UPDATE ON DIAGNOSIS AND MANAGEMENT OF FETAL GROWTH RESTRICTION

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www.fetalmedicinebarcelona.org
Neonatal and Fetal GA-adjusted “normal” weight in the same population
ISOLATED FETAL SMALLNESS = POORER PROGNOSIS
Perinatal and Long-term Outcomes

Exclude primary fetal defect
Exclude extrinsic cause

FGR vs. SGA: DIFFERENT MANAGEMENT

<table>
<thead>
<tr>
<th>Poor perinatal outcome + IUFD (Doppler) Signs of adaptation</th>
<th>Perinatal outcome normal - No IUFD NO signs of adaptation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IUGR</strong> Placental insufficiency</td>
<td><strong>SGA</strong> Unknown (constitutional + others)</td>
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</table>

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Prognostic criteria of “poor outcome”-SGA

CS for distress and/or neonatal acidosis

UtA >p95

CPR <p5 (<p15)

EFW CENTILE <3

N=509 SGA + 509 controls

Figueras 2013
IUGR = abnormal CPR or UtA or EFW < p3

early vs late-onset IUGR

Savchev 2013
RATIONALE FOR A STAGE-BASED APPROACH TO THE MANAGEMENT OF FGR

PLACENTAL DISEASE
Diagnostic/chronic markers
Early and Late IUGR
Increment placental impedance

HYPOXIA
Prognostic/Acute markers
Early IUGR

ACIDOSIS

SERIOUS INJURY
DEATH

CENTRALIZATION
Cardiac ischemia
Diastolic failure
Systolic cardiac failure

DIAGNOSTIC/CHRONIC MARKERS
Early and Late IUGR

PROGNOSTIC/ACUTE MARKERS
Early IUGR

STAGE FETAL DETERIORATION
Risks of prematurity

LOW
MODERATE
HIGH

Red Line EARLY IUGR
Red Line LATE IUGR

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1. Identify small fetus
2. FGR vs. SGA
3. Early vs. Late
4. Parameters for fetal follow-up
5. Stage-based management protocol
1. Identify small fetus

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5. Stage-based management protocol
Neonatal and Fetal GA-adjusted “normal” weight in the same population
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
1. Identify small fetus

2. FGR vs. SGA

3. Early vs. Late

4. Stage-based management protocol
ISOLATED FETAL SMALLNESS = POORER PROGNOSIS
Perinatal and Long-term Outcomes

FGR vs. SGA: DIFFERENT MANAGEMENT

IUGR
Placental insufficiency

SGA
Unknown (constitutional + others)
The discovery of UA and hemodynamics of IUGR

Constitutionally small  Placental insufficiency  Extrinsic cause

SGA  FGR  Primary fetal defect

FGR = abnormal UA Doppler
SGA: proportion of perinatal adverse outcomes in 376 consecutive cases

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

Figueras 2011
IMPACT OF NON-DETECTED IUGR ON LATE FETAL MORTALITY
Barcelona 2005-2010

Classification of stillbirth by relevant condition at birth (ReCoDe): population-based cohort study
Gardosi et al. BMJ 2005 and 2013

**IUGR as relevant condition identified in 43-60%**

*Overall stillbirth rate (/ 1000 births) 4.2, but only 2.4 in non-SGA pregnancies, increasing to 9.7 with antenatally detected IUGR and 19.8 in not detected IUGR.*
Prognostic criteria of “poor outcome” - SGA

CS for distress and/or neonatal acidosis

UtA >p95

CPR <p5

EFW CENTILE <3

N=509 SGA + 509 controls

Figueras 2012
Distribution of cases when IUGR = abnormal UA Doppler

Savchev 2013
Distribution of cases when IUGR = abnormal CPR or UtA or EFW

Savchev 2013
1. Identify small fetus
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IUGR = low CPR or high UtA or EFW<p3 or low PIGF

**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.
FETAL DETERIORATION IN PLACENTAL INSUFFICIENCY

PLACENTAL DISEASE
- Increment placental impedance
- UTERINE A. >p95
- CPR <p5
- UMBILICAL A. >p95
- Centralization
- MIDDLE CEREBRAL A. <p5
- Ao ISTHMUS >p95
- growth

COMPENSATED HYPOXIA

DECOMPENSATED HYPOXIA
- cardiac ischemia
- Diastolic failure
- DUCTUS VENOSUS >p95 and a-
- cCTG: reduced short-term variability

SERIOUS INJURY
- DEATH
- CTG ABNORMAL
- Systolic cardiac failure
FETAL DETERIORATION IN PLACENTAL INSUFFICIENCY
EARLY VS LATE IUGR (>34s)

PLACENTAL DISEASE
- Increment placental impedance
- UTERINE A. >p95
- CPR <p5
- UMBILICAL A. >p95
- Centralization
- MIDDLE CEREBRAL A. <p5
- Ao ISTHMUS >p95

COMPENSATED HYPOXIA
- minimal tolerance to hypoxia
- Placental injury <30%

DECOMPENSATED HYPOXIA
- cardiac ischemia
- Diastolic failure
- DUCTUS VENOSUS >p95 and a-

SERIOUS INJURY
- DEATH

CTG / BPP ABNORMAL
- Systolic cardiac failure

mild hypoxia
no cardiovascular adaptation

growth

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IUGR = low CPR or high UtA or EFW < p3 or low PIGF

<table>
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<tr>
<th>EARLY IUGR (1%)</th>
<th>LATE IUGR (5-7%)</th>
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<tr>
<td>PROBLEM: MANAGEMENT</td>
<td>PROBLEM: DIAGNOSIS</td>
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<tr>
<td>Placental disease: high (UA+, PE high)</td>
<td>Placental disease: low (UA-, PE low)</td>
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<td>Hypoxia ++: systemic CV adaptation</td>
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<td>Tolerance to hypoxia. Natural history</td>
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<td>High mortality and morbidity</td>
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32w @diagnosis
1. Identify small fetus

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4. Parameters for fetal follow up

4. Stage-based management protocol
umbilical artery
normal and anormal hemodynamics

Cardiac pump
normal function

<30%

placenta + cardiac ischemia

Placental status
middle cerebral artery
normal and abnormal hemodynamics

Normal oxygenation
- [normal waveform]

[mild vasodilation]

[marked vasodilation]

hypoxia
30 % venous return

REFLECTS DIASTOLIC PRESSURE IN RIGHT (AND LEFT) HEART
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
  - <26: >90%
  - 26-28: 30-40%
  - >28: <10%

- DVa (rev)
  - Yes: 19%
  - No: 60%

- Pathological CGT
  - cCTG-STV<3 ms

- 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

- Controls
- IUGR antegrade AoI
- IUGR retrograde AoI

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

Fouron 2004
Del Rio 2008
Cruz-Martinez 2012

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cardiac ischemia
Diastolic failure
Systolic cardiac failure

Centralization

cCTG: reduced STV
Systolic cardiac failure
Red Line LATE IUGR
Red Line EARLY IUGR

CLINIC
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Hospital Universitari

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Protocol IUGR
First step: UtA + CPR + EFW = SGA or IUGR

I  Low EFW (<p3) or mild placental resistance / redistribution

CPR <p5  Ut A >p95  MCA <p5

III Severe placental resistance / redistribution

AEDV  Aol >p95

III Severe hemodynamic adaptation
- Low suspicion acidosis

DV >p95  REDV

IV High suspicion of acidosis - High risk of death

DV (a rev)  CGT decelerations of reduced short-term variability

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## IUGR

### Management protocol according to severity stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
<th>Delivery</th>
<th>Follow-up</th>
<th>Mode</th>
<th>&lt;26w</th>
<th>26-28</th>
<th>28-32</th>
<th>32-34</th>
<th>34-37</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>DV (a)</td>
<td>cCTG abn.</td>
<td>CPR &gt;p95</td>
<td>UtA &gt;p95</td>
<td>MCA &lt;p5</td>
<td>LI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CTG dec.</td>
<td>REDV (a)</td>
<td>EFW &lt;p3</td>
<td>UtA &gt;p95</td>
<td>MCA &lt;p5</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>UV puls</td>
<td>AoI &gt;95</td>
<td>CPR &gt;p95</td>
<td>UtA &gt;p95</td>
<td>MCA &lt;p5</td>
<td></td>
<td></td>
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</tr>
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<td>UtA &gt;p95</td>
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<tr>
<td></td>
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**Follow-up**
- Hours/Daily: 1-2 d, 2/w, 1/w
- Mode: CS, CS or LI

**Mort.**
- >90%< 26w, 50% 26-28, <10% 28-32, 50% 32-34, 50% 34-37

**Morb.**
- >90%< 26w, 50% 26-28, <10% 28-32, 50% 32-34, 50% 34-37

[www.medicinafetalbarcelona.org/](http://www.medicinafetalbarcelona.org/)
Late FGR vs. SGA

GA 34.4

Gender Male

EFW 1950

CPR 1.85

UtA PI 0.85

Centile^1 4

z-value^2 -0.6

z-value^3 0.9

SGA
Follow up in 2 w

Repetir

2. Baschat A Ultrasound Obstet Gynecol 2003
Late FGR vs. SGA

GA: 34w 4d

EFW: 1850

Gender: Male

UA PI: 1.25

MCA PI: 1.35

UtA PI: 1.01

Calculate
Late FGR vs. SGA

GA 34.4

Gender Male

EFW 1850

CPR 1.08

UtA PI 1.01

Centile$^1$ 2

z-value$^2$ -2.2

z-value$^3$ 1.7

Late-IUGR

Follow up in 1 w

Repetir

2. Boschat A Ultrasound Obstet Gynecol 2003
Late FGR vs. SGA

GA 37.4

Gender Male

EFW 1850

CPR 1.08

UtA PI 1.01

Centile

z-value

Late-IUGR

Deliver

Repetir

2. Baschat A Ultrasound Obstet Gynecol 2003
The main goal in FGR is identification

Small fetus (EFW < p10) must be divided in:
- FGR (placenta, poor perinatal and long-term outcome)
- SGA (we don’t know, perinatal outcome N, poor long term)

Early and late-onset FGR (GA 32s) represent two distinct phenotypes of the same disease

Clinically, a single stage-based protocol allows optimizing decisions in all cases