Key issues in (early and late) IUGR

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Neonatal and Fetal GA-adjusted “normal” weight in the same population
EARLY IUGR (1%)

PROBLEM: MANAGEMENT

- Placental disease: high (UA+, PE high)
- Hypoxia ++: systemic CV adaptation
- Tolerance to hypoxia. Natural history
- High mortality and morbidity

LATE IUGR (5-7%)

PROBLEM: DIAGNOSIS

- Placental disease: low (UA-, PE low)
- Hypoxia +/-: central CV adaptation
- Low tolerance: no natural history
- Low mortality but poor long outcome.
Early-onset IUGR
(Doppler UA abnormal)

Late-onset IUGR
(Doppler UA normal)
FETAL DETERIORATION IN PLACENTAL INSUFFICIENCY

PLACENTAL DISEASE
- Increment placental impedance

COMPENSATED HYPOXIA
- Centralization
- MIDDLE CEREBRAL A.

DECOMPENSATED HYPOXIA
- Ao ISTHMUS
- DUCTUS VENOSUS
- Cardiac ischemia
- Diastolic failure
- CCTG: reduced short-term variability
- CTG ABNORMAL

SERIOUS INJURY
- Death

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umbilical artery
normal and anormal hemodynamics

Cardiac pump
normal function

Placental status

Cardiac pump
abnormal function

placenta + cardiac ischemia
middle cerebral artery
normal and abnormal
hrmodynamics

Normal oxygenation
[normal waveform]

[mild vasodilation]

[marked vasodilation]

hypoxia
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

no
Myocardial ischemia

compliance
IFI
VTI sistole + VTI diástole
VTI sistole

Fouron AJOG 2001, Del Río UOG 2006
Early-onset IUGR

PROBLEM #1: MORTALITY

Perinatal Mortality

>90%  30-40%  <10%

Pathological CGT

cCTG-STV<3 ms

DVa (rev)

Baschat 2003
Hecher 2003
Grivell 2009
Cruz-Lemini 2012

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Early-onset IUGR

PROBLEM #2: (NEUROLOGICAL) MORBIDITY

Brain US anomalies in 30w IUGR

Perinatal Mortality

>90% 30-40% <10%

Fouron 2004
Del Rio 2008
Cruz-Martinez 2012

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Fetal I+D Protocol early-onset IUGR
Sequence Doppler (and CTG) changes

I  Doppler normal but EFW<p3

II  Increased resistance
    Initial redistribution

III  Severely increased resistance
     and/or redistribution

IV  Severe hemodynamic alteration

V  High risk of death

CPR <p5  Ut A >p95  MCA <p5  AEDV  Aol >p95  DV >p95  REDV  UVpuls  DV (a rev)

CGT decelerations of reduced short-term variability

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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

Ⅱ LOW

Ⅲ MODERATE

Ⅳ HIGH

Risks of prematurity

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# Early-onset IUGR

Management protocol according to severity stages

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

<26w

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EARLY-ONSET IUGR

Key points for clinical management

1 - <28 w: PROBLEM IS MORTALITY
   First determinant: GA
   Second (most useful) determinant 26-28w: DV

2 - >28 PROBLEM IS NEUROLOGICAL MORBIDITY

3 - NATURAL HISTORY: USE A PROTOCOL

4 - (IF PREECLAMPSIA NATURAL HISTORY ALTERED)
Early-onset IUGR
(Doppler UA abnormal)

Late-onset IUGR
(Doppler UA normal)
SGA: proportion of perinatal adverse outcomes in 376 consecutive cases

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CLINICAL PROBLEMS

PROBLEM 1: DIAGNOSIS
detection <50%

PROBLEM 2: LATE-IUGR VS SGA
- Late-IUGR = poor perinatal outcome
- late-IUGR = 40% term IUFDs

PROBLEM 3: LONG TERM OUTCOME
Fetal programming

- 5-7% newborns
- detection < 50%
- > 40% late pregnancy IUFD
- Neurological, cardiovascular and metabolic impact
- diagnosis SGA vs. Late-IUGR

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

- **PLACENTAL DISEASE**
- **COMPENSATED HYPOXIA**
  - minimal tolerance to hypoxia
  - Placental injury <30%
  - Increment placental impedance
  - Centralization
  - MIDDLE CEREBRAL A.
  - growth

- **DECOMPENSATED HYPOXIA**
  - mild hypoxia
  - no cardiovascular adaptation
  - DUCTUS VENOSUS
    - cardiac ischemia
    - Diastolic failure

- **SERIOUS INJURY**
  - DEATH
  - CTG / BPP ABNORMAL
  - Systolic cardiac failure

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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 %
Today: identification of SGA and of cases with poor perinatal outcome

- EFW centile, UA, MCA, OV 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
Late-onset IUGR
Protocol for management of delivery

SGA>p3

Spontaneous/Induction

Late-onset IUGR

Labor Induction

Induction/Elective CS
IUGR vs SGA: the era of UA Doppler

A new notion: “late-onset” IUGR

Clinical implications for today

Clinical implications for tomorrow
GOALS OF MANAGEMENT?

PROBLEM 1: DIAGNOSIS

PROBLEM 2: POOR OUTCOME

PROBLEM 3: LONG TERM OUTCOME

• 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

Crispi 2010
Neurobehavior in SGA newborns

N=120 SGA vs 100 AGA

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

Bayley Score

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

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Satchev, 2012
Geva 2008
Figueras 2008
Eixarch 2010

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### Findings

<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>

### CPR (UA/MCA)

- Uterine Artery
- EFW Centile

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**HYPOTHESIS ON** DEGREES OF SEVERITY IN LATE-ONSET IUGR

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MANAGEMENT OF LATE-ONSET IUGR

Today: identification of poor perinatal outcome
EFW centile, UA, MCA and UtA Dopplers

(Tomorrow: improve identification + prediction of long term outcome)
LATE-IUGR: CLINICAL CONCLUSIONS

SGA + (EFW<3\text{th}, abnormal CPR, UtA or UV flow) = \text{IUGR}:
manage as IUGR with abnormal UA
# EARLY IUGR (1%)

**PROBLEM: MANAGEMENT**

- Placental disease: high (UA+, PE high)
- Hypoxia ++: systemic CV adaptation
- Tolerance to hypoxia. Natural history
  - High mortality and morbidity

# LATE IUGR (5-7%)

**PROBLEM: DIAGNOSIS**

- Placental disease: low (UA-, PE low)
- Hypoxia +/-: central CV adaptation
- Low tolerance: no natural history
  - Low mortality but poor long outcome.

Savchev 2013

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Fetal Medicine Course on Placental Disease
Intrauterine growth restriction and Preeclampsia
Update in clinical management
18th -19th April 2013 | Barcelona

Click on the link for more information:

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

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.

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KEY CURRENT ISSUES IN IUGR

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IMPACT OF NON-DETECTED IUGR ON LATE FETAL MORTALITY
Hospital Clínic 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

Normal heart

Globular heart
Cardiac remodelling

Cardiac shape

Systolic function

Diastolic function

Crispi et al. Circulation 2010
Risk of abnormal neurobehavior in SGA

* p<0.01

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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