Fetal Growth Restriction: Diagnosis & Management

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IUGR

Complex Problem:
- Various published definitions
- Poor detection rates
- Limited preventive or treatment options
- Multiple associated morbidities
- Increased likelihood of perinatal mortality

Outcome:
- Low Apgar scores & cord pH < 7.0
- Increased NICU admissions & sepsis
- Increased stillbirth and neonatal mortality
- Increased learning disabilities
- Increased adult onset cardiovascular disease

Treatment:
- Bed rest
- Aspirin
- Nutrient supplements with Calcium/Zinc
- Maternal oxygenation
- Heparin
- Plasma volume expansion
- Calcium channel blockers
- Hormonal therapy
- Smoking cessation

No Benefit

ACOG IUGR bulletin 2000. Reaffirmed 2010
IUGR

Prenatal detection:
- Serial fundal height measurements in low risk patients
- Third trimester ultrasound for high risk patients

ACOG IUGR bulletin 2000. Reaffirmed 2010

IUGR

Prenatal detection:
- Undetected in 30 - 50% of cases
- Incorrectly diagnosed in 50% of cases

ACOG IUGR bulletin 2000. Reaffirmed 2010
J Obstet Gynecol 1996;16:77

IUGR

Prenatal detection:
- Only 10% of SGA newborns were detected prenatally in a tertiary center
  - Younger maternal age
  - Size < dates
  - Sonogram within 4 weeks
  - History of substance abuse

Int J Gynecol Obstet 2010;109:140

IUGR

Prenatal detection:
- RCT in low risk patients
- US at 30-32 and 36-37 weeks
- Significantly reduced IUGR
- 6.9% vs 10.4% (RR 0.64)

Obstet Gynecol 2003; 101:630
IUGR

Benefit of Prenatal detection:

Manning, 1995

<table>
<thead>
<tr>
<th>Category</th>
<th>Number of Cases</th>
<th>Corrected Prenatal Mortality Rates (per 1,000 live births)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases</td>
<td>144,706</td>
<td>5.6</td>
</tr>
<tr>
<td>All low risk</td>
<td>103,350</td>
<td>5.8</td>
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<tr>
<td>All high risk</td>
<td>41,346</td>
<td>9.8</td>
</tr>
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<td>Screening high risk</td>
<td>33,740</td>
<td>2.2</td>
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<tr>
<td>All SGA (7% total population)</td>
<td>10,135</td>
<td>17.8</td>
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<tr>
<td>Unscreened SGA</td>
<td>7,485</td>
<td>29.3</td>
</tr>
<tr>
<td>Screened SGA</td>
<td>2,875</td>
<td>61.4</td>
</tr>
</tbody>
</table>

Definitions:

Perinatal Mortality

Manning, 1993

- EFW < 10th percentile
- EFW > 2 SD below mean (~3rd percentile)
- EFW < 5th percentile (most clinically applicable)

Use the correct curve:

High Altitude curve will underestimate IUGR by ~50% for sea level population

Creasy, 1986
**IUGR**

**Diagnosis**
- AC, most sensitive indicator
- AC sensitivity ~ 84 - 100%

![IUGR Chart]

- Normal 80%
- Pathologic 20%
  - SGA

**IUGR**

**Vermont Oxford Network Database**
(19,759 VLBW neonates/25 - 30 wks)
- No protective effect of IUGR
- IUGR has 3X increase mortality risk
- Increase in RDS and NEC
- Beneficial effects of steroids (0.5)

AJOG 2000;182:198

**IUGR**

**Neurodevelopmental Delay**
(38 severe IUGR / > 32 wks)
- Chronic fetal acidemia best predictor
- Fetal size is not a good predictor of neurodevelopmental delay or fetal acidemia

Ultrasound Obstet Gynecol 1992;2:80
IUGR

Fetal Hypoxemia

Fetal Acidemia

Adverse Outcome

IUGR

Challenge

- Diagnose true IUGR
- Identify markers of morbidity
- Intervene in a timely fashion

Fetal Surveillance / IUGR

What is the best test?

When should we intervene?

CST

Doppler

NST

Fetal Surveillance

CTG:

- Subjective
- Poor long term correlation
- High false positive rate

AJOG 1992;144:781
AJOG 1993;168:415
AJOG 1987;66:42
Fetal Surveillance

CTG

Unaided visual analyses of FHR records

have limited reliability & reproducibility

AJOG 1993;168:842
AJOG 1993;168:2517
AJOG 2000;183:391

Fetal Surveillance

CTG

Presence of overtly abnormal patterns

late sign of fetal deterioration
(advanced acidemia)

Early Hum Dev 1993;31:195
Ultrasound Obstet Gynecol 1997;9:152
NEJM 1993;328:692

Effect of Hypoxemia

IUGR Fetus

Early Changes / IUGR

Growth Delay

• ↑ RBC mass & O₂ extraction
• EFW < 10th percentile
• AC < 10th percentile

Br J Obstet Gynaecol 1999;106:453
**Early Changes / IUGR**

**Growth Delay**
- Normal UA Doppler
- Normal MCA Doppler
- Normal Venous Doppler
- Normal CTG

Fetal Hypoxemia
No fetal acidemia
No adverse effects

Br J Obstet Gynaecol 1999;106:653

**Early Changes / IUGR**

**Arterial Redistribution**

**Brain Sparing Reflex**
- ↑ impedance in UA (↑N/D)
- ↓ impedance in MCA (↓PI)

**Fetal Hypoxemia**

**Blood Flow Redistribution**

Brain Sparing Reflex

<table>
<thead>
<tr>
<th>Increased</th>
<th>Decreased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Lungs</td>
</tr>
<tr>
<td>Brain</td>
<td>GI</td>
</tr>
<tr>
<td>Adrenal</td>
<td>Skeletal</td>
</tr>
<tr>
<td>Spleen</td>
<td>Other</td>
</tr>
</tbody>
</table>

AJOG 1993;169:169
Obstet Gyne 1996;87:981

**Early Changes / IUGR**

**Arterial Redistribution**

- Abnormal UA Doppler
- Abnormal MCA Doppler
- Normal Venous Doppler
- Normal CTG

Fetal Hypoxemia
No fetal acidemia
No adverse effects

AJOG 1985;103:169
Obstet Gyne 1996;87:981
Umbilical Arteries

Normal Waveform

Abnormal Waveform

Umbilical Artery

AEDF

REDF

Fetal Hypoxemia / IUGR

UA↑ Impedance

• Obliteration of small muscular arteries in tertiary stem villi
• For A/REDF, need > 70% placental obliteration

Ultrasound Obstet Gynecol 1997;9:271
AJOG 1989;161:1055
Fetal Hypoxemia / IUGR

UA ↑ Impedance

- Meta-analysis of 18 trials (> 10,000 women), concluded that use of UA Doppler in high-risk women reduced perinatal death & obstetric interventions

*Syst Rev 2010;(1):CD007529*

Cerebral Vasculature

Middle Cerebral Artery

- Most accessible cerebral vessel
- Carries 80% of cerebral flow
- Constant 3% - 7% of CO
- Excellent reproducibility

*AJOG 1993;169:1393*

Circle of Willis

Middle Cerebral Artery

Normal Waveform

Abnormal Waveform
Cerebral Vasculature

Middle Cerebral Artery

• A limited number of studies have noted that MCA-PSV may be a better predictor of perinatal mortality in preterm IUGR than PI

Ultrasound Obstet Gynecol 2007;29:310

Late Changes / IUGR

Elevated Central Venous Pressure

Cardiac Decompensation

↑ EDP in RV (↑ afterload)
↑ Cardiac stiffness

Ultrasound Obstet Gynecol 1996;7:401

Late Changes / IUGR

Elevated Central Venous Pressure

• Abnormal UA Doppler
• Abnormal MCA Doppler
• Abnormal Venous Doppler
• Normal CTG

Ultrasound Obstet Gynecol 1996;7:401
Ultrasound Obstet Gynecol 1997;6:152

Ductus Venosus
Central Venous Circulation

Central Nervous System Hypoxia

- Spontaneous late decelerations
- Umbilical venous pulsations
- Abnormal BPP

Cardiovascular Collapse

Obstet Gynecol 1992;79:685
Ultrasound Obstet Gynecol 1994;4:139

Late Changes / IUGR

Central Nervous System Hypoxia

- Abnormal UA Doppler
- Abnormal MCA Doppler
- Abnormal Venous Doppler
- Abnormal CTG

Fetal Hypoxemia
Fetal acidemia
Adverse effects

Obstet Gynecol 1992;79:685
Ultrasound Obstet Gynecol 1994;4:139

Late Changes / IUGR

Central Nervous System Hypoxia

- Biometric changes
- Arterial Doppler
- Venous Doppler
- Heart rate tracing

Early Changes

Late Changes
Fetal Hypoxemia / IUGR

- Biophysical adaptation is a late sign of fetal deterioration
- Abnormal venous Doppler is noted in more than 60% of IUGR with low BPS

Abnormal fetal growth
- Abnormal arterial Doppler
  - 1-3 weeks
- Abnormal venous Doppler
  - ~1-2 weeks
- Abnormal CTG / BPP
IUGR / Fetal Surveillance

Arterial Redistribution

• Abnormal UA Doppler precedes decrease in MCA PI

Br J Obstet Gynaecol 1999;106:453

IUGR / Fetal Surveillance

MCA Doppler

• MCA PI has a ~ 98% negative predictive value at < 32 weeks

Radiology 1999;215:681

IUGR / Fetal Surveillance

Short-term Outcomes

• Compared with arterial / venous Doppler abnormalities, GA at delivery has the strongest association with postnatal complications

Ultrasound Obstet Gynecol 2000;16:487
IUGR / Fetal Surveillance

IUGR in Late Gestations

• Normal UA Doppler is common in IUGR fetuses in late gestations
• Cerebroplacental ratio has poor correlation in IUGR fetuses > 34 weeks
• Sequential deterioration is rare in fetuses beyond 32 – 34 weeks

AJOG 1999;180:750

Hypoxia

Placental Effects

Early Gestations
• Inhibits angiogenesis

Late Gestations
• Stimulates angiogenesis

Br Med J 1987;296:1641

IUGR / Fetal Surveillance

IUGR in Late Gestations

(Normal umbilical Doppler)

• Risk of fetal distress is 86 % when both uterine and MCA Dopplers are abnormal
• Risk of fetal distress is 4 % when both uterine and MCA Dopplers are normal

Ultrasound Obstet Gynecol 2002;19:225
Should Doppler be performed in low-risk women as a screening test?

Meta-analysis of 4 trials found no difference in outcome

Future Research

• Value of venous Doppler in clinical management
• Value of PSV of MCA in IUGR management
• Predictive power of uterine artery Doppler for pregnancy complications
• Risk assessment using combination of biochemical markers and Doppler