Key issues in (early and late) IUGR

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Maternal-Fetal Medicine Department, Hospital Clínic, University of Barcelona

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(early-onset) IUGR vs SGA: the era of UA Doppler

A new notion: “late-onset” IUGR

Clinical implications for today

Clinical implications for tomorrow

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IUGR vs SGA: the era of UA Doppler

(understanding and managing early IUGR)

Clinical implications for today

Clinical implications for tomorrow
Neonatal and Fetal GA-adjusted “normal” weight in the same population
The discovery of UA and hemodynamics of IUGR

Constitutionally small ➔ Placental insufficiency ➔ SGA

Extrinsic cause ➔ IUGR

Primary fetal defect

IUGR = abnormal UA Doppler

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FETAL DETERIORATION IN PLACENTAL INSUFFICIENCY

PLACENTAL DISEASE
- Increment placental impedance
- UTERINE A.

COMPENSATED HYPOXIA
- UMBILICAL A.
- Centralization
- MIDDLE CEREBRAL A.
- Ao ISTHMUS

DECOMPENSATED HYPOXIA
- cardiac ischemia
- Diastolic failure
- DUCTUS VENOSUS
- cCTG: reduced short-term variability
- CTG ABNORMAL
- Systolic cardiac failure

SERIOUS INJURY DEATH

UTERINE A.

growth

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umbilical artery
normal and abnormal hemodynamics

Cardiac pump
normal function

Cardiac pump
abnormal function

Placental status

<30%

placenta + cardiac ischemia

lunes, 3 de diciembre de 12
middle cerebral artery
normal and abnormal
hemodynamics

Normal oxygenation

[normal waveform]

[mild vasodilation]

[marked vasodilation]

hypoxia

lunes, 3 de diciembre de 12
30% venous return

REFLECTS DIASTOLIC PRESSURE IN RIGHT (AND LEFT) HEART

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ductus venosus
normal and abnormal
hemodynamics

Venous vessel: pulsation due to retrograde pressure
ductus venosus
normal and abnormal
hemodynamics

compliance right
chambers: effect sobre
on venous return

Myocardial
ischemia

compliance

no
Myocardial
ischemia

nonlunes, 3 de diciembre de 12
Early-onset IUGR

PROBLEM #1: MORTALITY

- Pathological CGT
- DVa (rev)
- cCTG-STV < 3 ms

Perinatal Mortality:
- <26: >90%
- 26-28: 30-40%
- >28: <10%

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Baschat 2003
Hecher 2003
Grivell 2009
Cruz-Lemini 2012
Early-onset IUGR

PROBLEM #2: (NEUROLOGICAL) MORBIDITY

Brain US anomalies in 30w IUGR

- Controls
- IUGR antegrade AoI
- IUGR retrograde AoI

Perinatal Mortality

- <29: >90%
- 29-32: 30-40%
- >32.0: <10%

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Fouron 2004
Del Rio 2008
Cruz-Martinez 2012
<table>
<thead>
<tr>
<th>I</th>
<th>Doppler normal but EFW &lt;p3</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>Increased resistance moderate</td>
</tr>
<tr>
<td></td>
<td>No redistribution</td>
</tr>
<tr>
<td>III</td>
<td>Severely increased resistance</td>
</tr>
<tr>
<td></td>
<td>and/or redistribution</td>
</tr>
<tr>
<td>IV</td>
<td>Severe hemodynamic alteration</td>
</tr>
<tr>
<td>V</td>
<td>High risk of death</td>
</tr>
</tbody>
</table>

- **CPR** <p5
- **Ut A** >p95
- **AEDV**
- **MCA** <p5
- **DV or AoI** >p95
- **REDV**
- **UVpuls**
- **DV** (a rev)

CGT decelerations of reduced short-term variability
FETAL DETERIORATION IN EARLY-ONSET IUGR

PLACENTAL DISEASE

COMPENSATED HYPOXIA

DECOMPENSATED HYPOXIA

SERIOUS INJURY

DEATH

Increment placental impedance

Centralization

cardiac ischemia
Diastolic failure

cCTG: reduced STV

Systolic cardiac failure

Risks of prematurity

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### Early-onset IUGR

Management protocol according to severity stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>V</th>
<th>IV</th>
<th>III</th>
<th>II</th>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up</td>
<td>Daily</td>
<td>1-2 d</td>
<td>2/w</td>
<td>1/w</td>
<td></td>
</tr>
<tr>
<td>When</td>
<td>DV(a-) cCTG abn. CTG dec.</td>
<td>(a) 28 w DV&gt;p95 / UV puls (b) 30 w ARDV / (*AoI&gt;p95)</td>
<td>(a) AEDV (b) MCA&lt;p5</td>
<td>EFW&lt;p3 CPR&gt;p95 UtA&gt;p95</td>
<td></td>
</tr>
<tr>
<td>Delivery</td>
<td>CS</td>
<td>CS</td>
<td>CS or LI</td>
<td>LI</td>
<td></td>
</tr>
<tr>
<td>Mort.</td>
<td>&gt;90%</td>
<td>50%</td>
<td>&lt;10%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Morb.</td>
<td>&gt;90%</td>
<td></td>
<td>50%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Follow-up:
- Daily <26w
- 26-28: 1-2 d
- 28-32: 2/w
- 32-34: 1/w

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**EARLY-ONSET IUGR**

Key points for clinical management

1. 
   - \(<28 \text{ w}: \ \text{PROBLEM IS MORTALITY}\)
     - First determinant: GA
     - Second (most useful) determinant 26-28w: DV

2. 
   - \(>28\ \text{PROBLEM IS NEUROLOGICAL MORBIDITY}\)

3. 
   - \text{NATURAL HISTORY: USE A PROTOCOL}\)

4. 
   - \text{(IF PREECLAMPSIA NATURAL HISTORY ALTERED)}\)
IUGR
SGA

%
IUGR vs SGA: the era of UA Doppler

A new notion: “late-onset” IUGR

Clinical implications for today

Clinical implications for tomorrow
SGA: proportion of perinatal adverse outcomes in 376 consecutive cases

- Neonatal acidosis
- CS for distress
- Abnormal NBAS
- Any

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Neurobehavior in SGA newborns

N=120 SGA vs 100 AGA

* p <0.05
Adjusted for GA, maternal age, socioeconomic status and smoking

Bayley Score

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FETAL DETERIORATION IN PLACENTAL INSUFFICIENCY
EARLY VS LATE IUGR (>34s)

PLACENTAL DISEASE

COMPENSATED HYPOXIA

DECOMPENSATED HYPOXIA

SERIOUS INJURY

DEATH

minimal tolerance to hypoxia

Placental injury <30%

MIDDLE CEREBRAL A.

UMBILICAL A.

Centralization

growth

minim tolerance to hypoxia

mild hypoxia

no cardiovascular adaptation

<table>
<thead>
<tr>
<th>DUCTUS VENOSUS</th>
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<tbody>
<tr>
<td>cardiac ischemia</td>
</tr>
<tr>
<td>Diastolic failure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CTG / BPP ABNORMAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic cardiac failure</td>
</tr>
</tbody>
</table>

www.fetalmedicinebarcelona.org/
IUGR

SGA

www.fetalmedicinebarcelona.org/
### EARLY IUGR vs LATE IUGR

<table>
<thead>
<tr>
<th>PROBLEM: MANAGEMENT</th>
<th>PROBLEM: DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degree placental disease: high</td>
<td>Degree placental disease: low</td>
</tr>
<tr>
<td>Frank hypoxia: cardiovasc. adaptation</td>
<td>Subtle hypoxia: no CV adaptation</td>
</tr>
<tr>
<td>Tolerance to hypoxia. Natural history</td>
<td>Low tolerance: no natural history</td>
</tr>
<tr>
<td>High mortality and morbidity</td>
<td>Low mortality but poorer outcome. Postnatal morbidity. Magnitude.</td>
</tr>
</tbody>
</table>
• 5-7% newborns
• detection < 50%
• > 40% late pregnancy IUFD
• Neurological, cardiovascular and metabolic impact
• diagnosis SGA vs. Late-IUGR
IUGR vs SGA: the era of UA Doppler

A new notion: “late-onset” IUGR

Clinical implications for today

Conclusions
Prognostic criteria of “poor outcome” - SGA
CS for distress and/or neonatal acidosis

UtA > p95
CPR < p5
EFW CENTILE < 3

N=447 SGA + 447 controls

Figueras 2012
LATE-IUGR: SELECTION OF HIGHER RISK CASES
MCA<p5 : CS AFTER INDUCTION >80 %

Cesarean section for distress
Neonatal acidosis

AGA
SGA normal MCA
SGA abnormal MCA

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Cruz et al, 2010
**MANAGEMENT OF LATE-ONSET IUGR**

**Today: identification of SGA and of cases with poor perinatal outcome**
- EFW centile, UA, MCA, UV and UtA Dopplers (plus BPP)
- All normal: control / 2 w
- One abnormal: control /1 w and manage as IUGR with abnormal UA (delivery 37 w)
- MCA abnormal: consider delivery at any time >34 w

**Tomorrow: improve identification + prediction of long term outcome**

**Exclusion of primary causes**
Late-onset IUGR
Protocol for management of delivery

SGA>p3

Spontaneous/Induction

Late-IUGR

Labor Induction

Induction/Elective CS

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IUGR vs SGA: the era of UA Doppler
A new notion: “late-onset” IUGR
Clinical implications for today
Clinical implications for tomorrow
5-7% newborns
• detection < 50%
• > 40% late pregnancy IUFD
• Neurological, cardiovascular and metabolic impact
• diagnosis SGA vs. Late-IUGR
Impact of prenatal severity on cardiovascular programming in late-IUGR

Fetuses EFW<p10 evaluated at 5 years

*Classified by CPR, p3 and UtA Doppler:*
- All normal: SGA
- Any abnormal: late-IUGR
Neurobehavior in SGA newborns

N=120 SGA
vs
100 AGA

No differences in relation with prenatal prognostic factors
(EEW<p3, CPR or UtA Doppler)

Bayley Score

- cognitive
- language
- motor
- socio-emotional
- adaptive behavior

Lunes, 3 de diciembre de 12
## Findings Perinatal Outcome Long Term Outcome

<table>
<thead>
<tr>
<th>Findings</th>
<th>Perinatal Outcome</th>
<th>Long Term Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>All normal (good reserve)</td>
<td>“Normal”</td>
<td>Abnormal</td>
</tr>
<tr>
<td>One or more abnormal (no reserve)</td>
<td>Higher risk poor outcome</td>
<td>Abnormal</td>
</tr>
<tr>
<td>MCA &lt;p5 (hypoxia)</td>
<td>Risk CS &gt;80%</td>
<td>Abnormal</td>
</tr>
</tbody>
</table>

(HYPOTHESIS ON) DEGREES OF SEVERITY IN LATE-ONSET IUGR

**EFW</p10**

CPR (UA/MCA)

Uterine Artery

EFW Centile

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IMPROVING DETECTION: THE DEFINITION OF “RESTRICTION”
PROBLEM 1: IMPROVING DETECTION: THE DEFINITION OF “RESTRICTION”
Birthweight inverse relation with perinatal outcome AND brain-cardiac remodelling

INTEGRATED 3T SCREENING FOR LATE-PREGNANCY COMPLICATIONS
Late-PE, Late-IUGR, Stillbirth

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PROBLEM 3:
INTEGRATED THIRD TRIMESTER SCREENING FOR THE PREDICTION OF PERINATAL AND LONG-TERM OUTCOME
(4P fetal medicine)
LATE-IUGR: CLINICAL CONCLUSIONS *(useful now)*

SGA + (EFW<3\text{th}, abnormal CPR, UtA or UV flow) = IUGR: manage as IUGR with abnormal UA

PHILOSOPHICAL CONCLUSIONS *(useful tomorrow)*

EFW<p10 is abnormal (normally)

“Late” IUGR has degrees (not always poor outcome)

Long term consequences of IUGR impact in public health

New definitions of fetal “restriction” will be developed
Fetal Medicine Course on Placental Disease
Intrauterine growth restriction and Preeclampsia
Update in clinical management
18th - 19th April 2013 | Barcelona

In spite of being among the most classical obstetrical complications, knowledge on PE and IUGR has been substantially renewed over recent years. Advances in management of these complications include prediction, integrating the notions of early and late onset disease, and counseling about long term impact in maternal and fetal health. Doppler fetal monitoring is still a mainstay in clinical management, but its correct use is still challenging for the average specialist.

The main goal of the course is to improve clinical competence, by ensuring the use of Doppler according to best practice and the application of systematic clinical protocols based on most recent evidence. All clinical lectures are based on real clinical cases, which are used to consolidate learning of the essential concepts. There is continuous electronic self-evaluation during the lectures. Given the important relationship with Doppler, one third of the course is dedicated to the basis and correct use of Doppler in fetal medicine, including a live demonstration session of all relevant vessels.

PROGRAMME

Thursday, April 18th

Panel 1: Feto-placental Doppler
09:00-09:30 Basis for the correct use of Doppler
09:30-10:15 Basic vessels: UA, UA
10:15-11:00 Live demonstration
11:00-11:30 Coffee
11:30-12:15 Brain circulation: MCA, AoI.
12:15-13:00 Venous vessels: DV, UV
13:00-14:00 Lunch

Panel 2: Early onset disease
14:00-14:45 Prediction and prevention
14:45-16:00 Management of early-onset IUGR
16:00-16:30 Coffee
16:00-18:00 Management of early-onset PE

Friday, 19th April

Panel 3: Late-onset disease
09:00-09:45 Prediction and the challenge of diagnosis.
09:45-11:00 Management of late-onset IUGR
10:45-11:15 Coffee
11:15-12:00 Management of late-onset PE
12:00-13:00 Special conference: Long term consequences of early and late IUGR and implications for parental counseling

• The correct use of Doppler in Fetal Medicine.
• Early and late-onset IUGR and preeclampsia.
• Systematic approach to clinical management based on evidence.

Click on the link for more information:
KEY CURRENT ISSUES IN IUGR

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www.medicinafetalbarcelona.org
IMPACT OF NON-DETECTED IUGR ON LATE FETAL MORTALITY
Hospital Clínica Barcelona 2005-2010

Classification of stillbirth by relevant condition at birth (ReCoDe): population-based cohort study
Gardosi et al. BMJ 2005

N=2625 stillbirths

FGR as relevant condition identified in 43%
1. Identification of IUGR
2. Pathophysiological insights
3. Goals of management
4. Suggestions according to evidence
5. Conclusions
Normal heart

Globular heart

IUGR
Cardiac remodelling

Cardiac shape

Systolic function

Diastolic function

Crispi et al. Circulation 2010

lunes, 3 de diciembre de 12
Risk of abnormal neurobehavior in SGA

* p<0.01

lunes, 3 de diciembre de 12
SGA = constitutionally small?

Significant increase in the risk of adverse perinatal outcome

Hershkovitz et al. Ultrasound Obstet Gynecol 2000
Severi et al. Ultrasound Obstet Gynecol 2002

Significant increase in the risk of adverse NEURODEVELOPMENT outcome

Eixarch et al. Ultrasound Obstet Gynecol 2008
Severi et al. Ultrasound Obstet Gynecol 2002