Intrauterine Growth Restriction

IUGR is a screening test for perinatal morbidity and mortality

Detection
Assessment
Delivery

ACOG Definitions

IUGR: EFW < 10th centile for GA
SGA: newborn birth weight < 10th centile for GA

Fetal Death

- The risk of fetal death 1.5%, twice the background rate of fetuses of normal growth.
- The risk of fetal death increases to 2.5% at fetal weights less than the 5th percentile for gestational age.
Neonatal Complications
- Hypoglycemia
- Hyperbilirubinemia
- Hypothermia
- Intraventricular hemorrhage
- Necrotizing enterocolitis
- Seizures
- Sepsis
- Respiratory distress syndrome
- Neonatal death

Antenatal Detection
- Clinical exam (take of the tope)
- Ultrasound biometry
- Current detection rates between 25 and 35%
  - Stillbirth rate is increased 8-fold in cases of unrecognized growth restriction
- It is clear that increased surveillance and timely delivery improves perinatal outcome in IUGR

Risk Factors
- Low pre-pregnancy weight
- Multifetal pregnancies
- Hypertensive disorders of pregnancy
- Diabetes mellitus
- Autoimmune diseases
- Congenital infections
- Substance abuse
- Therapeutic medications
- Genetic syndromes
- Placental and uterine anomalies

Classification of growth restriction
- Symmetric
- Asymmetric
- Early Onset < 32 w
- Late Onset ≥ 32 w

Early Onset < 32 w
Late Onset ≥ 32 w

Progressive placental dysfunction marked by increased placental resistance.

Vascular disorder due to abnormalities of the terminal villous vessels including infection/thrombosis.

- Fetal death
- Neurodevelopmental delay
- Prematurity

Placental insufficiency marked by different pathology (e.g. villous immaturity) with less effect on placental resistance.

Fetal Heart Rate
Biophysical Profile
Doppler
Biophysical Profile

Fig. 1. Incidence of cerebral palsy (rate per 1000 live births) as observed in 28,250 tested high-risk patients and 30,657 untreated patients. Incidence of cerebral palsy in tested populations (1.33 per 1000) was significantly lower than incidence observed among untreated patients (4.74 per 1000) (**p < 0.0001, Chi Square).

Fig. 2. Relationship between last fetal biophysical profile score (BPS) and incidence of cerebral palsy (CP). An inverse, exponential, and highly significant relationship is observed (R² = 0.965, p < 0.001).

Table 2: Indications for delivery of the study population (n = 48)

<table>
<thead>
<tr>
<th>Indication</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonreassuring fetal testing</td>
<td>7</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>7</td>
</tr>
<tr>
<td>Hemolysis, elevated liver enzymes, and low platelets</td>
<td>4</td>
</tr>
<tr>
<td>Floor growth</td>
<td>5</td>
</tr>
<tr>
<td>Abruption</td>
<td>2</td>
</tr>
<tr>
<td>Cholangiorheatitis</td>
<td>1</td>
</tr>
</tbody>
</table>

"This study brings into question how predictable the BPP is in fetuses with severe early diagnosed IUGR and whether there is a safe time duration after a BPP during which we can be reassured of the fetal status."
RESEARCH

A comparison of Doppler and biophysical findings between IUGR and normal growth-restricted fetuses

- 987 singleton pregnancies
- IUGR
- Doppler and BPP surveillance findings compared between live births and stillbirths.

- Abdominal circumference <5th percentile
- EFW <10th percentile
- Fetal head-to-abdominal circumference ratio >90th percentile
- AC growth rate <11 mm in a 16-day interval.

Doppler

Umbilical Artery

S/D ratio = systolic velocity/diastolic velocity
Pulsatility index = systolic velocity-diastolic velocity/time averaged mean
Resistance index = systolic velocity-diastolic velocity/systolic velocity

Placental Pathology in early IUGR

- Infarction (>5% involvement) in 42%
- Fetal thrombosis in 32%
- Result in increase placental resistance

Stillbirths <34 weeks (N=37)
- 7 stillbirths occurred within 1 week of a normal BPP
- Median interval between the last examination and delivery was 2.9 days
- All with birthweight <1st centile

Stillbirths >34 weeks (N=10)
- 8 stillbirths occurred within 1 week of a normal BPP
- Median interval between the last examination and delivery was 5.6 days
- Stillbirths in this group were not anticipated by the BPP
Doppler

Middle Cerebral Artery

- Fetus responds to placental dysfunction by lowering resistance in the cerebral vascular bed with an increase in diastolic flow through cerebral arteries.
- This is demonstrated in the MCA by q (all in all indices and is known as "head sparing")
  - Reduced PI (< 50th centile)
  - Reduced cerebroplacental ratio (MCA PI/Um PI)

Doppler

Ductus Venosus

Figure 3: The fraction of umbilical venous return shunted through the ductus venosus in low-risk pregnancies is 30% at mid-gestation but approximately 20% at 30–40 weeks, signifying the developmental importance of the fetal liver receiving 70–80% of the umbilical blood. Reproduced with permission from ref. 14.
So far...
- Ultrasound biometry can be used as a screening test for perinatal morbidity and mortality
- Early vs late onset
- Three assessment tools are available for isolated growth restriction
  - Fetal heart rate
  - Biophysical profile
  - Doppler

PORTO
Prospective Observational Trial to Optimise Paediatric Health in IUGR

“The objective of this study was to evaluate which sonographic parameters are associated with perinatal morbidity and mortality in pregnancies affected by IUGR, defined as EFW 10th centile.”

- No pre-specified management algorithms
- Delivery decision by managing physician
- AEDF cases delivered by 34 weeks’ gestation

Adverse Perinatal Outcomes
- IVH Periventricular leukomalacia
- Necrotizing enterocolitis
- Bronchopulmonary dysplasia
- Sepsis
- Death
All stillbirths had
- EFW < 3rd centile
- AEDF in the umbilical artery
- Occurred during inpatient care

Majority of perinatal deaths
- EFW < 3rd centile
- Abnormal UA Doppler velocimetrices

Cerebroplacental ratio
- 881 cases
- Abnormal defined as < 1
- 18% rate of adverse outcome

 Majority of perinatal deaths
- Associated with an abnormal CPR

"Pregnancies at increased risk of adverse outcome are those with associated abnormal UA or MCA Doppler and those with EFW <3rd centile with or without accompanying oligohydramnios."

TRUFFLE
Trial of Randomized Umbilical and Fetal Flow in Europe

"To establish whether the assessment of the ductus venosus could be a better method than cardiotocograph to trigger delivery of the very preterm growth restricted fetus."
Design
- Singleton pregnancies
- 26-32 weeks’ gestation
- IUGR
  - Abdominal circumference < 10th percentile
  - Umbilical artery Doppler pulsatility index (PI) > 95th percentile
- Estimated fetal weight > 500 g

Fetal Heart Rate Assessment

Short-term variation after 1 h of CTG tracing had to be ≤ 3.5 ms at 26-28 weeks and > 6 ms at 29-31 weeks.

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Short-term (ms)</th>
<th>Long-term (ms)</th>
</tr>
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<tbody>
<tr>
<td>Baseline</td>
<td>62.0</td>
<td>154.0</td>
</tr>
<tr>
<td>Short-term</td>
<td>3.3 (3.3 bpm)</td>
<td>28.1 (5.5 bpm)</td>
</tr>
</tbody>
</table>

Acceptable trace

Intervention Criteria
3 Groups

Reduced Short-Term Variability

Ductus Venous PI > 95th centile

Ductus Venosus Absent or Reversed a-wave
Intervention Criteria
3 Groups

Safety-Net interventions:
- Severe preeclampsia
- Recurrent late-decelerations
- Decreased umbilical artery diastolic flow > 30 weeks
- Absent umbilical artery diastolic flow > 32 weeks

Results
- 503 women/fetuses
- Median gestation age at delivery: 30.7 weeks
- Mean birthweight: 1019 g

40% of babies in each group had absent or reversed flow

Antenatal Fetal Deaths
12 deaths (2.4%)

Unexpected Fetal Deaths
7 Cases (1.3%)

In 6 of the 7 unexpected fetal deaths, the CTG short term variation was above the cut-off

Results
- 491 babies were liveborn
- Safety-net indicated delivery
  - STV group (15%)
  - DV p95 (23%)
  - DV no A (33%)

In 6 of the 7 unexpected fetal deaths, the CTG short term variation was above the cut-off
Interval to delivery

- STV group 7 days
- DVp95 group 7 days
- DV no A-wave group 9 days

In early onset growth restriction, a higher loss rate in the abnormal ductal groups was associated with a statistically significant reduction in neurodevelopmental impairment in the surviving infants of that group.
Accepted Manuscript

IS Cerebroplacental Ratio A Marker of Impaired Fetal Growth Velocity and Adverse Pregnancy Outcome?

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Consensus definition of fetal growth restriction: a Delphi procedure

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- Identify fetuses at risk
- Assist future research projects
- Aid in the comparison of different FGR studies

KEYWORDS: consensus definition, Delphi, fetal growth restriction, placenta, placenta-based FGR


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