surface areas at different gestational ages. (1) areas of intermediate villi; (2) areas of terminal villi. (Adapted from The Physiology of the Human Placenta, by Page K, Figure 2.7, published by UCL press).

Illustration of uterine and placental vasculature in the non-pregnant, pregnant and immediate post-partum state. Normal pregnancy is characterized by the formation of large arterio-venous shunts that persist in the immediate postpartum period. By contrast, pregnancies complicated by severe preeclampsia are characterized by minimal arterio-venous shunts, and thus narrower uterine arteries. Red shading = arterial; blue shading = venous. Adapted from Burton et al. Placenta 2009; 30 (6), 473-482. Adapted from Placenta, Burton et al. 2009

When
- Maternal risk factors
- Poor weight gain
- Size less than dates (fundal height)
- Pregnancy associated hypertension
- Abnormal placentation
- Abnormal serum screening
- Uncertainty in dating
- Timing of testing dependent upon risk factor

EGA

<table>
<thead>
<tr>
<th>Clinical or Sonographic</th>
<th>+/- 1 SD</th>
</tr>
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<tbody>
<tr>
<td>IVF</td>
<td>+/- 1 day</td>
</tr>
<tr>
<td>Ovulation induction or AI</td>
<td>+/- 3 days</td>
</tr>
<tr>
<td>Ultrasound EGA &gt; 8 6/7 (CRL)</td>
<td>+/- 5 days</td>
</tr>
<tr>
<td>9-13 6/7 (CRL)</td>
<td>+/- 7 days</td>
</tr>
<tr>
<td>14-15 6/7 (BPD, HC, AC, FL)</td>
<td>+/- 7 days</td>
</tr>
<tr>
<td>16-20 6/7 (BPD, HC, AC, FL)</td>
<td>+/- 10 days</td>
</tr>
<tr>
<td>20-27 6/7 (BPD, HC, AC, FL)</td>
<td>+/- 14 days</td>
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WHAT (test to use)?
- Cardiotocography or NST
- Biophysical profile
- Doppler studies

Nonstress test (NST)

<table>
<thead>
<tr>
<th>Normal Behavior (score = 2)</th>
<th>Abnormal Behavior (score = 0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal breathing movements (FBMs)</td>
<td>\begin{itemize} \item Intermittent, multiple episodes of more than 30 sec within a 30-min biophysical profile (BPP) time frame. \item Fick test count \end{itemize}</td>
</tr>
<tr>
<td>Body or limb movements</td>
<td>\begin{itemize} \item At least three discrete body movements in 30 min. \item Continuous, active movement episodes equal a single movement \item Includes face motor movements, rolling movements, and so on, but not rapid eye movements or mouthing movements \end{itemize}</td>
</tr>
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BPP – gradual hypoxia concept

- NST and FBM
- Movement
- Tone
- AFV (chronic)

<table>
<thead>
<tr>
<th>Test score reach</th>
<th>No. of cases</th>
<th>% of total cases</th>
<th>No. of tests</th>
<th>Rate per 1000 cases</th>
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<td>25,898</td>
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<td>6 (pregnant)</td>
<td>600</td>
<td>5</td>
<td>6</td>
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</tr>
<tr>
<td>5 (pregnant)</td>
<td>83</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>4 (pregnant)</td>
<td>17</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>3 (pregnant)</td>
<td>15</td>
<td></td>
<td>1</td>
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<tr>
<td>Total</td>
<td>26,207</td>
<td>199</td>
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*Excludes deaths due to either major congenital anomaly or severe fetal instrumentation.

Table IV. Test score distribution and associated corrected perinatal mortality

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BPP and cord pH

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BPP and medications

- Beta adrenergics
  - Possible increase in FBM
- Steroids
  - Reduction in FBM and FM and non-reactive NST has been described
- Magnesium sulfate
  - Possible decrease in FBM and NST
- Opioids
- Fasting
  - Hyperglycemia may increase FBM in presence of acidemia
  - Fasting may decrease FBM


Risk for mortality morbidity due to prematurity


Doppler studies

- Umbilical artery
- Middle cerebral artery
- Ductus venosus
- Uterine artery
Middle cerebral artery

The curves indicate the 5th, 10th, 90th, and 95th percentile values for pregnancies with and without morbidity and perinatal complications. The interval between Doppler imaging and delivery was less than 2 weeks.

- Open circles, <10th percentile, no morbidity
- Filled circles, <10th percentile, with morbidity

Cerebroplacental ratio (CPR) in relation to gestational age.

Abnormal MCA
Abnormal umbilical artery
Abnormal ductus venosus

Abnormal
"Although the difference in proportion of infants surviving without neuroimpairment was non-significant at the primary endpoint, timing of delivery based on the study protocol using late changes in the DV waveform might produce an improvement in developmental outcomes at 2 years of age."

Conclusions Fetal outcome in this study was better than expected from contemporary reports: perinatal death was uncommon (8%) and 70% survived without severe neonatal morbidity. The intervals to delivery, death and severe morbidity were related to the presence and severity of maternal hypertensive conditions. Copyright © 2013 ISUOG. Published by John Wiley & Sons Ltd.

TRUFFLE 2011

- Expansion in use of customized fetal growth charts
- Cell-free fetal DNA for evaluation of genetic syndromes
- Biochemical markers to help distinguish small normal from placental dysfunction
For immediate release: Thursday, June 18, 2015

Researchers design placenta-on-a-chip to better understand pregnancy


THANK YOU!