Update on the Ultrasound Detection and Surveillance of Intrauterine Growth Restriction

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Ultrasound

1972

The young resident went to Dr Anderson with a request to learn something about this new ultrasound technique and was handed the 1-year-old *Atlas of Ultrasonography in Obstetrics and Gynecology* by Mitsunao Kobayashi, MD, Louis M. Hellman, MD, and Ellen Cromb, RN (New York, NY: Appleton-Century; 1972). In the “Preface,” the authors made two statements about ultrasound.

The first, “With today’s equipment, technical excellence can only be achieved with patience and practice,” remains true and a cornerstone of learning ultrasound.

The second statement, “As machines improve in the future, so will the quality of the sonograms improve and the need for technical skill diminish,” was accurate only about quality.

Echoes From the Past, History of Obstetric Ultrasound
Lewis H. Nelson III, MD, RDMS, President AIUM July 1, 2003
IUGR: Introduction

- IUGR 2nd leading contributor to PNM rate
- Perinatal Mortality (PNM) rate increased 6-10 fold
- PNM rate 8/1000 background:
  - 120/1000 for all IUGR
  - 60-80/1000 when anomalies excluded
- **Normal growth** – 2 components
  - Genetic potential – Both parents
    - Mediated through growth factors
  - Substrate Supply
    - Essential to achieve genetic potential
    - Dependent on uterine and placenta blood supply

**Normal Weight Gain**

- 5g/day @ 14-15 weeks - 10g/day @20 weeks - 30-35g/day @ 32-34 weeks
- After which growth rate decreases
IUGR: Introduction

- 40% of stillbirths have IUGR
  - 53% of preterm stillbirths
  - 26% of term stillbirths

- Intrapartum asphyxia reported in up to 50% of IUGR fetuses

- > 60% of IUGR fetuses with FHR tracing abnormalities have hypoxia/acidosis
  - Pardi, NEJM 328:692, 1993
IUGR: Definition

- Birth weight < 10th percentile used to define growth restriction at birth

- Definition carried over to fetuses using ultrasound measurements (+/- 15%)

- Using 10th percentile, 70% will be constitutionally small (no increase risk)

- Two SD = less than 3rd percentile

- AC < 2.5th percentile has 95% sensitivity

- 3rd, 5th, 10th, 15th?
## IUGR: Etiology

<table>
<thead>
<tr>
<th><strong>Fetoplacental</strong></th>
<th><strong>Maternal</strong></th>
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<tbody>
<tr>
<td>Chromosomal</td>
<td>History of IUGR</td>
</tr>
<tr>
<td>Genetic</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Congenital malformation</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Infectious disease</td>
<td>MSAFP increase</td>
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<tr>
<td><strong>CMV</strong></td>
<td>APS</td>
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<tr>
<td><strong>Toxoplasmosis</strong></td>
<td>Chronic illness</td>
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<tr>
<td><strong>Rubella</strong></td>
<td>Weight &lt; 90% IBW</td>
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<tr>
<td><strong>Placental pathology</strong></td>
<td>Hemoglobinopathy</td>
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<tr>
<td><strong>Previa</strong></td>
<td>Substance abuse</td>
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<tr>
<td><strong>Abruption</strong></td>
<td>Anemia/Hypoxia</td>
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<td><strong>Mosaicism</strong></td>
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<td><strong>Infarction</strong></td>
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<tr>
<td><strong>Circumvallate</strong></td>
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<td><strong>Twins</strong></td>
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Normal Fetal Growth

- Characterized by

  - Cellular Hyperplasia (Early)
  
  - Cellular Hyperplasia and Hypertrophy
  
  - Hypertrophy alone (Late)
Classification of IUGR

- **Type 1 or Symmetrical IUGR (Intrinsic, Early)**
  - Hyperplastic stage – any insult leads to reduced number of cells
  - Reduced growth potential
  - **Causes include**
    - Intrauterine Infection
    - Chromosomal Disorders
    - Congenital Malformations

- **Type 2 or Asymmetric**
  - Result of restriction of nutrient supply (utero-placental insufficiency)
  - **Causes include – Maternal Diseases**
    - Chronic Hypertension
    - Renal Disease
    - Vasculopathies
Asymmetric IUGR (70-80%)

• The onset of growth restriction occurs usually after 28 wks of gestation i.e. in the stage of hypertrophy. The fetus has near normal total number of cells but cell size is reduced.

• There is brain sparing effect so that the head growth remains normal but the abdominal girth slows down.

• This asymmetry results from redistribution of fetal cardiac output with increased flow to brain and heart at the expense of reduced splanchnic circulation.
Intermediate IUGR (5-10% of all IUGR fetuses)

- It is a combination of type 1 and type 2.

- Fetal growth restriction occurs during *intermediate phase of growth* affecting *both hyperplasia and hypertrophy*, resulting in decrease in cell number as well as size.

- Causes include
  - Chronic Hypertension
  - Lupus nephritis
  - Maternal vascular diseases that are severe and have onset in early 2nd trimester
Other Maternal Causes

- **Smoking**- active or passive, especially during third trimester is important cause of IUGR. Nicotine has vasoconstrictive effect on the maternal circulation and leads to formation of toxic metabolites in fetus.

- **Alcohol and Drugs**- Alcohol crosses the placenta freely. It acts as a cellular poison reducing fetal growth potential.
  - Cocaine and opiates are potent vasoconstrictors.
  - Warfarin, anticonvulsants and antineoplastic agents are also implicated in growth restriction

- **Thrombophilias**- antiphospholipid antibody syndrome and other thrombophilias leading to placental thrombosis and impaired trophoblastic function.

- **Nutritional Deficiency**- poor intake
  - Inflammatory bowel
Opioid Addiction in Pregnancy

- Increased risk of low birth weight infants
- IUGR
- Preterm delivery
- Neonatal Abstinence Syndrome (NAS) (55-95%)
- Sudden Infant Death Syndrome (SIDS) 2-3 x greater

- Abrupt withdrawal – risk of miscarriage, stillbirth, or PTI
- Pregnancy provides motivation for lifestyle changes

- Methadone – detoxification or maintenance treatment
  - Synthetic opioid with along half-life (Once daily)
  - Completely removes withdrawal symptoms, but does not induce same high
  - May be associated with reduced fetal growth, but no evidence of teratogenicity
Opioid Addiction in Pregnancy

- Patients are usually stabilized on Methadone in the first and third trimesters
- If withdrawal is an option, best done in second trimester
- Reducing Methadone to 15mg or less by delivery, reduces the risk of NAS

- Subutex (Buprenorphine) – opioid partial agonist (Once daily)

- One study has tried to quantify the weight reduction due to opiates alone, concluding:
  - 489gm reduction in infants of pregnant heroin users,
  - 279gm reduction in methadone users and
  - 557gm reduction in those who take both in pregnancy
Methadone and buprenorphine for the management of opioid dependence in pregnancy. 
Jones HE¹, Finnegan LP, Kaltenbach K. 

The relationship between maternal use of heroin and methadone and infant birth weight. 
Hulse GK¹, Milne E, English DR, Holman CD. 
PMCID: PMC1891783

Substance Abuse in Pregnancy: Opioid substitution in a Northern Ireland Maternity Unit 
Sandra Mawhinney,¹ Robin G Ashe,¹ and Joanne Lowry² 
¹Department of Obstetrics and Gynecology, Antrim Area Hospital, 45 Bush Road, Antrim BT41 2RL, United Kingdom 
²Child Care Team, Antrim Area Hospital, 45 Bush Road, Antrim BT41 2RL, United Kingdom 
Correspondence to Dr Mawhinney Email: moc.xepip.lsd@yennihwamardnas
History of IUGR

- Prior history **#1 risk factor** for subsequent IUGR
  - 1 prior episode: 25% recurrence
  - 2 episodes: Fourfold increase

- 1/3 population “at risk”: 2/3 IUGR babies

- 2/3 population “low risk”: 1/3 of the IUGR babies, but most are constitutional (SGA)
IUGR: PNM and EFW

![Graph showing perinatal mortality per 1000 LB birth weight percentile]

Perinatal Mortality / 1000 LB

Birth Weight (percentile)
IUGR: Diagnosis

- **The Fundal Height Myth:**
  - best from 20-32 weeks: lightening
  - lag of 4 cm suspicious
  - Sensitivity of 27%, PPV of 18%

- **Fundal height of limited value**
  - risk factors more predictive
IUGR: Fetal Measurements

- Have you weighed a fetus lately?
  - EFW derived indirectly

- “Normal” growth curves difficult to establish

- PTL strongly associated with IUGR
  - BW derived charts inaccurate

- U/S growth curves more accurate over preterm age ranges
IUGR: Measurement Options

FH: poor predictive value

Growth curves (percentiles)

Individualized growth models
  (multiples study points needed)

Size ratios (HC/AC)

Some work being done to develop
Potential growth curves
Diagnosis of IUGR

- **Clinically**
  - *A lag in fundal ht. of 4wks is suggestive of moderate IUGR.*
  - *A lag of >6 wks is suggestive of severe IUGR.*

- **Sonographically**
  - most useful tool for diagnosis of IUGR
  - To differentiate between symmetrical and asymmetrical IUGR
  - To monitor the fetal condition.
Fetal Biometry

**BPD (Biparietal Diameter)** - determines gestational age and type of IUGR. When growth rate of BPD is below 5\textsuperscript{th} percentile, 82% of births are below 10\textsuperscript{th} percentile (i.e. IUGR).

**Head circumference (HC)** - better than BPD in predicting IUGR.

**Transeverse cerebellar diameter (TCD)** - can be used as a method to assess gestational age.

**Abdominal circumference (AC)** - **AC and fetal weight are most accurate ultrasound parameters for diagnosis of IUGR.**
- AC has highest sensitivity and greatest negative predictive value for sonographic diagnosis of IUGR
- An increase in fetal AC of less than 10 mm in 14 days has sensitivity of 85% and specificity of 74% for identification of IUGR.
**Appropriate Estimation of Due Date**

- **New Committee Opinion**
  - Committee of Obstetric Practice, AIUM, SMFM – October 2014

<table>
<thead>
<tr>
<th>Gestational Age Range (based on LMP)</th>
<th>Method of Measurement</th>
<th>Discrepancy Between Ultrasound and LMP Dating That Supports Redating</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 13 6/7 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• &lt; 9 weeks</td>
<td>CRL</td>
<td>&gt; 5 days</td>
</tr>
<tr>
<td>• 9 - &lt;14 weeks</td>
<td></td>
<td>&gt; 7 days</td>
</tr>
<tr>
<td>14 0/7 – 15 6/7 weeks</td>
<td>BPD, HC, AC, FL</td>
<td>&gt; 7 days</td>
</tr>
<tr>
<td>16 0/7 – 21 6/7 weeks</td>
<td>BPD, HC, AC, FL</td>
<td>&gt; 10 days</td>
</tr>
<tr>
<td>22 0/7 – 27 6/7 weeks</td>
<td>BPD, HC, AC, FL</td>
<td>&gt; 14 days</td>
</tr>
<tr>
<td>&gt; 28 weeks</td>
<td>BPD, HC, AC, FL</td>
<td>&gt; 21 days</td>
</tr>
</tbody>
</table>
Variables to consider when evaluating EFW

- Sonographer interobserver error
- Range of error
- Non-linear growth of fetus
Dr. Hadlock

Frank Hadlock, a tall, lanky Texan, gave an advanced obstetric ultrasound lecture on one of his visits to Winston-Salem and kept referring to the patients as “girls.” At the end of the lecture, he was cornered by a maternal-fetal medicine fellow, and one had to smile watching the short, plucky young woman shaking her finger up at one of the icons of ultrasound and setting him straight that these were women and not girls. His bemused response was, “Hell, I’m from Texas, and they are all girls, boys, or cows!”

Echoes From the Past
History of Obstetric Ultrasound
Lewis H. Nelson III, MD, RDMS, President
July 1, 2003
### IUGR: HC/AC Ratios

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Ratio</th>
</tr>
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<tbody>
<tr>
<td>&lt;32</td>
<td>&gt; 1.0</td>
</tr>
<tr>
<td>32-34</td>
<td>~ 1.0</td>
</tr>
<tr>
<td>&gt;34</td>
<td>&lt; 1.0</td>
</tr>
</tbody>
</table>

**Asymmetric**
- HC preserved, ratio > 1.0

**Symmetric**
- HC, AC both small, ratio ~ 1.0
IUGR: HC/AC Ratios

Asymmetric

Symmetric
IUGR: HC/AC Ratios

HC/AC: 85% of IUGR detected
False positives reduced

If HC difficult to obtain (late gestation), use FL
FL/AC = 22 consistently after 21 weeks
FL/AC > 23.5 = IUGR, even if GA not known
IUGR: Fetal Growth Patterns

When did you last watch a fetus grow?
I don’t always stop ordering Doppler indices…

But when I do, I make sure there are at least 2 EFWs above the <10%ile or that there is a trend of increasing EFW
Doppler – Moving structures - Red Blood Cells

\[ f_d = 2(f_t \cdot v \cdot \cos \theta)/c \]

Wall motion – high level NOISE!

Scattered waves - low level NOISE!
Doppler – Moving structures - Red Blood Cells
Doppler – Moving structures -Red Blood Cells

\[ f_t \]

\[ f \]

\[ ? \]
Doppler – Moving structures -Red Blood Cells

\[ f_t \]

\[ f \]

time

[Ultrasound image with Doppler settings and color scale]
Doppler – Moving structures - Red Blood Cells

Experimental Data

CCHE2D
Doppler modes are differentiated by the way the signal is processed
FFT – Fast Fourier Transform

- Algorithm to display multiple frequencies in a single time frame – **Spectral Doppler**
- Think of a single note versus a chord
- **Color Doppler** is an average of the spectral Doppler – it can’t show each frequency in a specific time unit
  - Standard display is BART – Blue away, Red towards
- **Density of blood cells displayed as an intensity of gray**
  - High density (power) – bright
  - Low density (power) – less bright
- **Is power useful in Spectral Doppler** – NO, but it is in **Power Doppler**
  - **Color tone determined by density (#) of cells**
Why Angle of Insonance is Important
Doppler Ultrasonography

\[
\frac{S}{D} = \text{S/D ratio (Stuart et al, 1980)}
\]

\[
\frac{S - D}{D} = \text{Resistance index (Pourcelot, 1974)}
\]

\[
\frac{S - D}{\text{Mean}} = \text{Pulsatility index (Gosling and King, 1975)}
\]

Christian J. Doppler was an Austrian physicist who described the Doppler effect in 1842.
Umbilical Artery

Flow velocity waveforms of the umbilical artery in a normal fetus from 11 to 40 weeks. Note the diastole that increases with advancing gestation. This indicates that the placental vascular resistance decreases in the normal fetus with advancing gestation.

Reference ranges for the umbilical artery RI, S/D ratio, and PI.
The pulsatility index is the only index that quantifies the waveforms in all of the cases.

A

The end-diastolic velocity (EDV) is equal to 0 in all 3 sets.

B

The A/B ratio is infinite (A/0) and, the RI is equal to 1 (A – 0/A) in all 3 cases.

C

The pulsatility index is different in the 3 cases (1.9, 2.5, 3.3), and it reflects the worsening of the condition.
Middle Cerebral Artery
MCA

- Placental Insufficiency
- Anemia (Isoimmunization / Parvo)
MCA – Placental Insufficiency

- **CerebroPlacental Ratio – CPR**
  - Originally used the anterior cerebral artery
  - Wladimiroff, et al.
  - RI c / RI u
  - >1 Normal, <1 Redistribution

- **MCA RI**
  - <70 Indicative of Redistribution

- **Others**
  - Umb Artery RI
  - Umb Artery PI
  - MCA PI
  - MCA TAMV
  - Thoracic Aorta PI
  - Thoracic artery TAMV
  - UA/MCA PI ratio
  - MCA/Thoracic Aorta PI ratio
  - MCA PI x Thoracic TAMV
MCA – Placental Insufficiency

- Valuable when fetus is reacting to hypoxia
- When physiological responses to hypoxia become exhausted, fetus cannot adapt further
  - Decline of forward cardiac function (increase venous doppler indices)
  - Deregulation of cardiovascular homeostasis may be seen and arterial circulation indices become less reliable.
MCA – Placental Insufficiency

Increased diastolic umbilical vein flow = GOOD

Increased diastolic cerebral flow - may signal placental problem
Ductus Venosus

Normal

Abnormal
Fetal hypoxia

Brain Sparing Reflex

Increased blood flow to brain, heart and adrenals

- Increased end diastolic Velocity in MCA
- Decreased S/D ratio, PI and RI

Decreased blood flow to Peripheral & placental circulation

- Decreased end diastolic Velocity in umbilical Vessels
- Increased S/D ratio, PI and RI
IUGR: Short Term Morbidity

- Early evidence of improved outcome

- Recent large studies:
  - More: RDS, NEC, IVH (+/-), mortality
  - More: meconium aspiration, hypoglycemia, hypocalcemia, polycythemia* (hyperviscosity, hyperbilirubinemia), hypothermia, thrombocytopenia

  - * baby height at cord clamping
IUGR: Long Term Morbidity

- The potential for normal long term growth is positive
  - late developing IUGR: excellent
  - early, prolonged IUGR: risk of suboptimal size (e.g. 50% with small HC have HC < 10th percentile at 8 years).
IUGR: Neurologic Outcome

- Depends:
  - degree of IUGR, especially small HC
  - timing of onset
  - GA at delivery
  - postnatal care

- CP risk is increased 4-6 times, for IUGR between 32-42 weeks