Detection and management of late onset FGR, and fetal well-being assessment in the third trimester.

Epworth Obstetrics and Gynaecology Symposium
Park Hyatt, Melbourne
Friday 19th August 2016
Late onset FGR
T3 wellbeing

Dr Elizabeth McCarthy
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Epworth
Park Hyatt
19th August 2016
Quiz

How often do your patients have 3\textsuperscript{rd} trimester ultrasound growth scans in your practice?

a) <20%
b) 21% to 50%
c) 51 to 80%
d) 81 to 100%
Quiz

How many of your patients use a smart phone App to record fetal movements?

a) < 20%
b) 21 to 50%
c) 51 to 80%
d) 81 to 100%
Quiz

Who famously complained soon after giving birth:
“I should be dancing the Tarantella, with my fella’ Italiano. Not dressed in hospital cotton, with a smarting front bottom”

a) Anna Pavlova, mother of Australia’s favourite dessert
b) Mrs Wormwood, mother of Mathilda
c) Pauline Hanson, mother of One Nation
d) Queen Victoria, mother of 9
e) Most urogynaecologists I know
Fetal growth restriction (FGR) is

* common at late gestation, especially > 34 weeks
* can be difficult to detect and/or distinguish from constitutional smallness
* associated with stillbirth, so an ideal target for stillbirth preventative strategies
* a common reason for obstetric interventions which elicit mixed feelings from both pregnant women and maternity caregivers

At the end of this talk, symposium participants will be updated about recent research into

- routine 3rd trimester biometry
- cerebro-placental ratio and other Doppler studies additional to umbilical artery
- fetal movement monitoring apps
- MRI
- placental RNA maps
- hopes for future prevention: can metformin, sildenafil, aspirin, clopidogrel, or mindfulness optimize fetal growth?
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- Routine 3rd trimester biometry
- What is the evidence?
- What charts?
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- Routine 3rd trimester biometry
- What is the evidence?
- What charts?
Routine 3rd trimester ultrasound

What is the evidence?

• Cochrane
  – Doesn’t prevent stillbirth, alter CS, IOL etc.

• France 30 to 34 week
  – 22% SGA detection

• Spain (ROUTE) 32 wk or 36wk
  – 33%, 60% detection

• Cambridge (POP)
  – 20% detection in routine care
  – 60% SGA detection if blinded 28 and 36 wk ultrasound

• Holland (DIGITAT)
  – 65% detection, late GA scan with IOL
Screening for the small fetus: a study of the relative efficacies of ultrasound biometry and symphysio fundalheight.

Harding K, et al

ANZJOg 1995
May;35(2):160-4

Figure 1. Receiver operator characteristic curves at 28, 34 and 38 weeks' gestation showing sensitivity on the vertical axis plotted against 1-specificity on the horizontal axis. The curves are constructed from a variety of cut-off values for measurements of symphysiofundal height (SFH), amniotic fluid index (AFI) and fetal abdominal circumference (FAC) measurement for the prediction of birth-weight <10th percentile.
Routine 3rd trimester ultrasound

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Ceiling for detection of SGA with current methods: 65%
Routine 3rd trimester ultrasound

Which charts?

- Fetal EFW NOT neonatal
  EBW
EFW is much preferred to EBW

- Preterm born babies are different, and smaller, than preterm fetuses
BUT....

• Liveborn babies are quite different from fetuses destined to grow in utero for variably further days to weeks
• Confounders can both
  – Promote preterm birth
  – Impair fetal growth

Placental bed disease
  – Preeclampsia
  – Abruption

Maternal
  – social class
  – Education
  – Smoking
  – other substance use
  – Infections
Zhang et al. BJOG 2007;114:474-477
Swedish data, Hadlock proportionality curves
Routine 3<sup>rd</sup> trimester ultrasound

Which charts?
- Fetal EFW NOT neonatal EBW
- IG21 cf with local “own”
- EFW pros: multiparameter = more information; clinically imaginable
- EFW cons: multimparamter = more error, assumes all sorts of implausible mathematics

Routine 3rd trimester ultrasound
Routine 3\textsuperscript{rd} trimester ultrasound: Unexpected findings

Anomalies 1.1\% as per Nicolaides group at 36 weeks

- Skeletal dysplasia
- Neurological
- Duodenal atresia
- Cardiac

Fetal diagnosis

- Certainty/uncertainty
- Family information/birth planning/ reproductive choices
- Multi-disciplinary
Risk of stillbirths
SGA, AGA, LGA Victoria
Lowest perinatal mortality

• Is not at 50\textsuperscript{th} centile

...the women are strong, the men are good-looking, and \textit{all the children are above average}
Not all SGA babies have poor outcome

• ~70 to 75% of fetuses referred for suspected SGA in PORTO had normal outcome: no NICU admission and no pre-specified morbidity or mortality

• are “constitutionally small”
Not all adverse outcomes are confined to SGA

Umbilical and fetal middle cerebral artery Doppler at 30–34 weeks’ gestation in the prediction of adverse perinatal outcome

S. BAKALIS*, R. AKOLEKAR*†, D. M. GALLO*, L. C. POON* and K. H. NICOLAIDES*

*Harris Birthright Research Centre for Fetal Medicine, King’s College Hospital, London, UK; †Department of Fetal Medicine, Medway Maritime Hospital, Gillingham, Kent, UK

KEYWORDS: middle cerebral artery Doppler; pyramid of antenatal care; small-for-gestational age; third-trimester screening; umbilical artery Doppler

Most infants suffering adverse outcome are non-SGA
• 71% of stillbirths
• 82% of CS for fetal distress
• 87% with arterial cord blood pH ≤7.0
• 81% with venous cord blood pH ≤7.1
• 83% with 5-min Apgar score <7
• 79% of NICU admissions
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- cerebro-placental ratio and other Doppler studies additional to umbilical artery
Doppler studies in late FGR

• Umbilical A Doppler
  – Well established
  – Marker of placental disease: reduced gas exchange area for whatever reason e.g. shallow placental bed, thrombo-occlusive but also placentitis, abnormal chromosomes; analogy with postnatal pulm circulation
  – Cochrane
  – NOT a dichotomiser of placental vs small-normal
Umbilical A Doppler studies in FGR

Early < 32 weeks FGR
• Well established place triage tool
• Does NOT time birth
• ? Entry into intervention trials
  – Sildenafil
  – Melatonin
  – Sleep studies/CPAP
  – NO donors
  – Nano-particle delivery
• Use GRIT/TRUFFLE to time birth
  e.g.
  – cCTG
  – Ductus venosus
  – Maternal complications (50%) pre-eclampsia/aabruption

Late > 32 weeks
• If abnormal, take seriously
  – Poor tolerance of labour if AREDF
• Need other markers in late FGR
  – Non-Umbilical A Doppler
  – Trials for other markers e.g. mRNA
Non-Umbilical A Doppler studies in late FGR

Middle cerebral artery  Cerebro-placental ratio
Uterine artery
Ductus venosus
Aside...Hazards of non-blinded studies

- I used my fancy new test* to determine the fetus is at TERRIBLY HIGH RISK
- I conveyed my concerns to the woman, her family, and other staff
- I went to extraordinary effort to perform an extremely challenging LSCS at a time convenient to myself
- The baby was ALIVE! My patient is ENDLESSLY grateful that the test prevented stillbirth (?????)
- The baby was admitted to NICU: positive association between my test and NICU admission
- The baby had morbidity: need for prolonged ventilation, NEC, IVH: positive association between my test and morbidity

fancy new test* = ? ANA positivity, NK cell subtype, Rotem coagulation test, sFLT-1 at 10 weeks
Other Doppler studies in late FGR

/ = 2 = ok
Other Doppler studies in late FGR

= 1 = NOT ok
Other Doppler studies in late FGR

Middle Cerebral Artery

Umbilical Artery

1 to 2
Non-Umbilical A Doppler studies in late FGR

Middle cerebral artery
Cerebro-placental ratio
Uterine artery
Ductus venosus

Of these, CPR has advantages

• >0 blinded study
• Large retrospective studies where CPR wasn’t necessarily used by clinicians
• Fewer false +ve cf with MCA PI < 5th
• Biologically plausible
Crossing centiles?

• Delphi consensus for FGR 32+ weeks
  – 2 quartile growth drop or abnormal Doppler with EFW 3rd to 10th
• 30% points in MHW study correlated with CPR change
• POP study:
  – calculator to be released
  – Centile change from 20 week scan
  – Correlates with hard outcome combined mortality/morbidity

• Does rely on EFW not birth weight charts
• All fetuses appear to cross BW centiles due to small fetuses being disproportionately represented in preterm births
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- fetal movement monitoring apps
Fetal movement monitoring apps

Baby Kicks Monitor Free - Fetal Movement & Kick Counter on the App ...
Free - iOS
Mar 11, 2016 - Baby Kicks Monitor Free is designed for all the pregnancy Mums as a baby kicking counter. From about 28 weeks or when you feel kicks ...

Count The Kicks App - 3rd Trimester? Start Counting!
www.countthekicks.org/app/
Use this app every day during your third trimester of pregnancy to track your baby’s movement patterns. Be sure to alert your provider immediately if you notice ...

Kickme - Baby Kicks Counter - Android Apps on Google Play
One of the most exciting moments in your pregnancy is when you feel those first little flutterers of your baby kicking. These tiny movements reassure you that your ...

Best baby movement apps for ios (Top 100) – AppCrawlr
appcrawlr.com/ios-apps/best-apps-baby-movement
Discover the top 100 best baby movement apps for ios free and paid. Top ios apps for baby movement in AppCrawlr!

My Baby's Movements App - ABC Melbourne - Australian ...
www.abc.net.au/local/stories/2014/02/28/3954323.htm
Feb 28, 2014 - Could a smart phone application help women monitor their baby's movements in 

Fitbit for the fetus?

- Actogram
- Magnetic field
- Accelerometer
My Baby’s Movements: a stepped wedge cluster randomised controlled trial to raise maternal awareness of fetal movements during pregnancy

Trial registered on ANZCTR

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<thead>
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- Way out stuff... not in clinical practice yet
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Go beyond the ceilings of current practice
Save this date in the future
For a date with the future......

Mercy Global Obstetric Update 2016 — Science
1 - 3 December 2016, Park Hyatt Melbourne

GOU 2015 told you how to practice today....

GOU 2016 will amaze you how we will be practicing tomorrow...

Presented by Tong Vader ...Sue Sky-Walker... Hui-Solo ... R2-Ali D-2
Why “way out” stuff might be worth looking at to prolong pregnancy

- MRI
  - Tissue density specific so perhaps better EFW/ body composition to distinguish small-healthy from small-undernourished

- Short gestation is an easy answer to prevent stillbirth
  - But iatrogenic late preterm birth attracts all the wrong attention otherwise

PRACTICE POINTS 1 to 8
5. No pregnancy is to be ended prior to 38+ weeks’ gestation unless there is a medical or obstetric justification.
Induction versus expectant monitoring for intrauterine growth restriction at term: randomised equivalence trial (DIGITAT)

K E Boers, obstetrician, S M C Vijgen, health economist, D Bijlenga, psychologist, senior researcher, J A M van der Post, obstetrician, D J Bekedam, obstetrician, A Kwee, obstetrician, P C M van der Salm, obstetrician, M G van Pampus, obstetrician, M E A Spaanderman, obstetrician, K de Boer, obstetrician, J J Duvekot, obstetrician, H A Bremer, obstetrician, T H M Hasaart, obstetrician, F M C Delemarre, obstetrician, K W M Bloemenkamp, obstetrician, C A van Meir, obstetrician, C Willekes, obstetrician, E J Wijnen, obstetrician, M Rijken, neonatologist, S de Cessie, statistician, F J M E Roumen, obstetrician, J G Thornton, obstetrician, J M M van Lith, obstetrician, B W J Mol, obstetrician, S A Scherjon, obstetrician on behalf of the DIGITAT study group

ABSTRACT

Objective To compare the effect of induction of labour with a policy of expectant monitoring for intrauterine growth restriction near term.

Design Multicentre randomised equivalence trial (the Disproportionate Intrauterine Growth Intervention Trial At Term (DIGITAT)).

Setting Eight academic and 44 non-academic hospitals in the Netherlands between November 2004 and November 2008.

Participants Pregnant women who had a singleton pregnancy beyond 36+0 weeks' gestation with suspected

Conclusions In women with suspected intrauterine growth restriction at term, we found no important differences in adverse outcomes between induction of labour and expectant monitoring. Patients who are keen on non-intervention can safely choose expectant management with intensive maternal and fetal monitoring; however, it is rational to choose induction to prevent possible neonatal morbidity and stillbirth.

Trial registration International Standard Randomised Controlled Trial number ISRCTN10363217.
Acknowledgements

• Epworth O&G Clinical Institute:
  Prof Gab Kovacs, Dr Steve Cole, Meg Dalmau, Mikayla Jones

• Mercy Hospital for Women and University of Melbourne:
  Prof Sue Walker, Dr Hannah Skryzpek