Intrauterine Growth Restriction

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Terminology

- Low birthweight (LBW) = < 2500g at birth
- Small for gestational age (SGA) - < 10th centile for growth - NEONATAL
- Intrauterine growth restriction (IUGR or FGR) < 10th centile for growth - OBSTETRICAL

Maternal Causes

- Maternal disease
- Substance abuse
- Malnutrition
- Teratogen exposure
- Environmental

Fetal Causes

- Multiple gestation
- Genetic abnormalities
- Structural abnormalities

Placental Causes

- Placental separation, infarction
- Congenital infections
- Abnormal placentation
- Primary placental disease
- Confined placental mosaicism
Patterns of IUGR

<table>
<thead>
<tr>
<th>Insult</th>
<th>IUGR</th>
<th>Neonatal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early/Prolonged</td>
<td>Symmetric</td>
<td>HC = L = WT all &lt; 10 cent%</td>
</tr>
<tr>
<td>Late</td>
<td>Asymmetric</td>
<td>HC = L &gt; WT WT &lt; 10 cent%</td>
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</tbody>
</table>

(Compatible with autopsy studies)

Threshold Risk for Neonatal Encephalopathy

- Large, population-based case control study
- >9th % OR = 1.54
- 3-9th % OR = 4.37
- <3rd % OR = 38.2


IUGR Versus Prematurity

<table>
<thead>
<tr>
<th></th>
<th>IUGR</th>
<th>PREMATURITY</th>
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<tbody>
<tr>
<td>Asphyxia</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Temperature instability</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Polycythemia</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Acidosis</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Meconium aspiration</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Congenital malformations</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>RDS</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>IVH</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>NEC</td>
<td>-</td>
<td>+</td>
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IUGR Diagnosis

IUGR : Diagnosis

Suspect
- History of IUGR
- Maternal disease
- Fundal height

Detect
- Sonography
- Cardiotocography
- Doppler
Sonographic Growth Curves

Diagnosis: Sonography
- EFW
- Biometric sonographic measurements (BPD, HC, AC, FL) in formulas
- Accuracy $\pm$ 8-20%
- Serial fetal assessment
- AC most important parameter

16 – 18 Week Evaluation
- Size should equal dates, $\pm$ 1 week
- If there is a greater discrepancy, don’t change dates
  Investigate

IUGR: Monitoring
- Cardiotocography
- BPP
- NST
- Doppler
  - Arterial
    - Umbilical artery
    - Middle cerebral artery
  - Venous
    - Ductus venous

IUGR Monitoring
IUGR: Monitoring

- Timing of delivery is the most critical step
- Avoid chronic acidemia
- Doppler detects acidemia earlier than tocoographic studies
- Delay delivery for fetal maturity only if safe

Fetal Adaptation to Worsening Placental Function - BPP

- BPP
  - Heart rate reactivity – may be absent
  - Low AFV
  - FBM
  - Loss of FM
  - Loss of tone
  - Sequential loss of variables correlates with worsening acidemia, hypoxemia, hypercapnea
  ([Vintzeleos AJOG 1991:165:707])

IUGR: Monitoring

- Serial assessment of fetal growth
- Antepartum fetal monitoring
  - Suspected: at diagnosis
    - NST, AFI weekly
  - Confirmed: at diagnosis
    - NST, AFI 2x weekly

Miller et al AJOG 1987; 157:583
Nageotte et al AJOG 1994; 170: 1672

IUGR: Doppler Ultrasound

- Restricted fetal growth
- Increased fetal cerebral blood flow
- Decreased aortic flow
- Decreased amniotic fluid volume
- Fetal measurements below 5th centile
- Moderate to severe redistribution
- Abnormal fetal venous flow
- Abnormal fetal heart rate tracings

Fetal Doppler Studies

- umbilical artery
- middle cerebral artery
- Aorta
- IVC
- ductus venous
Doppler Arterial Velocimetry

- Limited oxygen and nutrients
- Fetal adaptation results in vascular redistribution sparing vital organs
- ↑ umbilical vascular resistance
- ↓ cerebral vascular resistance

Doppler Arterial Velocimetry

- Allows observation of blood flow
- Waveform changes reflect redistribution of fetal blood flow and placental resistance
- Normal Dopplers in IUGR fetuses are reassuring findings
- Reduce interventions and improve fetal outcomes in pregnancies at risk for IUGR

Doppler: Umbilical Artery

**Normal**
- Systole
- Diastole

**Abnormal Waveforms**
- Increased indices
- Absent EDV
- Reversed flow

Doppler: MCA

**Normal**
- Abnormal

**Abnormal umbilical arterial Doppler indices**
- Brain-sparing
- Abnormal venous Doppler
**Doppler: Venous**
- Abnormalities indicate direct fetal cardiac compromise
- Abnormal waveforms occur prior to abnormal BPPs
- Sequence may vary

**Doppler: Ductus Venosus**

**IUGR: Monitoring**
- Fetal assessment
  - BPP, sonography, Doppler
  - Once or twice weekly, possibly more frequent
- NST
  - May not be reactive
  - May show decelerations
- Protocols may vary

**IUGR Monitoring**
- GA of 28 or more weeks predicts survival
- Ductus venosus: only predictor of intact survival and is the most reliable indicator after 27 week

604 singletons with:
- AC = < 5th centile
- Increased UA Pulsatility Index
- Delivering between 24 and 32+6 weeks

61 singletons with:
- EFW = < 3 centile
- Umbical artery = PI = <95 centile
- Delivery for:
  - Nonreactive NST
  - Worsening maternal condition
  - BPP = < 4/10

Baschat et al Obstet & Gynec 2007; 196: 253-261
Mari et al J Ultrasound Med 2007
IUGR Monitoring

- Logistic regression: perinatal mortality predictors
  - Gestational age
  - Abnormal MCA peak systolic velocity
  - Reverse flow in Ductus venosus
  - When delivered before 29 weeks = 94% mortality

Mari et al. Journal of Ultrasound in Medicine 2007;26: 555-569

IUGR Monitoring

- 151 fetuses – retrospective cohort
  - FGR = EFW < 5th centile
  - NST – twice weekly
  - BPP prn
  - Doppler prn
  - Delivery for BPP <6 twice in 6 hours
  - Only abnormal Dopplers were associated with adverse outcomes.

Gonzalez et al. AJOG 2007; 196: 48-51

IUGR Management

- First change: umbilical artery Doppler resistance
- Absent end-diastolic UA 7-9 days PTD (50%)
- PI abnormal in MCA 4 days PTD (50%)
- Reversal of flow in DV and UA 1-2 days PTD
- These precede NR, NST and abnormal BPP
- Standard is to wait for NST or BPP for delivery


IUGR Management

- Patients generally require hospitalization for intensive fetal evaluation
- Antenatal steroids for pulmonary maturation
- Delivery required for:
  - Oligohydramnios
  - Abnormal Doppler indices
  - Worsening fetal condition (NST, BPP)

A Randomized Trial of Timed Delivery for the Compromised Preterm Fetus: short term outcomes and Bayesian Interpretation

The Growth Restriction Intervention Trial Study Group

An RCT of pregnant women with compromised fetuses between 24 and 36 weeks gestation to study outcomes of immediate compared to delayed delivery

548 women (588 babies) 496 FGR, 234 HPTN, 37 Twins

BJOG: an international journal of obstetrics and gynaecology Jan 2003 Vol. 110; 27-32
Original GRIT

Purpose:
To compare early delivery to prevent severe intrauterine hypoxemia with delaying delivery to gain maturity.

Methods:
Recruitment 69 hospitals in 13 European countries from 1993 to 2001
496 babies with FGR at 24-36 weeks
Umbilical artery dopplers recorded
Clinicians uncertain whether to deliver or defer.
Randomized to immediate delivery 48 hours (for steroids), or delay until physician believed they could no longer be safely deferred.
Mode of delivery and monitoring strategies decided by clinician.

BJOG: an international journal of obstetrics and gynaecology Jan 2003 Vol 110; 27-32

Infant wellbeing at 2 years of age in the Growth Restriction Intervention Trial: multi-centered randomized controlled trial

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<thead>
<tr>
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<th>Immediate</th>
<th>Delayed</th>
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<tbody>
<tr>
<td>Deliveries</td>
<td>290 (98%)</td>
<td>283 (97%)</td>
</tr>
<tr>
<td>Death/ Sev Dis</td>
<td>55 (19%)</td>
<td>44 (14%)</td>
</tr>
<tr>
<td>Griffith DQ &lt; 70 24-30 wk</td>
<td>9 (12%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Griffith DQ &lt; 70 31-36 wk</td>
<td>4 (2%)</td>
<td>7 (4%)</td>
</tr>
</tbody>
</table>

At 2 years, more disability in immediate delivery group but no overall difference in Griffith DQ
Most disabilities in babies less than 31 weeks at randomization

The GRIT Study Group: The Lancet Vol. 364 August 7, 2004

The Growth Restriction Intervention Trial: Long term outcomes in a randomized trial of timing of fetal growth restriction

Of 376 babies, 302 (80%) had known outcome either dead or evaluated at 6-13 years old

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<tr>
<td>Died or disabled</td>
<td>21 (14%)</td>
<td>25 (17%)</td>
</tr>
<tr>
<td>Mean cognition</td>
<td>95 (15%)</td>
<td>96 (14%)</td>
</tr>
<tr>
<td>Motor scores</td>
<td>8.9 (7.0)</td>
<td>8.7 (6.7)</td>
</tr>
<tr>
<td>P/A behavior</td>
<td>10.5 (7.1)</td>
<td>10.5 (6.9)</td>
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Neonatal Management
IUGR

**Neonatal Management**

- FGR becomes SGA
- Decreased fat stores: monitor for hypothermia
- Decreased liver glycogen: monitor for hypoglycemia
- Chronic hypoxemia: monitor for polycythemia
- Provide catch-up growth calories

**Long Term Monitoring**

- Monitor growth percentiles
- Monitor WT/L for balanced growth
- Monitor neurodevelopment: need for long term follow-up with special attention to hearing screen

**References**


ACOG Practice Bulletin #12, Intrauterine Growth Restriction January 2000

Walker DM, Marlow N et al Growth Restriction Intervention Trial: long-term outcomes in a randomized trial of timing of delivery in fetal growth restriction AJOG 2011; 204-234

SMFM Diagnostic approach to the small fetus Contemporary OB/GYN 2011

Gracias