University Medical Center, Utrecht, the NL

Updated viewpoint in managing

Early-Onset Fetal Growth Restriction

Gerard H.A.Visser

Early vs Late FGR

- High impact on mortality & morbidity
- However, diagnosis is generally easy and clear management guidelines

Early FGR vs late FGR

- Rare
- Even more so with early screening and Aspirin
- No treatment (~~oxygen~~, ~~Viagra~~)
- All diagnostic tests work appropriately
- Diagnosis not too difficult since there will be a PE in the majority of cases
- Management according to TRUFFLE guidelines

Early FGR; management easy:

Refer to level 3 hospital

Early FGR; management easy:

As long as that hospital knows how to measure DV and uses cCTG

ISUOG world congress Berlin Oct 2019

Comments:

- USA: Ductus Venosus too difficult; only CTG/Biophysical profile. Computer CTG not used

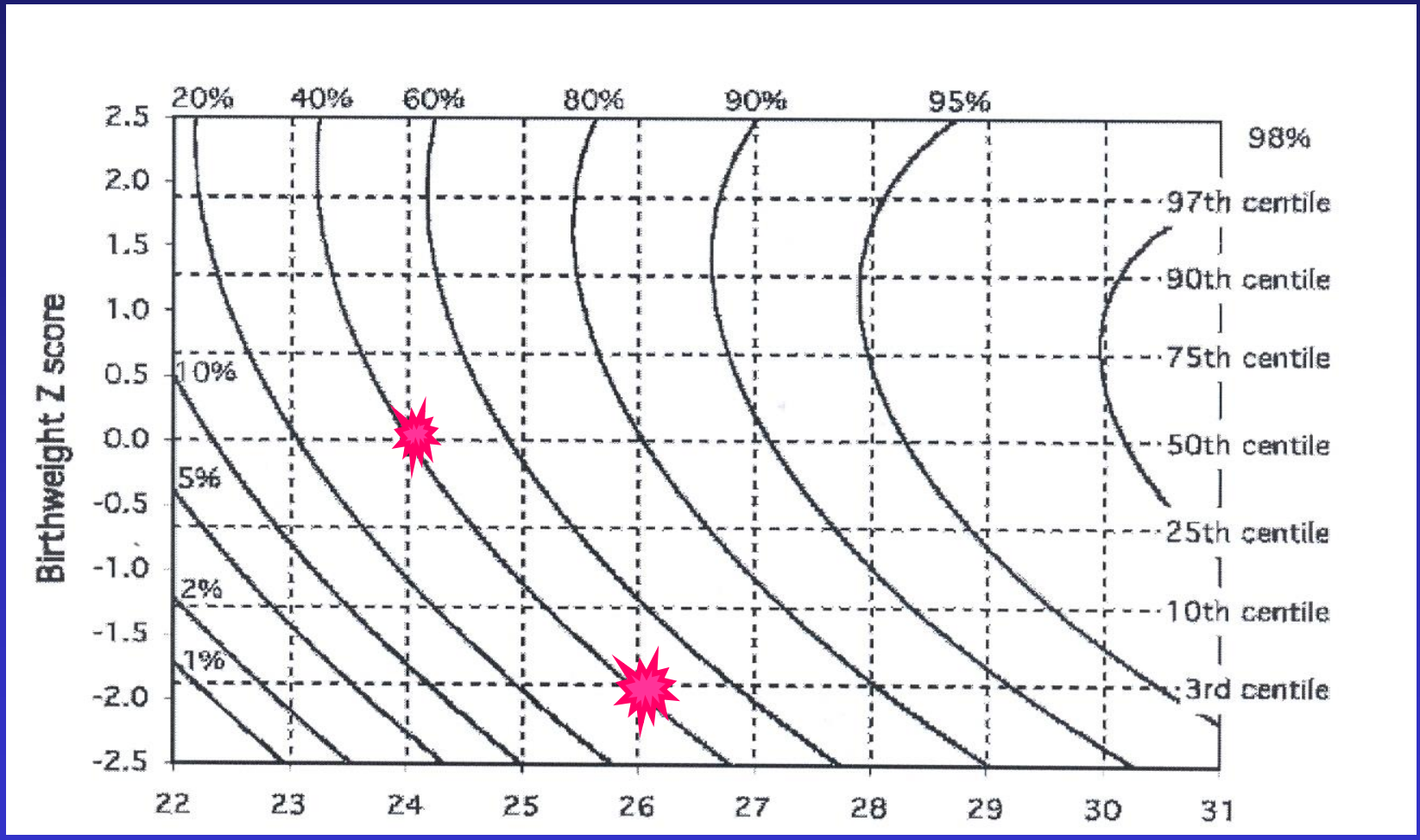
Level 3/4 centers should provide optimal quality, otherwise they do not deserve that accreditation

Early FGR; management easy:

And, most importantly, those hospitals should have an appropriate level 3 Neonatal Care Unit

FRG at the limits of viability

Prognosis early FGR: PREM-score



Cole et al, Arch Dis Child Fetal Neonatal Ed 2010;95:F14-19

Survival SFD/FGR infants

- Comparable to that of appropriate for dates infants with a 2 wks shorter gestational age

Survival SFD/IUGR infants

- Comparable to that of appropriate for dates infants with a 2 wks shorter gestational age

So ,if you would normally advocate an active management to try to keep the baby alife from 24 weeks onwards, you may decide to wait till 26 weeks (and/or>600g) in case of FGR

Timing of delivery of the early IUGR fetus

< 26 wks

- Refrain from intervention?

Visser et al. IUGR survival at the limits of viability Fetal Diagn Ther, 2014

TRUFFLE Group

Inclusion 26-32 wks; AC<p10, PI Umb art>p95, EFW>500g

CTG STV	**DV>p95**	**DV no A**
<3.5msec at<29wks < 4msec > 29 wks		

Safety net: computerized CTG (STV<2.6msec <29wks or <3msec 29-32wk), FHR decelerations, ReDF umb art >30 wks
Delivery> 32 wks, according to local protocol

2 years outcome (Lees et al, Lancet 2015)

- **Primary outcome**: proportion of infants surviving without neuroimpairment:

CTG STV	DVp95	DVnoA
77%	84%	85%

- Proportion of survivors without neuroimpairment

CTG STV		DVnoA
85% (78-90)	P=0.005	95% (90-98)

But, that is not correct

Since the DV arm had a cCTG safety net, whereas the CTG arm had no DV safety net

But, that is not correct

In fact,

in deliveries for fetal reasons<32 wks:

Early DV, 51% deliveries based on CTG safey net
Late DV, 83% deliveries based on CTG safety net

Visser et al, UOG, 2017

Timing of delivery of the early IUGR fetus (<32 weeks); n=217 (Visser et al, UOG 2017)

TRUFFLE delivered<32 weeks for fetal reasons:

- 165 Abn CTG * (decel in 59% of cases)
- 45 DV 49
- 7 REDF umb art (>30wks)

- * STV< 3.5 msec (<29wks) or 4.0 (>29wks)

Or safety net criteria: 2.6 and 3.0 msec, respectively

TRUFFLE, delivery<32 wks, because of CTG or DV abnormality

Proportion of infants surviving without handicap

- N= 217

- CTG abnormality n=165 Normal 132 (83%)
- DV abnormality n= 45 Normal 36 (80%)
- ReDF umb art n= 7 Normal 7

Visser et al, UOG, 2017

2 year neurodevelopmental and intermediate perinatal outcomes in infants with very preterm fetal growth restriction (TRUFFLE): a randomised trial

Lancet 2015

*Christoph C Lees, Neil Marlow, Aleid van Wassenaer-Leemhuis, Birgit Arabin, Caterina M Bilardo, Christoph Brezinka, Sandra Calvert, Jan B Derks, Anke Diemert, Johannes J Duvekot, Enrico Ferrazzi, Tiziana Frusca, Wessel Ganzevoort, Kurt Hecher, Pasquale Martinelli, Eva Ostermayer, Aris T Papageorghiou, Dietmar Schlembach, K T M Schneider, Baskaran Thilaganathan, Tullia Todros, Adriana Valcamonico, Gerard H A Visser, Hans Wolf, for the TRUFFLE study group**

N=503, age at delivery 30.7 wks, birth weight 1019 g

• F.death	12	8%
• Neonatal/infant death	29	
• Impairment at 2 y		10%
• Favourable 2 y outcome		82%

Cerebral palsy in early IUGR at 2 y

- Torrance et al, UOG 2009, Utrecht,
  1 out of 158

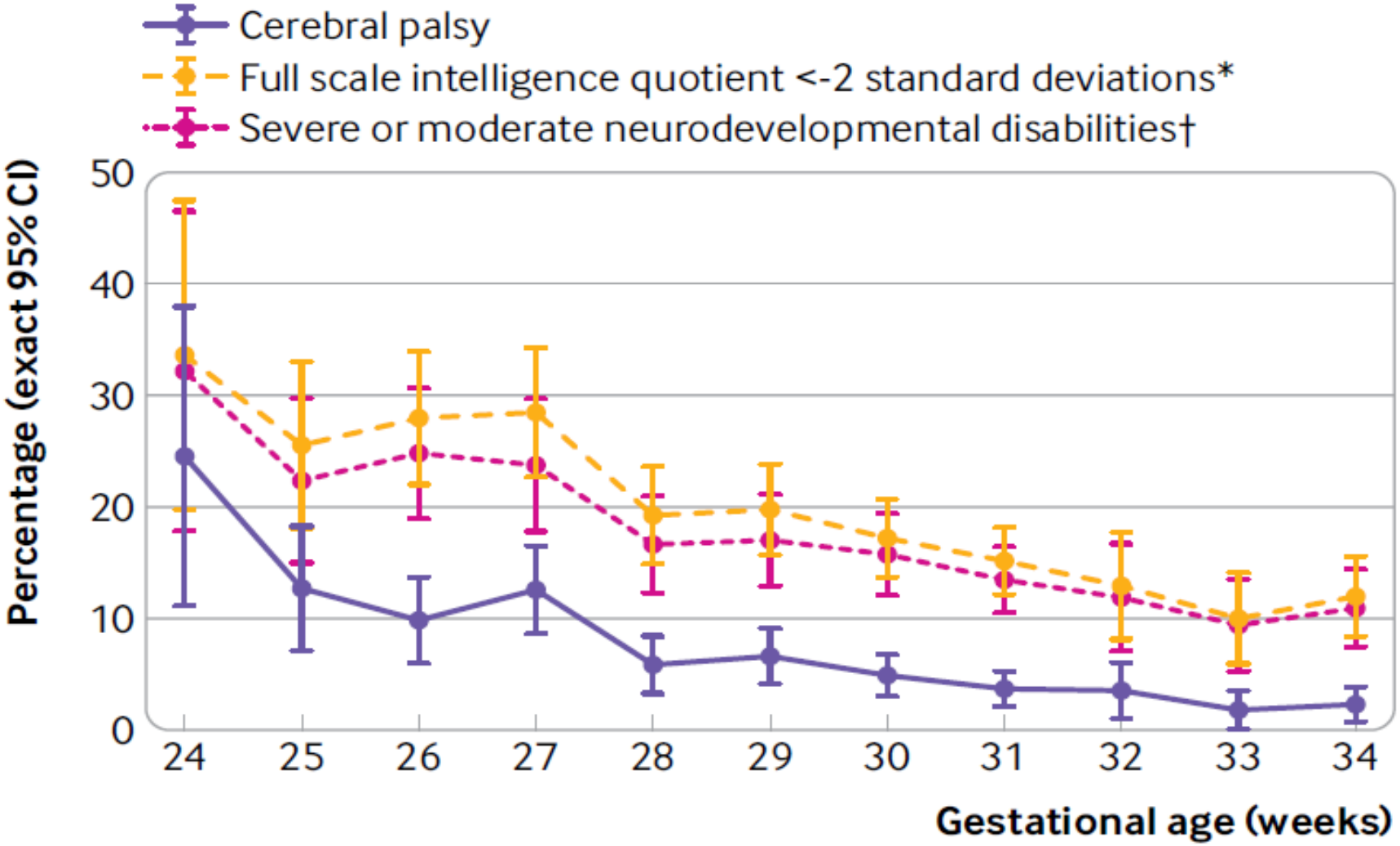
- TRUFFLE, Lees et al, 2016
  6 out of 402

1 %

Neurodevelopmental outcomes at age 5 among children born preterm: EPIPAGE-2 cohort study

Véronique Pierrat,[1,2] Laetitia Marchand-Martin,[1] Stéphane Marret,[3,4] Catherine Arnaud,[5,6,7] Valérie Benhammou,[1] Gilles Cambonie,[8] Thierry Debillon,[9,10] Marie-Noëlle Dufourg,[11] et al

BMJ March 2021



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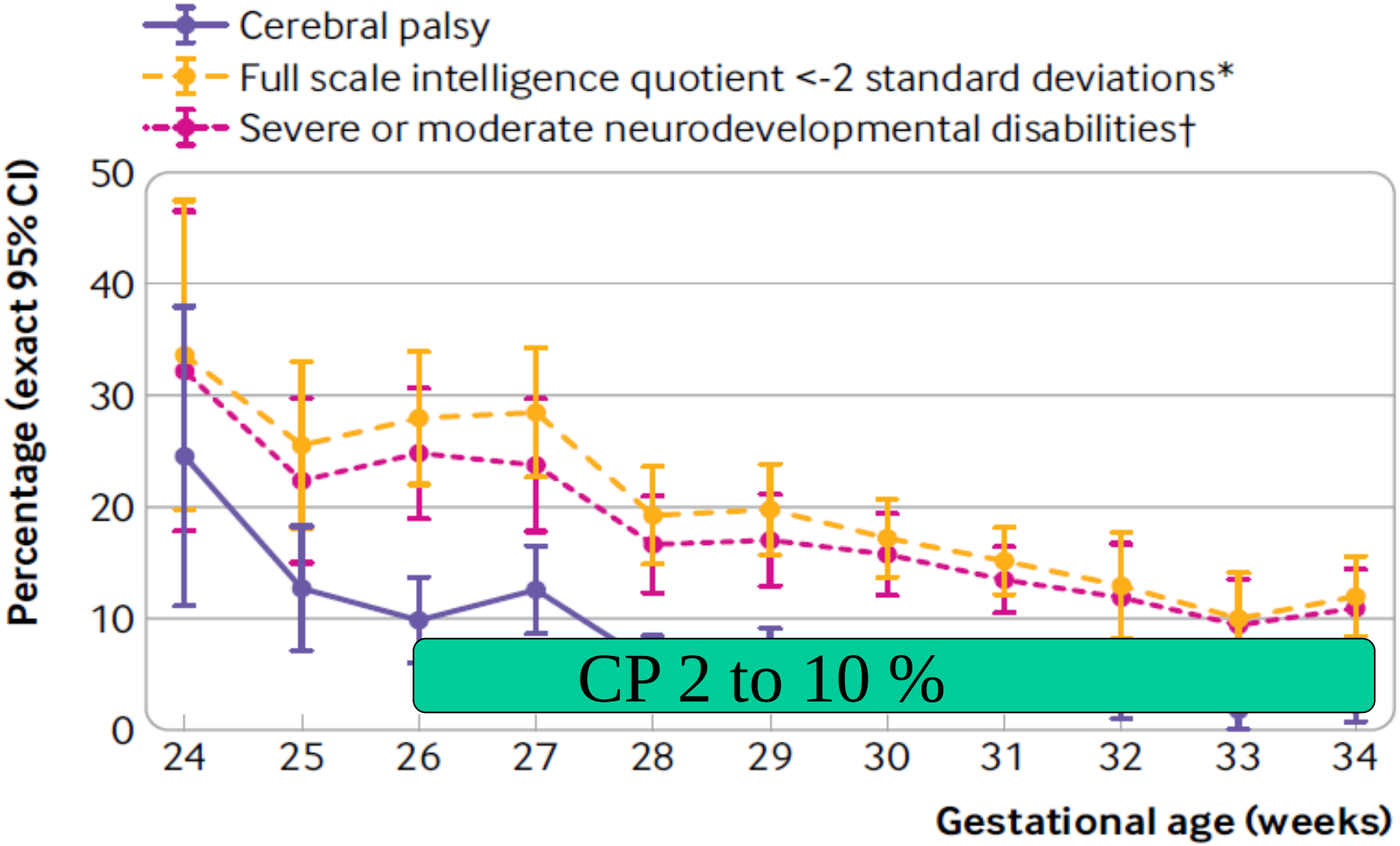

Cerebral Palsy

- Is linked to localised brain lesions, due to (acute) asphyxia

- The TRUFFLE data may well indicate that delivery took place before such lesions occurred

Favourable outcome TRUFFLE trial

Why?

- Hawthorne effect
- NICU
- DV and cCTG assessment?
- All delivered by Csection

Timing of delivery of the early IUGR fetus (<32 weeks)

< 26 wks

- Refrain from intervention?

>26 wks

- Abnormal DV PI or reduced c-CTG STV or FHR decelerations. Use a computer analysis to assess FHR variation. Delivery by CS in level-3 center.

>30 wks

- Idem or ReD flow umb art

FMF Algorhythm SGA Management

The Fetal Medicine Foundation

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Prediction of risk
- Preeclampsia
  - 11+0 to 14+1 weeks NEW
  - 19+0 to 24+6 weeks NEW
  - 30+0 to 37+6 weeks NEW
- Trisomies
- Gestational diabetes
- Miscarriage
- Stillbirth
- Fetal growth restriction
- Fetal macrosomia
- Preterm birth - history
- Preterm birth - cervix

Assessment / management
- SGA management NEW
- Pregnancy dating
- Fetal growth assessment
- Birth weight assessment
- Fetal Doppler assessment
- Uterine PI assessment
- NT assessment

Performance audits
- Mean arterial pressure
- Uterine artery PI
- Nuchal translucency
- Ductus venosus PIV
- Serum sFLT-1
- Serum PLGF
- Serum PAPP-A
- Serum free β-hCG

Research tools
- Batch MoMs calculation NEW
- Batch preeclampsia risks

18th World Congress in Fetal Medicine

25th - 29th June 2019
Alicante, Spain
For more information click here
For online registration click here

SGA management

This application aims to assist with the management of pregnancies with small for gestational age (SGA) fetuses.

The essential fields are gestational age, estimated fetal weight (EFW) and presence or absence of preeclampsia.

In some countries assessment is primarily based on Doppler and in other countries on fetal heart rate pattern (FHR) and biophysical profile score (BPS). This application can provide a suggested management using any combination of these.

Please record the following information

Gestational age: 31 weeks ____ days

Estimated fetal weight: ◉ Calculated ○ From biometry
950 grams (centile: <1)

The size of the fetus is small for gestational age.

Preeclampsia: ◉ Yes ○ No
○ Severe PE[4] ○ Not severe PE[4]

Umbilical artery EDF[4]: ◉ Absent ○ Reversed ○ Positive

Ductus venosus a-wave: ○ Absent or reversed ◉ Positive
PIV[4] ____ (centile:)

Amniotic fluid deepest pool: ____ cm

FHR repetitive decelerations[4]: ◉ No ○ Yes

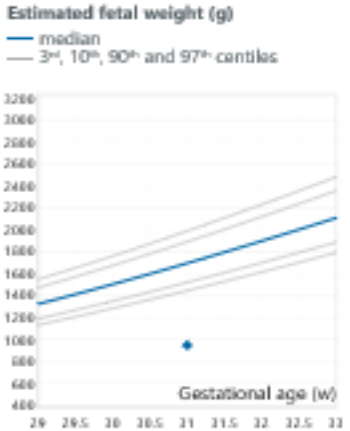
FHR short term variation[4]: 3.8 ms

Biophysical profile score: ○ 0 ○ 2 ○ 4 ○ 6 ○ 8 ○ 10 ○ Calculate

Findings
- The mother has preeclampsia
- Absent umbilical artery end diastolic flow
- Low fetal heart rate short-term variation

Suggested management
- Consider administration of steroids, magnesium sulphate and delivery

Reset form



Bashat, Figueros, Nicolaides, Visser

Computerised CTG, advantages

- Numerical assessment
- Objective, eliminates interobserver variation
- Enables to observe trends
- Likely to result in more consistent clinical responses
- Facilitates multicenter studies and research

Early FGR: Duration of CTG recording: 1 hour (shorter rec time, many more with low variation, and large fluctuations over the days)

What if you do not have a cCTG monitor?

- Eye-balling fetal heart rate variation
- Assessment of FHR decelerations (present in 59% of cases in the TRUFFLE study)

Remaining issues:

- Cut-off values Short term FHR variation: the ones used in the CTG arm, or the slightly lower values as used in the safety net?
- Antenatal corticosteroids ?
- MgSO4 before CSection/delivery ?

“ I am a fetus in the womb
I fear it may become my tomb
if only I could give a shout
to get my stupid doctor to get
me out!”

a British Medical Student

Thank you