Late Onset FGR: Fetal Monitoring, Delivery Time

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Acıbadem University Obstetric And Gynecology Department
Neonatal Weight, Size and Condition

- Genetically Growth Potential
- Placenta
- Health of the Fetus
- Mother
**FGR-Etiology**

**Placenta / umbilical Cord:**
velamentous cord. ins., Single Umblical Artery

**Perinatal infections:**
TORCH, Parvovirus, Syphilis

**Genetic:**
anoploidy, single gen disease

**Structural:**
Cardiac, GIS anomaly
FGR

- Sonographic estimated fetal weight < 10th percentile

- Poor detection rate
- Limited preventive treatment option
- Increased perinatal mortality
- Multiple asc. morbidities

Decrease intellectual performance and long term effects
Placental insufficiency in second trimester- early onset FGR-preterm labor

Delivery Time?

First Option
Early
neonatal mortality - prematurity

Second Option
Wait
I.U. hypoxia, acidosis, stillbirth, asphyxia

Long term and Adult affects
Early Onset FGR

AC < 2.5 to 10th percentile

Anatomy survey and amniotic fluid volume
  - Fetal anomaly
  - Polyhydramnios

Normal anatomy, normal AFI, or oligohydramnios

Umbilical artery
  Middle cerebral artery Doppler
    - Elevated index, A/REDV
    - Brain sparing

If both normal
  Cerebroplacental ratio
    - Decreased ratio
      - Normal
      - Repeat examination at 14 days
        - If normal
          - Constitutionally small fetus

Placental insufficiency

Baschat, High risk pregnancy
Early Onset FGR

4-6 Weeks

- Normal umbilical artery
- Elevated Doppler index
- Absent/reversed end-diastolic velocity
- Normal middle cerebral artery
- ‘Brain sparing’
- Normal ductus venosus
- Elevated Doppler index
- Absent/reversed a-wave

FHR variation loss
Late decelerations
Declining amniotic fluid volume
Loss of breathing
Loss of movement
Loss of tone

Baschat, UOG, 2011
Late Onset FGR

- Half of stillbirths occur > 37 weeks

- 60-65% of unexplained stillbirth are (customized) FGR and small placenta

- In >60% of all stillbirth significant placental and cord pathology is present

96% of Births

Gebelik Haftası

TAJEV 2014
increased Perinatal Mortality

Detection antenataly decrease mortality

Vashevnik et al., 2007

Gardosi et al., BMJ, 2013
## Perinatal Mortality Risk
### Birth Weight percentile at term

<table>
<thead>
<tr>
<th>BW centile</th>
<th>PND(n)</th>
<th>%</th>
<th>Adj OR*</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1&lt;sup&gt;st&lt;/sup&gt; %ile</td>
<td>77</td>
<td>1.78</td>
<td>15.61</td>
<td>(11.52, 21.14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1-3&lt;sup&gt;rd&lt;/sup&gt; %ile</td>
<td>63</td>
<td>0.62</td>
<td>5.51</td>
<td>(4.01, 7.59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3-5&lt;sup&gt;th&lt;/sup&gt; %ile</td>
<td>46</td>
<td>0.47</td>
<td>4.13</td>
<td>(2.90, 5.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5-10&lt;sup&gt;th&lt;/sup&gt; %ile</td>
<td>90</td>
<td>0.34</td>
<td>3.11</td>
<td>(2.33, 4.15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>10-25&lt;sup&gt;th&lt;/sup&gt; %ile</td>
<td>185</td>
<td>0.23</td>
<td>2.10</td>
<td>(1.64, 2.69)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>25-50&lt;sup&gt;th&lt;/sup&gt; %ile</td>
<td>244</td>
<td>0.17</td>
<td>1.58</td>
<td>(1.25, 2.01)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>50-75&lt;sup&gt;th&lt;/sup&gt; %ile</td>
<td>166</td>
<td>0.11</td>
<td>1.06</td>
<td>(0.82, 1.36)</td>
<td>0.655</td>
</tr>
<tr>
<td>75&lt;sup&gt;th&lt;/sup&gt; - 90&lt;sup&gt;th&lt;/sup&gt; %ile</td>
<td>99</td>
<td>0.11</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90-95&lt;sup&gt;th&lt;/sup&gt; %ile</td>
<td>40</td>
<td>0.13</td>
<td>1.28</td>
<td>(0.88, 1.85)</td>
<td>0.193</td>
</tr>
<tr>
<td>95&lt;sup&gt;th&lt;/sup&gt; - 97&lt;sup&gt;th&lt;/sup&gt; %ile</td>
<td>18</td>
<td>0.14</td>
<td>1.33</td>
<td>(0.81, 2.21)</td>
<td>0.263</td>
</tr>
<tr>
<td>97-99&lt;sup&gt;th&lt;/sup&gt; %ile</td>
<td>17</td>
<td>0.13</td>
<td>1.14</td>
<td>(0.67, 1.95)</td>
<td>0.615</td>
</tr>
<tr>
<td>&gt;99&lt;sup&gt;th&lt;/sup&gt; %ile</td>
<td>26</td>
<td>0.3</td>
<td>2.79</td>
<td>(1.81, 4.30)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

614.000 birth, 1999-2008

Francis, 2012
Table 3 Outcomes of >72,000 Live-Born Singleton Term Infants Born at ≥37 Weeks of Gestation in Relation to Birth-Weight Percentile

<table>
<thead>
<tr>
<th>Outcome</th>
<th>≤3rd (n = 3184)</th>
<th>4th-5th (n = 2065)</th>
<th>6th-10th (n = 5254)</th>
<th>11th-15th (n = 5400)</th>
<th>16th-25th (n = 10,857)</th>
<th>26th-75th (n = 55,601)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apgar score ≤3 at 5 min</td>
<td>7 (0.2)*</td>
<td>1 (&lt;0.1)</td>
<td>6 (0.1)</td>
<td>5 (0.1)</td>
<td>9 (0.1)</td>
<td>38 (0.1)</td>
</tr>
<tr>
<td>Umbilical-artery blood pH ≤7.0</td>
<td>28 (0.9)*</td>
<td>12 (0.6)</td>
<td>28 (0.5)</td>
<td>27 (0.5)</td>
<td>37 (0.3)</td>
<td>212 (0.4)</td>
</tr>
<tr>
<td>Intubation in delivery room</td>
<td>70 (2.2)*</td>
<td>11 (0.5)</td>
<td>39 (0.7)</td>
<td>39 (0.7)</td>
<td>70 (0.6)</td>
<td>317 (0.6)</td>
</tr>
<tr>
<td>Seizures during first 24 h</td>
<td>14 (0.4)*</td>
<td>4 (0.2)</td>
<td>14 (0.3)*</td>
<td>9 (0.2)</td>
<td>16 (0.1)</td>
<td>68 (0.1)</td>
</tr>
<tr>
<td>after birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis (positive blood culture)</td>
<td>15 (0.5)*</td>
<td>6 (0.3)</td>
<td>12 (0.2)</td>
<td>15 (0.3)</td>
<td>28 (0.3)</td>
<td>125 (0.2)</td>
</tr>
<tr>
<td>Death in first 28 days</td>
<td>9 (0.3)*</td>
<td>2 (0.1)</td>
<td>2 (&lt;0.1)</td>
<td>3 (0.1)</td>
<td>3 (&lt;0.1)</td>
<td>18 (&lt;0.1)</td>
</tr>
</tbody>
</table>

Values are n (%).
Reprinted with permission from McIntyre et al.5
*P < 0.05 for the comparison with the infants with birth weights in the 26th through 75th percentiles for gestational age.

McIntyre et al., NEJM, 1999

Other neonatal morbidities...
Estimated Birth weight should be adjusted or customized

- Sex
- Maternal characteristics.
  - Height
  - Weight
  - Parity
  - Ethnic

Perinatal mortality rate (PMR) and SGA by customized (SGAcust) and population-based centiles (SGApop), according to maternal body mass index (BMI). Comparison test for difference of slopes: PMR vs SGAcust: \( P = .753 \); PMR vs SGApop: \( P = .007 \).
Customized Growth Chart

Mrs. Small

Mrs. Large

A
B
**“Customized growth standards”**

<table>
<thead>
<tr>
<th>Customized Grow</th>
<th>Ethnicity, Maternal weight (before pregnancy), Maternal height, Fetal gender, Parity</th>
</tr>
</thead>
</table>

* GROW = Gestation Related Optimal Weight

- Improve the ability of fetal biometry to detect high-risk fetuses.
- Decrease false negative SGA (<10.p.) fetuses 28% normal
- LGA (>90.p.) fetuses 22% normal
- Increase specificity

Decrease unnecessary advanced care and maternal anxiety

Gardosi et al., Lancet, 1992
Late Onset FGR
Difficult to diagnosis

1- Perinatal mortality high

2- Diagnosis is difficult

: Fundal height measurement sensitivity %17, PPD %20

Sparks, 2011

Estimated fetal weight by US:
+/-15 % failure, at the edge accuracy low

Scioscia, 2008

Umbilical artery Doppler:
Almost normal (can't be used for “screening”)
Does slow growth mean that placental insufficiency?

**Fetal adaptation:**
At the advanced pregnancy weeks with slow grow MCA PI decrease ("brain sparing")
<table>
<thead>
<tr>
<th></th>
<th>SGA</th>
<th>AGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight &lt;3 percentile</td>
<td>54.2%</td>
<td>9.9%</td>
</tr>
<tr>
<td>Histological</td>
<td>78.2%</td>
<td>25.4%</td>
</tr>
</tbody>
</table>

Latent insufficiency in uteroplacental blood supply. Need for new markers of placental disease.

Parra-Saavedra. et al Placenta 2013:34 1136-1141
Late Onset FGR

- Abnormal Doppler’s in umbilical artery only occur in case of 30-50% reduction of placental function/capacity.

- Late in pregnancy fetus cannot live just only %50 percent capacity of placenta.
### Risk Factors For 3rd Trimester Stillbirth

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR Multivariate multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>FGR</td>
<td>7 (3.3-15.7)</td>
</tr>
<tr>
<td>Age &gt;35</td>
<td>4.1 (1.0-16.5)</td>
</tr>
<tr>
<td>BMD &gt;25</td>
<td>4.7 (1.1-10.2)</td>
</tr>
<tr>
<td>Education &lt;10 years</td>
<td>3.4 (1.2-9.6)</td>
</tr>
<tr>
<td>FGR+ &gt;BMD 25</td>
<td>71 (14-350)</td>
</tr>
</tbody>
</table>

Froen, Gardosi. Et al. 2004
Acta Obstet Gynecol Scan.
Late Onset FGR And Doppler Uterine Artery

Table 4 Concordance between first- and third-trimester abnormal mUoA-PI z-scores

<table>
<thead>
<tr>
<th>mUoA-PI z-scores</th>
<th>Third trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>normal (&lt;2 SD)</td>
</tr>
<tr>
<td>First trimester, normal (&lt;2 SD)</td>
<td>878</td>
</tr>
<tr>
<td>First trimester, abnormal (≥2 SD)</td>
<td>31</td>
</tr>
</tbody>
</table>

mUoA-PI, mean uterine artery pulsatility index; SD, standard deviation.
Perinatal complications and long-term neurodevelopmental outcome of infants with intrauterine growth restriction

Anne-Karen von Beckerath; Martina Kollmann, MD; Christa Rotky-Fast, MD; 

<table>
<thead>
<tr>
<th>Long-term outcomes</th>
<th>IUGR (n = 146)</th>
<th>SGA (n = 215)</th>
<th>P value</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Neurodevelopmental outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>110</td>
<td>75.34</td>
<td>203</td>
<td>94.42</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Abnormal</td>
<td>36</td>
<td>24.66</td>
<td>12</td>
<td>5.58</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grade of disability</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>22</td>
<td>15.07</td>
<td>7</td>
<td>3.26</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Moderate</td>
<td>8</td>
<td>5.48</td>
<td>5</td>
<td>2.33</td>
<td>ns</td>
</tr>
<tr>
<td>Severe</td>
<td>6</td>
<td>4.11</td>
<td>0</td>
<td>0</td>
<td>.004</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Impaired domain</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor</td>
<td>20</td>
<td>13.70</td>
<td>8</td>
<td>3.72</td>
<td>.01</td>
</tr>
<tr>
<td>Speech</td>
<td>22</td>
<td>15.07</td>
<td>8</td>
<td>3.72</td>
<td>.0002</td>
</tr>
<tr>
<td>Cognition</td>
<td>17</td>
<td>11.64</td>
<td>3</td>
<td>1.40</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Hearing</td>
<td>1</td>
<td>0.68</td>
<td>1</td>
<td>0.47</td>
<td>ns</td>
</tr>
<tr>
<td>Vision</td>
<td>13</td>
<td>8.90</td>
<td>2</td>
<td>0.93</td>
<td>.0002</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cerebral palsy</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Diplegia</td>
<td>2</td>
<td>1.37</td>
<td>0</td>
<td>0</td>
<td>ns</td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>1</td>
<td>0.68</td>
<td>0</td>
<td>0</td>
<td>ns</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infant growth</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Appropriate</td>
<td>115</td>
<td>78.77</td>
<td>199</td>
<td>92.56</td>
<td></td>
</tr>
<tr>
<td>Dystrophic</td>
<td>31</td>
<td>21.23</td>
<td>16</td>
<td>7.44</td>
<td>.0002</td>
</tr>
</tbody>
</table>

Long-term outcome of infants with IUGR compared with constitutionally SGA fetuses.
CI, confidence interval; IUGR, intrauterine growth restriction; ns, not significant; OR, odds ratio; SGA, small for gestational age.

Cerebral Palsy and restricted growth status at birth: population based study: 334 infants with CP

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Early preterm</td>
<td>&lt;34</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.4-1.4)</td>
</tr>
<tr>
<td>Late preterm</td>
<td>34-37</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.4-3.4</td>
</tr>
<tr>
<td>Term</td>
<td>&gt;37</td>
<td>5.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.7-10.1</td>
</tr>
</tbody>
</table>

- Severely SGA birthweights had a 5- to 7-fold risk of CP
- Combination of malnutrition and fetal hypoxia

Jacobsson L BJOG 2008
Late-onset SGA infants are at increased risk for axonal loss in the retina and present specific visuomotor difficulties.
Late Onset FGR And Doppler Studies
Middle Cerebral Artery & Cerebro-Placental Ratio

- CPR becomes abnormal earlier than MCA-PI
- UtA and UA Doppler do not deteriorate
- progression from 37 weeks with worsening CPR and MCA

\[
\text{CPR} = \frac{\text{MCA PI}}{\text{Umbilical artery PI}}
\]

Oros et al., UOG, 2011
more direct and physiological measurement of vascular placental function

UV blood flow with spectral brain Doppler allows better identification late-onset IUGR at risk of non-reassuring fetal status during labor and of neonatal metabolic acidosis.

Geç başlangıçlı IUGG & Doppler: MCA & CPR


TAJEV, 2014
Associations between UA Doppler and neurodevelopment manifest differently across patterns of fetal growth delay.

Abnormal UA Doppler is a less prominent feature and developmental abnormalities.
### Table 1. Summary of the main differences between early- and late-onset forms of FGR

<table>
<thead>
<tr>
<th>Early-onset FGR (1–2%)</th>
<th>Late-onset FGR (3–5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Problem: management</strong></td>
<td><strong>Problem: diagnosis</strong></td>
</tr>
<tr>
<td>Placental disease: severe (UA Doppler abnormal, high association with pre eclampsia)</td>
<td>Placental disease: mild (UA Doppler normal, low association with pre eclampsia)</td>
</tr>
<tr>
<td>Hypoxia ++: systemic cardiovascular adaptation</td>
<td>Hypoxia +/–: central cardiovascular adaptation</td>
</tr>
<tr>
<td>Immature fetus = higher tolerance to hypoxia = natural history</td>
<td>Mature fetus = lower tolerance to hypoxia = no (or very short) natural history</td>
</tr>
<tr>
<td>High mortality and morbidity; lower prevalence</td>
<td>Lower mortality (but common cause of late stillbirth); poor long-term outcome; affects large fraction of pregnancies</td>
</tr>
</tbody>
</table>

Fig. 1. Distribution of a large population of small fetuses (n = 656) in FGR or SGA.

*FGR is defined by an UA PI > 95th centile only.*  
*FGR is defined using a combination of CPR < 5th centile, UtA PI > 95th centile and an EFW < 3rd centile.*  
*Note how a remarkable proportion of 'SGA' defined by UA PI are reclassified as true FGR when the combined definition is used, particularly among late-onset FGR fetuses.*
Respiratory Morbidity

McIntyre et al., NEJM, 1999
abour induction affects neither the rate of adverse neonatal outcomes nor the rates of intru- mental vaginal delivery or caesarean section.

Boers et al BMJ 2010

However, neonatal admissions are lower after 38 weeks of pregnancy

Boers et al. AJOG 2012

<table>
<thead>
<tr>
<th></th>
<th>Induction</th>
<th>Expectant Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>321</td>
<td>329</td>
</tr>
<tr>
<td>C/S</td>
<td>14%</td>
<td>13.7%</td>
</tr>
<tr>
<td>BW&lt;3 per</td>
<td>12.5%</td>
<td>36.7%</td>
</tr>
<tr>
<td>PN mortality</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Composite Morbidity</td>
<td>5.3%</td>
<td>6.1%</td>
</tr>
</tbody>
</table>
neither a policy of induction of labor nor expectant management affect developmental and behavioral outcome when compared to expectant management

the Ages and Stages Questionnaire (ASQ) and Child Behavior Checklist (CBCL)

NO DIFFERENCE

van Wyk L. AJOG 2012
Where are we?

TAJEV, 2014
Diagnostic markers

Weeks

UtA PI >p95

CPR <p5

MCA PI <p5

AoI PI >p95

Acute deterioration

Hours

AoI reverse

CTG decelerations
Stage I: EFW <3rd centile or CPR <5th centile or MCA pulsatility index <5th centile (both persisting 12 h apart) or mean UtA pulsatility index >95th centile

SGA: ≥40 weeks

≥37 weeks

Repeat in 1 week

Repeat in 2 weeks

No

Labor induction
“customisation”:

- improve the ability of fetal biometry to detect high-risk fetuses

- First Trimester risk assessment
- 30 wks uterine artery Doppler (+ plasma proteins)
- Longitudinal growth assessment
- 30 wks if growth <25 percentile
  - CPR
  - Umbilical vein
  - FHR acceleration capacity
If you have any doubt take your baby out