7th International Conference on Fetal Growth

Milan 2018

Programme & Abstracts

CONTENTS

Abstracts

GENERAL INFORMATION

Venues
see map page 83

Welcome Reception - Milan Hilton
Monday 1 Oct, 18:00 – 20:00

Wifi
Unique access code provided
in your delegate pack

Gala Dinner - Blue Note Jazz Club
Tuesday 2 October, 20:00 for 20:30
Dress: smart- casual
.

Admission to the conference is with
name tag only. In interest of safety,
please make sure it is visible at all times.

Milan attractions and tours: See
www.fetalgrowth.org/2018/milan

Welcome! Benvenuti!

A warm welcome to Milan and to the Seventh International Conference on Fetal Growth.

This year's meeting is being organised by the Perinatal Institute in partnership with the Lombardy Society of Obstetrics and Gynaecology and again assisted by our international scientific committee.

Since its inception in 2012, this specialised conference has grown year on year, which confirms an increasing awareness of the importance of fetal growth, its central role in maternal and perinatal care, and the need for a dedicated meeting to track developments in this field. Accordingly, Fetal Growth 2018 has received the highest number of abstracts yet, as well as a record number of registrations. Once again, the conference will follow the model of a single stream of presentations and e-posters of the latest evidence, with ample opportunity for discussion and critical evaluation.

The meeting has been endorsed by the Società Italiana di Ginecologia e Ostetricia (SIGO) and the Associazione Ostetrici Ginecologi Ospedalieri Italiani (AOGOI). It has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME®).

We would like to thank the Regione Lombardia for hosting the meeting, and our sponsors and exhibitors for their support. Special thanks also to the staff that have been busily working to make this event happen - Marianna Mancini, Emma Hassan (Birmingham) and Chiara Capitanio (Milan).

Patrizia Vergani
Professor of Obstetrics & Gynaecology
Milano-Bicocca University, Milan, Italy

Jason Gardosi
Professor and Director
Perinatal Institute, Birmingham, UK

Francesc Figueras
Professor of Maternal-Fetal Medicine
University of Barcelona, Spain

Lesley McCowan
Professor of Obstetrics & Gynecology
University of Auckland, New Zealand

Ahmet Baschat
Professor of Gynecology & Obstetrics
Johns Hopkins University, Baltimore, USA

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MONDAY 1st OCTOBER

Pre-Conference Workshops – Hilton Milan Via Luigi Galvani 12, Milan, 20124

09:00 Registration

WORKSHOP 1: Growth Assessment Protocol (GAP)

SUE TURNER - GAP Lead UK| MANDY WILLIAMS - GAP Lead International |
MARIANNA MANCINI - Specialist Midwife | Prof JASON GARDOSI – Director, Perinatal Institute, UK

09:30	Welcome and Introduction; fetal growth restriction and pregnancy outcome; SGA and FGR; customised GROW charts: principles and clinical implications; Q&A
11:00	Refreshment Break
11:30	Standardised fundal height measurement and plotting; referral protocols – indications for further investigation; clinical and practical application; documentation and record keeping; case studies and clinical scenarios; Q&A
12:30	Lunch
13:30	Implementation; baseline audit; routine recording of referral and detection rates; automated reporting and benchmarking; missed case audit tool; identifying and addressing problems; Q&A
15:00	Refreshment Break
15:30	Ultrasound biometry; risk assessment and surveillance algorithms; routine scans for all? - the evidence. General discussion
17:00	Close

WORKSHOP 2: Ultrasound and Doppler

Prof AHMET BASCHAT, USA | Prof FRANCESC FIGUERAS, Spain
Prof TORVID KISERUD, Norway; Prof PATRIZIA VERGANI, Italy

09:30	Ultrasound biometry Structural scans Audit and Quality Assurance
11:00	Refreshment Break
11:30	Live Demonstration
12:30	Lunch
13:30	Doppler – Basics Doppler Investigation I (UA, ACM, CPR, UtA) Live Demonstration
15:00	Refreshment Break
15:30	Biophysical profile & amniotic fluid Doppler Investigation II (UA, DV) Live Demonstration
17:00	Close
18:00	**Welcome Reception – Hilton**

TUESDAY 2nd OCTOBER

Conference Day 1

| K | Keynote 15+5 min | O | Oral 7+3 min | PO | Poster Oral 2+1 min |

07:30   Registration

08:30   Welcome

08:40   **SESSION 1: Fetal Growth & Neonatal Outcome**

08:40 | **K** | **IRENE CETIN**
1.1 | Maternal & environmental factors

09:00 | **K** | **KAREL MARSAL**
1.2 | Neurodevelopmental outcome after early onset FGR

09:20 | **O** | **ANOUK PELS**
1.3 | Neurodevelopmental outcomes at five years after early-onset FGR, analyses in a Dutch subgroup participating in a European management trial

09:30 | **O** | **MARIA F PAZ Y MINO**
1.4 | Severe fetal-growth restriction and normal doppler: neurodevelopmental evaluation at 54 months of age

09:40 | **K** | **ENRICO BERTINO**
1.5 | Standards for neonatal size and catch up growth

10:00 | **O** | **DANIELA DI MARTINO**
1.6 | Prenatal assessment of IUGR versus postnatal diagnosis of SGA based on newborn weight charts: a muliticentre study

10:10   Discussion

10:20   Refreshment Break

10:40   **SESSION 2: Standards for Fetal Growth**

10:40 | **K** | **TULLIA TODROS**
2.1 | INTERGROWTH 21st

11:00 | **K** | **TORVID KISERUD**
2.2 | The WHO fetal growth standard

11:20 | **K** | **KATHERINE GRANTZ**
2.3 | The NICHD program on fetal growth

11:40 | **K** | **JASON GARDOSI**
2.4 | Customised GROW charts

12:00 | **O** | **TINA LAVIN**
2.5 | Concordance between Intergrowth-21st and South African fetal growth standards for identification of SGA in stillbirths

12:10 | **O** | **OLIVER HUGH**
2.6 | The effect of mixed parentage on ethnic variation in birthweight

12:20   Discussion

12:30   Lunch

6

TUESDAY 2nd OCTOBER

Conference Day 1 (cont'd)

13:15   **SESSION 3: Poster Oral**

14:00   **SESSION 4: Risk factors, Screening and Prevention**

14:00 | **K** | **PATRIZIA VERGANI**
4.1 | Stillbirth and fetal growth

14:20 | **O** | **PAOLA D'ALOJA**
4.2 | Perinatal mortality surveillance: a pilot project in three Italian regions

14:30 | **O** | **SARA ORNAGHI**
4.3 | Use of customized curves for estimation of fetal weight and identification of late onset FGR at risk of adverse outcomes

14:40 | **K** | **LESLEY MCCOWAN**
4.4 | Risk assessment and prevention

15:00 | **O** | **JOYCE COWAN**
4.5 | The Growth Assessment Protocol (GAP): New Zealand experience

15:10 | **O** | **LYNN SADLER**
4.6 | A reduction in perinatal mortality in New Zealand from 2008 to 2016 among small for gestational babies by customised birthweight centile

15:20 | **O** | **MANDY WILLIAMS**
4.7 | Reduction in SGA stillbirths in England

15:30   Discussion

15:50   Refreshment Break

16:10   **SESSION 5: Surveillance Strategies for Detection of Growth Restriction and Macrosomia**

16:10 | **O** | **ISABELLE MONIER**
5.1 | Comparison of the Hadlock and Intergrowth 21st formulas for calculating estimated fetal weight among preterm infants: a population cohort study in France

16:20 | **O** | **RAIGAM J MARTINEZ-PORTILLA**
5.2 | Performance of third trimester ultrasound for the prediction of smallness-for-gestational age: a diagnostic test accuracy meta-analysis

16:30 | **O** | **DILETTA FUMAGALLI**
5.3 | Perinatal outcome of term fetuses born <10th centile: are small for gestational age and growth restricted fetuses different?

TUESDAY 2nd OCTOBER
Conference Day 1 (cont'd)

K Keynote 15+5 min   **O** Oral 7+3 min   **PO** Poster Oral 2+1 min

16:40 **O** **JENS HENRICHS | VIKI VERFAILLE**
5.4 | Effectiveness and cost-effectiveness of routine third trimester ultrasound screening: the IUGR risk selection study (IRIS)

16:50 **PO** **FRANCESCO D'AMBROSI**
5.5 | Combined sequential ultrasound screening at 29 – 32 weeks and 35 – 37 weeks in detection of SGA fetuses

16:53 **PO** **FRANCESCO D'AMBROSI**
5.6 | Screening for small for gestational age fetuses with universal ultrasonography between 35 – 37 weeks in singleton low risk pregnancies: a prospective cohort study

16:56 **PO** **ANDREW SHARP**
5.7 | The current management of the small for gestational age fetus in the UK: A survey of practice

16:59 **O** **GRÁINNE MILNE**
5.8 GAP: How is it working for us?

17:10 **O** **SUSAN TURNER**
5.9 | GAP audit: national antenatal detection rates of SGA babies and analysis of missed cases

17:20 **O** **ANDREA DALL'ASTA**
5.10 | Identification of large-for-gestational age fetuses using antenatal customized fetal growth charts: can we improve the prediction of abnormal labor course?

17:30 **O** **LAUREN JADE EWINGTON**
5.11 | Accuracy of antenatal ultrasound in predicting large-for-gestational age fetuses

17:40 **O** **TRACY TOMLINSON**
5.12 | Validation of a prediction model for fetal overgrowth in pregnancies complicated by diabetes

17:50   Discussion

18:00   Close

20:00   **Gala Dinner and Dance**

WEDNESDAY 3rd OCTOBER

Conference Day 2

K Keynote 15+5 min	**O** Oral 7+3 min	**P O** Poster Oral 2+1 min

07:30   Registration

08:30   **SESSION 6**: **Fetal Growth Restriction - Early Onset**

08:30 **K**   **AHMET BASCHAT**
6.1 | Diagnosis and management of placenta based FGR <32 weeks

08:50 **K**   **ENRICO FERRAZZI**
6.2 | Haemodynamics in pregnancies with growth restricted fetuses

09:10 **O**   **DAMIANO LO PRESTI**
6.3 | Role of maternal haemodynamic evaluation in the definition of fetuses with growth restriction outcome

09:20 **O**   **MANEL MENDOZA**
6.4 | Pravastatin to treat early-onset fetal growth restriction

09:30 **O**   **JANA BRODSZKI**
6.5 | Management of very early onset IUGR. Single center experience 1998-2015

09:40 **O**   **TAMARA STAMPALIJA**
6.6 | Uterine arteries blood flow volume in fetuses with inappropriate growth for gestational age and normal doppler velocimetry

09:50 **O**   **ANDREW SHARP**
6.7 | A prediction model for short-term neonatal outcomes in severe early-onset IUGR

10:00   Discussion

10:10   Refreshment Break

10:30   **SESSION 7: Fetal Growth Restriction - Late Onset**

10:30 **K**   **FRANCESC FIGUERAS**
7.1 | Investigation and management of late onset FGR

10:50 **P O**   **M SERRA**
7.2 | Placental findings in small for gestational age and growth restricted fetuses

10:53 **O**   **MAREK LUBUSKY**
7.3 | Maternal serum levels of PlGF and sFlt-1 in predicting delivery of an SGA newborn

11:03 **P O**   **VALENTINA GIARDINI**
7.4 | Placental growth factor (plGF) as a marker of fetal growth restriction (FGR) caused by placental dysfunction: correlation with uterine arteries doppler and placental histology

11:06 **P O**   **FEDERICA FUSÈ**
7.5 | sFlt-1/PlGF ratio in pregnancies complicated by placental insufficiency

11:09 **P O**   **FEDERICA FUSÈ**
7.6 | sFlt-1/PlGF ratio and maternal hemodynamics in pregnancies complicated by placental insufficiency

| K | Keynote 15+5 min | O | Oral 7+3 min | PO | Poster Oral 2+1 min |

11:12 **PO** **SERENA RIGANO**
7.7 | The no man's land between late IUGR and AGA fetuses: the constitutionally small fetus.

11:15 **PO** **RAIGAM J MARTINEZ-PORTILLA**
7.8 | Higher-risk of adverse perinatal outcome in adequate-for-gestational age fetuses with abnormal cerebro-placental ratio

11:18 **PO** **JOSÉ MORALES ROSELLO**
7.9 | Comparison among cerebroplacental ratio, Intergrowth-21st standards, customized growth and local population references for the prediction of fetal compromise. Which is the best approach?

11:21 **PO** **JOSÉ MORALES ROSELLO**
7.10 | Is it possible to predict late antepartum stillbirth by means of cerebroplacental ratio and maternal characteristics?

11:24 **PO** **ALICE ZAVATTA**
7.11 | Is labour induction the right choice in term IUGR fetuses?

11:27 **PO** **EVA MELER**
7.12 | Perinatal outcomes when electively inducing low fetal weight

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11:30 **SESSION 8: Fetal Growth in Twins**

11:30 **O** **TULLIO GHI**
8.1 | The Italian multicentre study

11:40 **O** **KATHERINE GRANTZ**
8.2 | The NICHD fetal growth studies on dichorionic twin pairs

11:50 **PO** **MARIANO LANNA**
8.3 | Twin-specific doppler nomograms in uncomplicated monochorionic twins

11:53 Discussion

12:06 **PO** **CARMAN WING SZE LAI**
8.4 | Perinatal outcomes among twin with severe growth discordance more than 30% in a 7-year retrospective cohort

12:09 **PO** **MARIANO LANNA**
8.5 | Monochorionic twin pregnancies complicated with twin-twin transfusion syndrome and selective growth restriction of donor twin

12:12 **PO** **MARIANO LANNA**
8.6 | Perinatal outcome in monochorionic twin pregnancies complicated with selective intrauterine growth restriction

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12:15 Lunch

WEDNESDAY 3rd OCTOBER

Conference Day 2   (cont'd)

| **K** | Keynote 15+5 min | **O** | Oral 7+3 min | **s O** | Short Oral 5 min |

13:00   **SESSION 9**: **Poster Oral 2**
Please see page 14 for full list.

14:00   **SESSION 10: Therapies for Placental Insufficiency - The EVERREST Studies**

14:00 **O**   **ANNA DAVID**
10.1 | Scientific rationale and aims of the consortium

14:10 **O**   **REBECCA SPENCER**
10.2 | Ethical issues in a trial of maternal gene therapy

Understanding Early Onset FGR: The EVERREST Prospective study

14:20 **s O**   **KASIA MAKSYM**
10.3 | Outcomes of early onset FGR: the fetus

14:25 **s O**   **FRANCESC FIGUERAS**
10.4 | Early onset FGR - baseline medical and obstetric characteristics: 6 year prospective study

14:30 **s O**   **INGRAN LINGAM**
10.5 | Outcomes of early onset FGR: the neonate at 12 months

14:35 **s O**   **MERRYL HARVEY**
10.6 | Pregnant women's experiences and perceptions of study participation

14:40 **O**   **KAREL MARSAL**
10.7 | Challenges in recruitment in studies of FGR

14:50 **s O**   **TOMMI HEIKURA**
10.8 | Reproductive toxicology studies: human placenta and pre-clinical rabbit

14:55   Discussion

Developing and Planning The EVERREST Clinical Trial

15:05 **s O**   **TOMMI HEIKURA**
10.9 | Developing the ATIMP (Advanced Therapy Investigational Medicinal Product) for EVERREST

15:10 **s O**   **ROBERT SHAW**
10.10 | Manufacturing the EVERREST IMP (Investigational Medicinal Product)

15:15 **s O**   **ANNA DAVID**
10.11 | FGR as an orphan disease

15:20 **s O**   **REBECCA SPENCER**
10.12 | Inclusion and exclusion criteria and predicting outcome of early onset FGR

15:25 **s O**   **REBECCA SPENCER**
10.13 | Developing standard maternal and fetal adverse event criteria for FGR clinical trials

15:30 **s O**   **JADE DYER**
10.14 | Regulatory Process - MHRA

15:35   Discussion; Closing Remarks

| K | Keynote 15+5 min | O | Oral 7+3 min | P O | Poster Oral 2+1 min |

15:50 Refreshment Break

16:10 **SESSION 11: Debate: Are We Placing Too Much Emphasis on Fetal Size?**

16:10 **O** **WESSEL GANZEVOORT**
Yes; let's get away from dichotomisation

16:20 **O** **JASON GARDOSI**
No; size does matter when assessing growth

16:30 Discussion

16:45 **SESSION 12: Policies & Protocols: do they reflect the evidence?**

16:45 **K** **LESLEY MCCOWAN**
12.1 | Overview of international guidelines on fetal growth

17:05 **O** **PATRIZIA VERGANI**
Protocols in Lombardy and Italy

17:15 Plenary / Open Forum: General discussion and take-home messages

17:45 Best abstracts: Awards & Presentations

18:00 Close

E-POSTER ORAL
Presentations

SESSION 3: Poster-Oral 1

FIDA ALI
3.1 | Are our SGA babies slipping through the net?

JM ARRAEZ
3.2 | Screening programme for fetal growth restriction in low risk population

SIMA DELAVARI
3.3 | To evaluate GROW customised charts in the classification of term birthweight infants <2.5kg and their predictive value for neonatal care unit admission

SABRINA DEMIRDJIAN
3.4 | Perinatal outcome and morbidity in small for gestational age newborns with and without prenatal diagnosis

NANDINI HALDER
3.5 | Retrospective analysis of small for gestational age (SGA) babies at our health board following implementation of the growth assessment protocol (GAP)

DITTE NYMARK HANSEN
3.6 | Screening for small-for-gestational-age fetuses in Denmark

GRAHAM TYDEMAN
3.7 | The rising number of growth scans and an audit of screening for SGA in women with a low PAPP-A

ANDREA DALL'ASTA
3.8 | Accuracy of the symphysis-fundal height as a screening test for small-for-gestational age fetuses at birth within a low risk population

ANDREA DALL'ASTA
3.9 | Prediction of small for gestational age neonates and adverse outcomes in late onset fetal growth restriction: a comparison of standard and Intergrowth charts

ANNA CARLI
3.10 | Identification of fetal growth restriction in a population of stillbirths: a comparison of three different growth curves

OLIVER HUGH
3.11 | Stillbirth risk and SGA rate in subgroups according to maternal size: comparison of GROW, WHO and IG21 fetal growth standards

LESLEY MCCOWAN
3.12 | The effect of maternal going-to-sleep position on birthweight: a secondary analysis of an individual participant data meta-analysis of going-to-sleep position and the risk of late stillbirth

SESSION 9: Poster-Oral 2

IRENE BEUNE
9.1 | Definitions of fetal growth restriction in existing literature over time: A systematic review

IRENE BEUNE
9.2 | Consensus based definitions of fetal growth restriction

SABRINA DEMIRDJIAN
9.3 | Subtle cardiovascular changes in small for gestational age fetuses may be associated with neonatal morbidity

V PRIYADARSHINI
9.4 | Cardiac function and doppler indices before and after administration of steroid in fetuses with growth restriction

GRAZIA TIRALONGO
9.5 | A Pilot study of fetal growth, maternal hemodynamics and plasma and placental expression of epidermal growth factor

JOSEPHINE LUPPINO
9.6 | Physiopathology of adrenal sparing: ultrasound and functional evaluation of foetal adrenal glands in relation to foetal growth restriction and pre-eclampsia

CLARA BRUIN
9.7 | TInter- and Intra-observer variability in ductus venosus blood flow measurement

MEGAN SHARPS
9.8 | Elevated numbers of placental macrophages in pregnancies complicated with fetal growth restriction

TAMARA STAMPALIJA
9.9 | Umbilical vein blood flow volume in fetuses with inappropriate growth for gestational age and normal doppler velocimetry

TAMARA STAMPALIJA
9.10 | Uterine and umbilical vein blood flow volume in fetuses detected antenatally as inappropriate for gestational age but with normal birthweight

CATERINA NERI
9.11 | Fetal dopplers at term in pregnancies affected by gestational diabetes: role in prediction of perinatal outcomes

FRANCESC FIGUERAS
9.12 | Evaluation of the quality and reliability of middle cerebral artery (MCA) and umbilical artery (UA) doppler images in a randomized controlled trial

MADDY SMIES
9.13 | Birthweight/placenta weight ratio in clinically unexpected stillbirth

SANNE GORDIJN
9.15 | Free thiols in maternal serum and urine for the detection of fetal growth restriction

14

E POSTERS   (Abstracts – see p 62)

NB - Electronic posters will be on display throughout the conference.

GERARD ALBAIGÉS
P1 | Early growth velocity and mode of conception in the prediction of small for gestational age (SGA)

EZRA AYDIN
P2 | Anogenital distance in male and female fetuses at 26 to 30 weeks gestation

CLARA BRUIN
P4 | A study of STV calculation algorithms – comparison of two applications for computerized CTG analysis

RICARDO CIAMMELLA
P5 | Is low cerebro placental ratio (CPR), as a placental disfunction marker, a limitant to reach the optimal weight in dichorionic pregnancies?

MAGDALENA ZGLICZYNSKA
P6 | Partial molar pregnancy coexisting with a live diploid fetus, complicated by intrauterine growth restriction and eclampsia

MAGDALENA ZGLICZYNSKA
P7 | The association between expression of microrna-21 and microrna-141 with the occurrence of intrauterine growth restriction

EDEL CLARE
P8 | Fundal height measurements - size does matter

ALEX COLLISTER
P9 | Clinical evaluation of the effectiveness of low PAPP-A in the identification of small-for-gestational-age babies: A GDH audit

JOYCE COWAN
P10 | Fundal height measurement accuracy pre-and post training

ASEELA DASSANAYAKE
P11 | Audit: Was there adequate utilisation of the customised growth chart and its principles in the detection of all growth restricted babies below the 10th centile, delivered in a small DGH

ANNA KAJDY
P12 | Is it better to be big or small? - Adverse perinatal outcomes comparison

RYAN LAVERY
P13 | Accuracy of antenatal ultrasound estimation of fetal weight within South-Eastern Health & Social Care Trust (SEHSCT)

REBECCA LAWES
P14 | Student midwives' perception of the growth assessment protocol (GAP): Preparation for clinical practice

FLURINA MICHELOTTI
P15 | Accuracy of fetal weight by ultrasound

HANNAH MISTRY
P16 | Identification and management of antenatal risk factors for growth restricted babies in a district general hospital

RACHAEL O'FLAHERTY
P18 **|** Experience of GROW programme in Causeway Hospital, Northern Ireland

C PERRY
P19 | Screening, detection and management of small for gestational age fetuses at the Liverpool Women's Hospital

MINI POOTHAVELIL
P20 | Circumvallate placenta and early onset intrauterine growth restriction

FADIMATU ALIYA UMARU
P21 | A case of Non-Hodgkin's lymphoma in pregnancy

RADHIKA VISWANATHA
P22 | Outcome of large for gestational age fetus in an unselected population in non-diabetic mothers who delivered before 40 weeks' gestation

AMIRA YOUNIS
P23 | Effect of diabetes mellitus in pregnancy on fetal liver length measurements

STEFANO FAIOLA
P24 | Longitudinal assessment of interventricular septum thickness in monochorionic biamniotic twins complicated by TTTS and treated with laser coagulation of placental anastomoses

VALENTINA GIARDINI
P25 | A possible role of placental growth factor (PlGF) in the management of fetal growth restriction (FGR) with abnormal umbilical artery doppler velocimetry

JOSEPHINE LUPPINO
P26 | Preterm infants outcomes: Is more important the weight or the gestational age?

EDURNE MAZARICO
P27 | Birth weight and nutritional indices prediction using fractional limb volume and estimated fetal weight

CARLO PERSONENI
P28 | Labour, maternal and neonatal outcomes in IUGR fetuses induced at term

LYNNE WARRANDER
P29 | Prediction of pregnancy outcome in extreme early-onset fetal growth restriction: An exploratory prognostic factor study

HEATHER WATSON
P30 | Treasure hunting: Establishing a Midwife-Led fetal growth assessment (MFGA) clinic to identify the high risk fetus in the low risk pregnancy

NOHA AL-OKDA
P31 | Umbilical artery intima-media thickness: A predictor of poor perinatal outcome in fetal growth restriction

ABSTRACTS - ORAL PRESENTATIONS

Session 1 Fetal growth and neonatal outcome

1.1 | Maternal & environmental factors

K

Cetin I | Parisi F | Mandò C | Dept of Biomedical and Clinical Sciences, ASST FBF Sacco, University of Milano, Italy

Pregnancy represents a period of susceptibility to environmental factors and to increased nutritional needs for both mother's adaptation to pregnancy and for fetal demands. Nutrients (both macro and micro), together with environmental factors such as smoke, pollution, alcohol, social conditions, may determine epigenetic signatures in the placenta, thus influencing its development. Both restricted and accelerated fetal growth may result from inadequate maternal exposures before and during pregnancy. These conditions are also associated with the burden of prematurity and with increased risks for non communicable diseases in later life.

Pregnancy is a dynamic state, during which the mother switches from an anabolic condition during early pregnancy to a catabolic state during late pregnancy, with qualitative differences in dietary requirements during early and late pregnancy.

Energetic adaptations are also a function of maternal body mass index (BMI), with gestational weight gain (GWG) being the major determinant of incremental energy needs.

Since requirements for micronutrients increase more than energy intake, in recent years studies have shown that both BMI and dietary patterns during the periconceptional period as well as during pregnancy are main determinants of intrauterine growth trajectories and birthweight.

The degree of Mediterranean-diet adherence seems to be positively associated not only with birthweight, but already with parameters of embryo growth and development in the first trimester.

Renal intrauterine development and programming seem to be particularly susceptible to environmental and nutritional exposures, with nephron number strictly related to birthweight.

Even in industrialized countries intake of micronutrients such as iron, folate, vitamin D and iodine is inadequate during pregnancy. These nutritional imbalances need to be evaluated, together with counselling on smoking and alcohol, already in the preconceptional phase. Evidence with RCT trials is available only for folate and there is a need for further research.

1.2 | Neurodevelopmental outcome after early onset FGR

K

Karel Marsal | Lund University, Lund, Sweden

Fetal growth restriction (FGR) is associated with increased risk of intrauterine death and with suboptimal neurodevelopment in survivors. In growth restricted infants delivered very preterm, either spontaneously or actively on fetal indication, the negative effects of FGR on development after birth are combined with those of prematurity. The gestational age is considered as the strongest predictor of postnatal development. However, in a clinical context, attempts to prolong early-onset FGR pregnancies have to be balanced against the risk of intrauterine demise. The rates of severe neurodevelopmental impairment like cerebral palsy have not been found higher than in groups of antenatally normally grown infants delivered at very preterm gestational age. Very varying and sometimes conflicting results have been reported for various Doppler variables and the postnatal neurodevelopment. Deterioration of ductus venosus Doppler findings was found to be negatively associated with fetal neurodevelopment; other authors were not able to confirm such association.

Similar is true for the antenatal finding of cerebral redistribution. The predictive value of umbilical artery ARED flow in cases of early-onset FGR is questioned. Nevertheless, recent studies indicate that early intervention in very preterm FGR with reverse end-diastolic flow leads to postnatal neurodevelopment not different from that of infants with less pronounced impairment of fetoplacental blood flow. This suggests that proactive perinatal management in early-onset FGR might be justified. The above mentioned disparity in results reported in the literature is obviously due to big differences in the studies regarding antenatal management (expectative or proactive), gestational age and infant condition at birth, occurrence of neonatal complications, postnatal age at follow-up, presence or lack of controls, etc. It also reflects how difficult it is to perform well-designed long-term follow-up studies. Nevertheless, such studies are urgently needed in order to establish a basis for clinical management protocols improving postnatal neurodevelopment in early-onset FGR.

1.3 | Neurodevelopmental outcomes at five years after early-onset FGR, analyses in a Dutch subgroup participating in a European management trial

A Pels[1], OC Knaven[1] | BJ Wijnberg-Williams[2] | MJC Eijsermans[3] | SM Mulder- de Tollenaer[2] | CSH Aarnoudse-Moens[5] | C Koopman- Esseboom[3] | J van Eyck[6] | JB Derks[4] | W Ganzevoort[1] | AG van Wassenaer-Leemhuis[5] | [1]Department of Obstetrics and Gynecology | Academic Medical Centre, Amsterdam, the Netherlands | [2]Department of Pediatrics, Isala Hospital, Zwolle, the Netherlands | [3]Child Development & Exercise Center, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, the Netherlands | [4]Department of Obstetrics, Gynecology and Neonatology, Wilhelmina Children's Hospital University Medical Center, Utrecht, the Netherlands | [5]Department of Pediatrics, Academic Medical Centre, Amsterdam, the Netherlands | [6]Department of Obstetrics and Gynecology, Isala Hospital, Zwolle, the Netherlands

Objective
Extreme early-onset fetal growth restriction (FGR) is associated with severe neonatal morbidity and long-term sequelae at age two and above. In a European trial on timing of delivery in early-onset FGR, developmental outcome was assessed at age two. No further follow up was scheduled. The Dutch follow-up program gave the opportunity to study developmental outcome at corrected age five years in a (Dutch) subset of the participating FGR children. The aim of the study was to explore developmental outcomes at five years after extreme FGR and their perinatal risk factors.

Methods
Retrospective data analysis of prospective follow- up of infants born very preterm after FGR. At five years of age IQ, movement ABC-II (M-ABC-II-NL) and neurosensory outcomes were assessed.

Results
Seventy-four very preterm FGR children underwent follow- up at five years. They had a mean gestational age at birth of 30 weeks and birth weight of 910 grams, 7% of the children had a Bayley score <85 at two years. Mean five years' full scale IQ (FSIQ) was 98, 16% had a FSIQ <85, and 35% had one or more IQ scores <85. Motor score ≤ 7 was seen in 39%. Neurodevelopmental impairment increased from 6.8% at age two to 15% at age five. An abnormal IQ scale score was related to birthweight and severity of FGR, and abnormal motor score to male sex and bronchopulmonary dysplasia (BPD).

Conclusions
Overall, mean cognitive outcome at five years was within normal range, but 35% of the children had any abnormal IQ score, depending on the IQ measure, and motor impairment was seen in 39% of the children. Severity of FGR was the most important risk factor for cognitive outcome.

1.4 | Severe FGR and normal doppler: neurodevelopmental evaluation at 54 months of age

Maria F Paz y Mino | Raigam J. Martinez-Portilla | Antoni Borrell | Francesc Figueras |
Fetal i+D Fetal Medicine Research Center, BCNatal - Barcelona Center for Maternal-Fetal and Neonatal Medicine (Hospital Clínic and Hospital Sant Joan de Déu), IDIBAPS, University of Barcelona, Spain.

Objective
To assess the neurodevelopment of children born at term with extreme low birthweight and normal Doppler.
Methods: We constructed a cohort of women with singleton pregnancies delivered at term (>37 weeks) with extreme low birthweight defined as birthweight <3SD and normal Doppler. Infants with diagnosed genetic syndromes were excluded. A prospective evaluation of these infants was conducted by the Ages and Stages Questionnaire (ASQ), a validated tool comprising five main areas: communication, gross motor movement, fine motor movement, problem solving, and personal-social behaviour. The lower the score in each area, the higher the probability the children may need further assessment with a professional. Descriptive statistics were used.
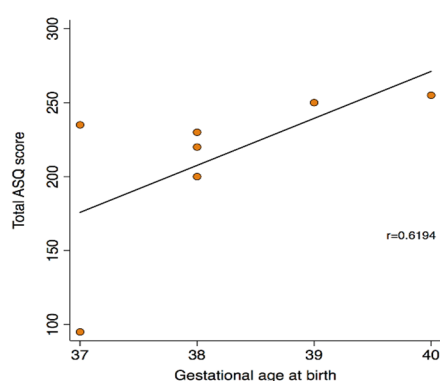

Fig 1. Linear relation between GA at birth and the overall ASQ score at 54 months.

Results
Of 15057 babies born between July 2013 and December 2017, 40 had a BW<3SD (0,26%). Of them A 23 had an abnormal Doppler evaluation before delivery and 2 had B a genetic syndrome diagnosed, leaving 17 infants for analysis. Neurodevelopment assessment will be performed.
The mean maternal age was 37 (SD 6.5) years. The mean GA at birth was 38 (SD 1.4) weeks, and the mean BW was 1,800 (SD 389) grs. From the 17-selected woman, 41% (7/17) completed the ASQ. Overall performance in the communication area was 48 points (SD 14), were only 14% (1/7) had an abnormal score <31.85 points. The mean score for gross motor area was 46 (SD 19) points, where 29% (2/7) were considered abnormal (<35.18 points). Fine motor area score was 31 (SD 11), all considered normal (>17.32 points). Problem solving area score was 40 (SD 15) and 14% (1/7) were abnormal (<28.12 points). And finally, personal-social area had a score of 46 (SD 7), where 14% (1/7) were below the threshold of normality (32.33 points). In the general section of the questionnaire we ask if they think their children speak like children of their age and 57 %(4/7) answered that they think they do not.
Spearman correlation showed a trend towards higher overall ASQ scores when babies were born later in pregnancy (r=0.619), while there was no correlation with birthweight (r=0.193).

Conclusion
There is an overall better neurodevelopmental performance in children born with severe FGR and normal Doppler when delivery takes place later in pregnancy.

1.5 | Standards for neonatal size and catch up growth

K

Enrico Bertino[1] | Francesca Giuliani[2]
[1] Neonatal Unit of the University, [2] Ospedale Infantile Regina Margherita, City of Health and Science University Hub, Turin

No consensus exists regarding how the growth of preterm infants should be monitored or what constitutes their ideal pattern of growth, especially after term-corrected age. The concept that the growth of preterm infants should match that of healthy fetuses is not substantiated by data and, in practice is seldom attained, particularly for very preterm infants. Hence, by hospital discharge, many preterm infants are classified as postnatal growth–restricted. In a recent systematic review, 61 longitudinal reference charts were identified, most with considerable limitations in the quality of gestational age estimation, anthropometric measures, feeding regimens, and how morbidities were described. We suggest that the correct comparator for assessing the growth of preterm infants, especially those who are moderately or late preterm, is a cohort of preterm newborns (not fetuses or term infants) with an uncomplicated intrauterine life and low neonatal and infant morbidity.

Such growth monitoring should be comprehensive, as recommended for term infants, and should include assessments of postnatal length, head circumference, weight/length ratio, and, if possible, fat and fat-free mass. Preterm postnatal growth standards meeting these criteria are now available and may be used to assess preterm infants until 64 weeks' postmenstrual age (6 months' corrected age), the time at which they overlap, without the need for any adjustment, with the World Health Organization Child Growth Standards for term newborns.

Despite remaining nutritional gaps, 90% of preterm newborns (ie, moderate to late preterm infants) can be monitored by using the International Fetal and Newborn Growth Consortium for the 21st Century Preterm Postnatal Growth Standards from birth until life at home.

1.6 | Prenatal assessment of IUGR versus postnatal diagnosis of SGA based on newborns weight charts: a muliticentre study

O

Enrico Ferrazzi[1] | Daniela Di Martino[1] | Tamara Stampalija[2] | Sara Zullino[3] | [1]Unit of Obstetrics, IRCCS Fondazione Cà Granda Policlinic of Milan, University of Milan, Italy | [2]Unit of Prenatal Diagnosis IRCCS Burlo Garofalo, Trieste, Italy | [3]Unit of Obstetrics and Gynecology, University of Pisa, Italy

Objective
A major hiatus there exists between prenatal and neonatal reference charts. We hypothesize that reference charts based on newborns weight at delivery are limited by a poor sensitivity in the detection of IUGR fetuses, not only as regards early and severe IUGR, but also as regards late IUGR, as such these neonatal charts are unable to identify newborns who require special nutritional and follow-up requirements.

Methods
We recruited pregnant patients admitted in five Italian MFM centres for Hypertensive Disorders of Pregnancy associated with AGA fetuses or IUGR fetuses (abdominal circumference -AC- below the 10th centile or with a growth reduction of >40th centiles from mid-trimester biometry, with abnormal Uterine Doppler PI) Prenatal Diagnosis of fetal growth restriction was compared with neonatal Italian weight charts for parity and gender (Bertino et al. 2010)

Italian newborn chart for parity and gender		prenatal diagnosis of IUGR	Sensitivity of newborn chart
n of cases	329	124	
>10th	239	42	
<10th	90	82	66,1
>5th	270	70	
<5th	59	54	43,5
>3rd	296	93	
<3rd	33	31	25,0

Results
Table 1 one shows the sensitivity of Italian neonatal weight charts vs. prenatal diagnosis of IUGR based on Italian prenatal growth charts for SGA newborns. Overall sensitivity of IUGR at 5th centile was only 43,5%. For IUGR delivered after 34 weeks of gestation sensitivity of the 5th centile for newborns weight charts was 61.8%.

Conclusions
Newborns weight charts even when based on local standards suffer of a poor sensitivity in the detection of IUGR fetuses. This sensitivity is improved for late IUGR, but we strongly believe that it remains dramatically poor for clinical purposes in the neonatal and pediatric treatment and follow-up.

Session 2 Standards for fetal growth

2.1 | INTERGROWTH 21st

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Tullia Todros | University of Turin, Turin, Italy

The aim of this study was to investigate the pattern of normal growth among healthy fetuses and newborn babies. Before, most ultrasound charts of size by gestational age were obtained from very relatively studies conducted at local or Country level and may not be appropriate for use internationally. INTERGROWTH has been conducted in eight different countries simultaneously over a five-year period. We screened 13.108 women, of whom 4607 were eligible.

The population consisted in 4321 women (94% of eligible women) who had pregnancies without major complications and delivered live singletons without congenital malformations. In this population we found very low maternal and perinatal mortality and morbidity and these findings underline that our population is really at low risk.

We measured fetal crown-rump length before 14 weeks and 0 days of gestation, and head circumference, abdominal circumference and femur length from 14 weeks and 0 days to 42 weeks and 0 days of gestational age. Each woman was subjected to 6 scans scheduled at 5 weeks interval -14-18 weeks, 19-23 weeks, 24-28 weeks, 29-33weeks, 34-38 weeks and 39-42 weeks.

These measurements allowed to develop international charts of fetal growth standard. Interestingly we also found that fetal growth is not so different across different geographical setting when women's health and nutrition are adequate and when risk factors for fetal growth are low.

2.2 | The WHO fetal growth standard

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Torvid Kiserud | Gilda Piaggio | Guillermo Carroli | Mariana Widmer | José Carvalho | Lisa Neerup Jensen | Daniel Giordano | Alexandra Benachi | Lawrence D. Platt et al. for the WHO Fetal Growth Consortium
Dept. Clinical Science, University of Bergen, Norway | Dept. Clinical Science, University of Bergen, Norway

WHO established fetal growth charts for common ultrasound biometric measurements including estimated fetal weight (EFW) in 2017. Based on 10 different countries, these reference ranges are intended for international application. Briefly, with 1,362 participants recruited according to prescriptive criteria, and 8,203 sets of ultrasound measurements entering the final statistics, the study could also show significant differences and variations across the population concerning intrauterine growth in EFW. And, there were differences between countries concerning gestational age at birth (p<0.001) and birthweight even after adjusting for gestational age (p<0.001).

The study results leave some interesting conclusions for discussion:

1. The idea that optimized maternal condition results in optimally sized neonate is not supported by the wide variation of EFW (5-95 percentile span 2,849-4,312g at 40 weeks) and birthweight (5-95 percentile span 2,880-4,251g at 40 weeks).

2. Fetal growth variation is asymmetric; e.g. during late pregnancy, the dispersion is wider above the 50th percentile than below indicating biological dynamics in addition to pure random distribution.

3. Maternal age, parity, height and weight influence EFW percentiles but rarely more than 2% each, which leaves a major part of variation unexplained. Second, these maternal covariates have differential effect across the percentiles.

4. Significant differences in EFW and growth trajectories among countries were only partially explained by maternal factors.

5. Fetal sex influences the growth percentiles 3.5-4.5%.

Final comments
The WHO growth charts based on multi-national observations across the world seem more appropriate for clinical and epidemiological use than existing references based on single populations. The population variation and a sex difference, suggests that refinement in diagnostic performance can be achieved by customization. Further, the wide individual growth variation prompts a more individualized approach and demands additional information to optimize clinical management and understand long term health development.

2.3 | The NICHD Fetal Growth Study Approach in Context with INTERGROWTH-21st and the World Health Organization Multicentre Growth Reference Study

Katherine Laughon Grantz | Epidemiology Branch, Division of Intramural Population Health Research Eunice Kennedy Shriver National Institute of Child Health and Human Development National Institutes of Health, USA

This presentation will compare and contrast the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Fetal Growth Studies with two international cohort studies that have developed fetal growth standards, INTERGROWTH-21st (INTERGROWTH) and the World Health Organization Multicentre Growth Reference Study (WHO Fetal), in light of differences in aims, sampling frames, and analytical approaches.

Despite all three studies including low-risk status women, the percentiles for fetal dimensions and estimated fetal weight (EFW) varied among the studies. For example, at 39 weeks, the 50th percentile for EFW was 3502 g for whites, 3330g for Hispanics, 3263 g for Asians and 3256 for blacks in the NICHD Study, compared with 3186 g for INTERGROWTH and 3403 g for WHO Fetal.

When applying these standards to a clinical population, it is important to be aware that different percentages of small- (SGA) and large-for-gestational age (LGA) fetuses will be identified. Ideally, a comparison of diagnostic accuracy, or misclassification rates, of SGA and LGA in relation to morbidity and mortality using different criteria is necessary to make recommendations. Identification of the appropriate percentile cut-offs in relation to neonatal morbidity and mortality is needed in local populations depending on which standard is used.

On a final point, assessment of fetal growth with one-time measurement remains standard clinical practice, despite recognition that a single measurement can only indicate size. At least two measurements separated in time are needed to estimate a trajectory, and perhaps one of the greater contributions of these prospective studies will be the ability to estimate fetal growth velocity. Recent findings on fetal growth velocity from the NICHD Study will also be presented.

2.4 | The customised GROW standard for fetal growth and birthweight

Jason Gardosi | Andre Francis | Oliver Hugh | Sue Turner | Mandy Williams | Perinatal Institute, UK

One size does not fit all. The computer-generated customised chart is individually adjusted for each pregnancy, according to constitutional variables that have consistently, in multiple databases, been shown to influence the growth and birthweight of the baby: maternal height, weight at booking, parity and ethnic origin. The GROW chart (Gestational Related Optimal Weight) provides an optimal curve and normal ranges for fetal weight achievable in an uncomplicated pregnancy. The model does not adjust for pathological factors such as smoking or diabetes so that their effect on fetal growth is more easily recognised.

Birthweight and fetal weight centiles calculated by this method have been found to be better at detecting pathology. Customised SGA is more closely related to adverse outcomes such as stillbirth and neonatal death and perinatal morbidity 1. In a recent 10 country, 1.2 million birth comparison with the Intergrowth 21st fetal growth standard, GROW identified significantly more babies at risk of stillbirth 2. Customised charts also confirm normality, thereby reducing false alarms causing unnecessary anxiety, investigations and intervention. This is of particular relevance in subgroups of the population where babies are (normally) smaller.

The GROW software now includes 120 ethnic or country of origin coefficients derived from 3.7 million births from 28 countries. It is provided freely as individual and bulk centile calculators to clinicians and researchers to assess fetal weight and birthweight, and as growth charts with appropriate training.

Following endorsement by guidelines from the Royal College of Obstetricians and Gynaecologists', national roll-out of GROW charts as part of the Growth Assessment Protocol (GAP) has been associated with a year on year drop in stillbirth rates in England to their lowest ever levels. To a large extent, this is attributed to increased antenatal recognition and clinical confidence in the management of fetal growth restriction.

References
1. Gardosi J, Francis A, Turner S, Williams M. Customized growth charts: rationale, validation and clinical benefits. Am J Obstet Gynecol 2018 Feb;218(2):S609-618
2. Francis A, Hugh O, Gardosi J. Customized vs INTERGROWTH-21st standards for the assessment of birthweight and stillbirth risk at term. Am J Obstet Gynecol 2018 Feb;218(2):S692-699

2.5 | Concordance between Intergrowth-21st and South African fetal growth standards for identification of SGA in stillbirths

Tina Lavin | L Nedkoff[2] | DB Preen[1] | G Theron[3] | R Pattinson[4] | [1] Centre for Health Services Research, School of Population and Global Health, The University of Western Australia; [2] Cardiovascular Research Group, School of Population and Global Health, The University of Western Australia; [3] Department of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town; [4] SAMRC Maternal and Infant Health Care Strategies Unit, University of Pretoria

Objective
To compare the ability of INTERGROWTH-21st to identify small-for-gestational-age (SGA) fetuses in stillbirth cases with local standards (Theron) in the South African setting.

Methods
Secondary analysis of the South African Perinatal Problems Identification Program (PPIP) database was used to investigate all stillbirths (>500g and >28 weeks) between October 2013 to December 2016 across South Africa (n=14,776). The study applied the INTERGROWTH-21st standards to classify perinatal deaths as <10th centile (SGA) or >10th centile (AGA) for stillbirths in South Africa as compared to Theron (population-based) growth charts. This was assessed across pregnancy and at specific gestational ages (28-40 weeks).

Results
The prevalence of SGA was estimated at 32.2% and 31.1% by INTERGROWTH-21st and Theron growth charts, respectively. When considering each gestational age separately INTERGROWTH-21st classified 13.8% more stillbirths as SGA in earlier gestations (28-30 weeks, p<0.001) but 4.0% (n=315) fewer events between gestations of 33-38 weeks (p<0.001). Observed agreement ranged from 76.4% (28w) to 99.6% (39w) with Kappa scores lower at earlier gestations (0.42, 28 w) and at 34-36 weeks (0.84-0.89).

Conclusions
Our findings show that there are differences in the proportion of stillbirths considered SGA at each gestational age using different classification systems. This highlights the importance of future research to consider SGA at each gestational age rather than the entire pregnancy period when considering adopting INTERGROWTH-21st.

2.6 | The effect of mixed parentage on ethnic variation in birthweight

Oliver Hugh | Andre Francis | Jason Gardosi | Perinatal Institute, UK

Objective
We wanted to examine whether there is an observable 'dose response' relationship between ethnic origin and birthweight by comparing the effect of same and mixed ethnic parentage on neonatal weight at birth.

Method
We studied a routinely collected, multi-ethnic dataset of 128,609 singleton, normally formed, term pregnancies. Of a total of 11 ethnic categories recorded, there were 7 ethnic groups with sufficient data for analysis: English, East European, African, African-Caribbean, Middle Eastern, Indian and Pakistani. 8,060 (6.3%) of the pregnancies had mixed parentage, which in all cases included one parent being English. Multivariable analysis of birthweight was undertaken, adjusted for physiological characteristics (maternal height, weight, parity), sex and gestational age at birth, and pathological factors including smoking, hypertension, and social deprivation (IMD scores 4 and 5). Birthweight was calculated for each ethnic category, standardised to gestation length of 280 days, maternal height 163 cm, weight 64kg, parity 0, unadjusted for sex, and excluding pathological factors and social deprivation.

Fig 1. Ethnic differences in birthweights, same and mixed parentage pregnancies. Mean standardised birthweight and 95% C.I. are shown. Ethnic groups: Eng=English; EE=East European; Afr=African; AfC= African Caribbean; ME=Middle Eastern; Ind=Indian; Pak=Pakistani.

Results
The average birthweight after a standard uncomplicated pregnancy with English parentage was 3433g. Figure 1 shows the comparative same and mixed parentage standard birthweights in all ethnic groups. For each group, the mixed parent effect lies between the same ethnic parentage and the English reference.

Conclusion
The results confirm previous reports of ethnic differences in birthweight in normal pregnancy, after excluding pathological factors and social deprivation. There is a dose dependent relationship between ethnicity and birthweight, in that pregnancies with mixed parentage display a lesser effect than those with the same parentage.

Session 4 Risk factors, Screening and Prevention

K

4.1 | Stillbirth and fetal growth

Patrizia Vergani | Milan Bicocca University, Italy

Stillbirth has been related to both an impaired and an excessive fetal growth. The relationship between fetal growth and stillbirth is still difficult to determine. Fetal growth restriction (FGR), and its after-birth proxy small for gestational age (SGA) neonate, is one of the most important predictors of stillbirth. However, proper recognition of in utero FGR can be challenging, requiring serial evaluation of antenatal growth. Conversely, SGA is easier to define but can include a proportion of small but normally grown neonates. Customised growth charts have been shown to improve the distinction between pathological and constitutional smallness, thus reducing the rate of unexplained stillbirths. On a cohort of stillbirths diagnosed at the Department of Obstetrics and Gynecology, University Milano-Bicocca, Monza, Italy, identification of stillbirth cases associated with impaired growth was increased by using customized growth charts as compared to standard-of-care Italian Neonatal Curves (39% vs 11%).

Fetuses with intrauterine growth restriction but with normal birthweight represent a limitation of this approach. In presence of suboptimal growth velocity there is an increased risk for neonatal morbidity. Serial ultrasound evaluation, uterine artery Doppler velocimetry, blood test indicating placental dysfunction could allow antenatal detection of inadequate placental support and help reducing the rate of avoidable stillbirths in late FGR cases with normal umbilical artery Doppler. Stillbirth with excessive fetal growth (LGA) has been reported, although the causes have not been elucidated. LGA stillbirths may have large but inefficient placentas, thus being inadequate to support the high metabolic demands. Post-partum morphologic assessment of the placenta can help in proper classification of stillbirths, thus allowing to detect underlying maternal risk factors. Notwithstanding recent improvements the underlying cause/s of the majority of stillbirths would still remain unidentified either because of inaccurate fetal growth assessment or because not associated with growth abnormalities.

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4.2 | Perinatal mortality surveillance: a pilot project in three Italian regions

P D'Aloja, I I Lega | A Maraschini | V Occhiodoro | S Donati | National Centre for Disease Prevention and Health Promotion, Istituto Superiore di Sanità - Italian National Institute of Health, Rome, Italy

Objective
To implement and validate the feasibility and the effectiveness of a multiregional pilot project on perinatal mortality surveillance in Italy, named SPItOSS. The long-term project's goals are population-based estimates of perinatal mortality and prevention of the avoidable deaths.

Method
The surveillance system considers any stillbirth occurring ≥28 gestational weeks and any neonatal death ≤ 7 days of life in three Italian regions (Lombardy, Tuscany and Sicily) with different perinatal mortality rates detected by routine vital statistics (fig.1). All participating health facilities are required to notify every incident case that is subsequently confidentially assessed by a panel of experts at local, regional and national level to establish the cause of death and to assess quality of care. The surveillance system collects also detailed information on the organizational characteristics of the health facilities where the death occurred.

All SPItOSS reference persons and a representative of the clinical risk management network for each facility received a residential training on the operational aspects of the surveillance and a training package cascade teaching to all professionals in their health facility. The final shared assessment includes the classification of the perinatal death according to the ICD-PM classification, the attribution of its cause and the definition of the quality of care that is described as: appropriate with unavoidable outcome, improvable with unavoidable outcome, substandard with avoidable

Results
From July 2017 to April 2018, 272 perinatal deaths have been reported. Among them, 180 occurred antepartum, 11 intrapartum and 81 in the first 7 days of neonatal life.

Conclusions
SPITOSS, modelled on the UK experiences with maternal and perinatal death reviews, enables the critical review of incident cases of perinatal death with the aim of providing clinicians with recommendations to improve care and reduce avoidable perinatal mortality. The present study is funded by the Italian Ministry of Health.

Fig 1. Perinatal deaths in participating regions / 1000 live births - Italy 2013
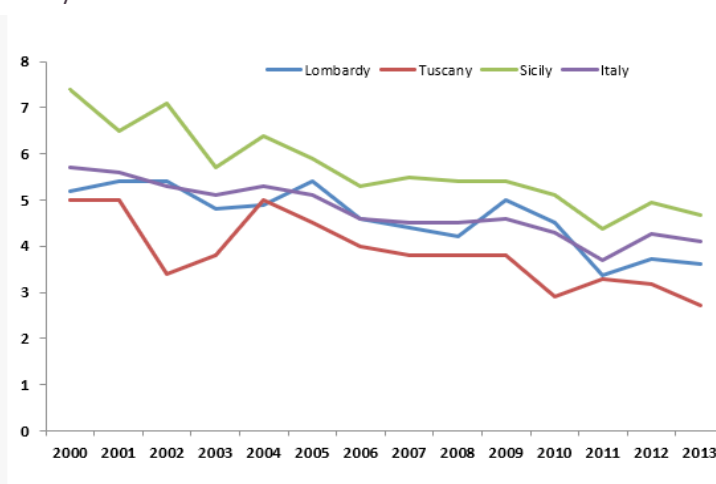
Source: ISTAT 2013 – Investigation of cause of death demographic

O
4.3 | Use of customized curves for estimation of fetal weight and identification of late onset FGR at risk of adverse outcomes

Sara Ornaghi | S Dell'Oro | NJ Pezzotta | E Acampora | N Roncaglia | P Vergani | Department of Obstetrics and Gynecology, Maternal-Fetal Medicine Unit, Foundation MBBM, University of Milano-Bicocca, Monza, Italy

Objective

To investigate the role of customized fetal growth curves on identification of late-onset growth restricted fetuses at increased risk for adverse outcomes.

Method

Singleton patients managed and delivered at our center from 07/2011-2017 with diagnosis of fetal growth restriction (FGR) >320/7 weeks (late-onset). FGR was defined as AC <10th percentile for GA. Customized EFW (C-EFW) percentile was calculated in fetuses with both AC and EFW (Hadlock's formula, H-EFW) <10th percentile at last ultrasound evaluation within 2 weeks before delivery. FGR cases were classified into three groups according to EFW percentile and Doppler assessment: 1) EFW <3rd, 2) 3rd<EFW<9th and abnormal Doppler, and 3) 3rd<EFW<9th with normal Doppler.

Results

During the study period, diagnosis of late-onset FGR was performed in 170 cases, 165 (97.1%) of which also had H-EFW <10th percentile at last scan.

Calculation of C-EFW percentile was possible in 163/165 fetuses. According to H-EFW, 90 (55.2%) fetuses belonged to group 1, 27 (16.6%) to group 2, and 46 (28.2%) to group 3.

After applying customized curves, 22 (13.5%) fetuses appeared to have normal EFW (NO-FGR group). Among the remaining 141 growth restricted fetuses, 68 (48.2%) were in group 1, 31 (22.0%) in group 2, and 42 (29.8%) in group 3. Table displays maternal characteristics and gestational, fetal, and neonatal outcomes among the four C-EFW groups. Of note, NO-FGR fetuses were more likely to be females from Bangladeshi or Indian mothers and to have higher H-EFW percentiles. Also, lower rates of adverse delivery and neonatal outcomes were identified in NO-FGR group and group 3 compared to the other groups.

Conclusions

Our results suggest that use of customized curves for fetal growth could improve the correct diagnosis of FGR and help, alongside with Doppler assessment, the distinction of FGR cases at increased risk for adverse outcomes from 'physiologically' small fetuses.

K
4.4 | Risk assessment and prevention of SGA

Lesley McCowan | University of Auckland, Auckland, New Zealand

Identification of major risk factors for small for gestational age (SGA) infants in early pregnancy is standard practice in many countries. Major risk factors present in early pregnancy include: previous SGA or stillborn infant, maternal chronic hypertension, renal or autoimmune disease, diabetes with vascular disease, age >40, smoking (especially >10 per day), drug abuse, and low PAPPA. These risk factors are often considered as indications for a plan for serial growth scans in the third trimester. Late pregnancy major risk factors include abnormal fundal height measurements (low or crossing centiles), hypertensive disease, unexplained antepartum haemorrhage and low gestational weight gain. These risk factors should also prompt a tailored plan for third trimester scanning.

In women with major early pregnancy risk factors for SGA, especially those also associated with risk for preeclampsia, low dose aspirin (LDA) started by 16 weeks' reduces the risk of an SGA infant. Administration of LDA in the evening is more effective for prevention of SGA and preeclampsia and a dosage of 100-150mg is optimal.

Smoking is a major risk factor for SGA. Cessation early in pregnancy is associated with SGA rates similar to non-smokers and cessation later in pregnancy is associated with an increase in birthweight compared to women who continue to smoke. The most effective strategies to achieve smoking cessation in pregnancy include incentive-based programs and opt-off referral (rather than opt-in) to smoking cessation services. Smoke free legislation also improves pregnancy outcomes. Folic acid taken prior to pregnancy also reduces the risk of an SGA infant and should be a goal for all women planning a pregnancy. Going to sleep on the back in the third trimester may be a novel and modifiable risk factor associated with reduced birthweight.

4.5 | The Growth Assessment Protocol (GAP): New Zealand experience

Joyce Cowan[1] | Lesley McCowan[2] | Mandy Williams[3] | Jason Gardosi[3]
[1] Auckland University of Technology New Zealand, [2]University of Auckland, New Zealand, [3]Perinatal Institute, UK

Objective

To assess progress with a pilot programme to implement the Perinatal Institute's Growth Assessment Protocol (GAP) in New Zealand (NZ).

Method

The GAP programme was adapted by incorporating customised coefficients from a multi-ethnic database derived from National Women's Health, Auckland, NZ. GAP protocols, referral algorithms and e-learning modules were configured to align with NZ SGA guidelines. Since
2016, a training programme was established which included a series of hands-on GAP workshops at 9 District Health Boards. Training included use of growth charts, risk selection and management of SGA and audit tools for antenatal detection of SGA neonates.

Results

A total of 25 multidisciplinary workshops were held, with a total of 875 professionals trained. In addition, there were 726 registrations for e-learning. The rate of pregnancies managed with customised growth charts has increased to over 30,000 per year. A post GAP audit in a large DHB has shown that detection of SGA has more than doubled from a baseline of 22.9% to 53.6% (p<0.001) with GAP training. Barriers to optimal implementation were able to be highlighted and included inequity of access to scanning and follow up after detection of SGA.

Conclusions

The GAP programme was successfully implemented in the first New Zealand units and is already showing improvement in detection of SGA. In 2018, the programme has received funding for a co-ordinated national roll-out.

4.6 | A reduction in perinatal mortality in New Zealand from 2008 to 2016 among small for gestational babies by customised birthweight centile

Lynn Sadler | Ngaire Anderson | Lesley McCowan |
Auckland District Health Board and University of Auckland, New Zealand.

Objective

To determine whether there has been a reduction in perinatal mortality rate (PMR) (stillbirth and neonatal death to 27 days) by customised birthweight centile (CBC) among singleton non- anomalous babies 26 weeks; and to determine the CBC with lowest PMR.

Method

CBC was calculated, using data from the national maternity dataset for the 87% of NZ births under community lead maternity caregivers from 2008- 2016. Perinatal deaths were identified from the PMMRC national collection. For stillbirths gestation at death was used to calculate CBC. SGA was defined as CBC<10th and LGA CBC>90th; and centiles further grouped to determine deciles with lowest PMR.

Results

CBC was available for 95.2% of births and 93.7% of deaths. The PMR in SGA babies reduced from 10.38 to 7.28/1000 births from 2008-2016 (score test for trend p=0.046). PMR was lowest in babies in the 50th-90th CBCs.

Conclusions

A statistically significant reduction in PMR in NZ from 2008-2016 among SGA babies supports the hypothesis that close attention to recognition and management of SGA improves perinatal outcomes.

Figure: Perinatal mortality rate (PMR) by CBC group among singleton non-anomalous births from 26 weeks gestation.

4.7 | Reduction in SGA stillbirths in England

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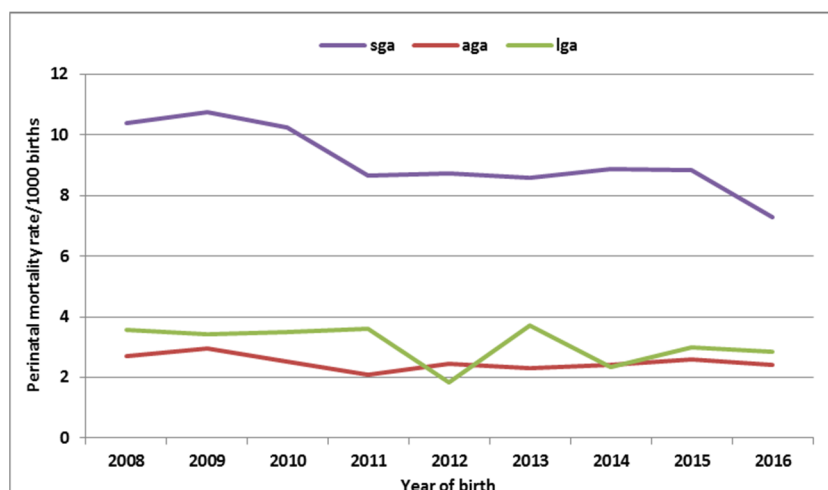
Mandy Williams | Sue Turner | Oliver Hugh | Andre Francis | Jason Gardosi | Perinatal Institute, UK

Objective

The Growth Assessment Protocol (GAP) has been rolled out to 80% of NHS Trusts over the last 5 years and has been accompanied by a significant reduction of stillbirths in England. Part of the GAP programme is the postnatal recording of pregnancy outcome. We wanted to assess whether the lowered stillbirth rate reflected a reduction of fetal deaths with smallness of gestational age (SGA).

Method

The cohort studied consisted of all births entered on GROW software from English Trusts in the GAP programme within 2015–2018. Using the customised centiles produced at the time of submission, with adjustment for intrauterine death-to- delivery delay, the proportion of stillbirths that were SGA (<10th centile) were calculated. Differences between rates over time were assessed using the Z Test.

Results

748,415 deliveries were recorded on GROW software during 2015-2018 and included 3,142 stillbirths (4.2/1000). Of these 1,074 (34.2%) were SGA at birth over the whole period. The proportion of SGA cases decreased significantly from 38.3% in Q1/2, 2015/16 to 33.3% in Q1, 2018/19 (p=0.02) – See Figure.

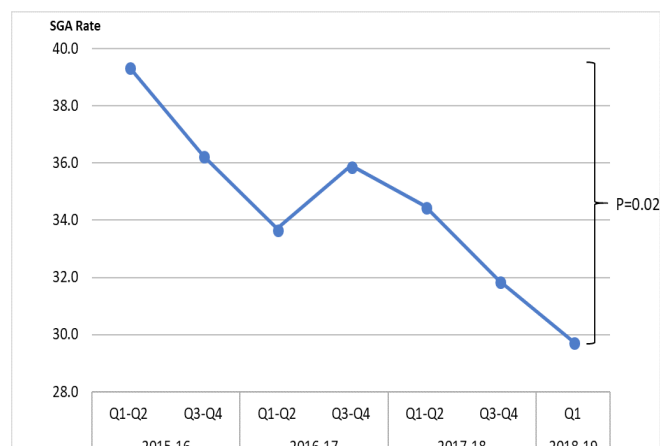**Figure**: Proportion of SGA stillbirths in England, 2015-2018

Conclusions

The national roll-out of the GAP programme has led to the reduction in stillbirths in England. This analysis demonstrates that the improvement was associated with the increase in antenatal detection of SGA babies (reported separately), which in turn has led to fewer intrauterine deaths of SGA babies.

Session 5
Surveillance Strategies for Detection of Growth Restriction and Macrosomia

5.1 | Comparison of the Hadlock and INTERGROWTH-21st formulas for calculating estimated fetal weight among preterm infants: a population cohort study in France

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Objective
To compare the accuracy of the Hadlock and INTERGROWTH formulas for the estimation of fetal weight among preterm infants.

Method
Using the EPIPAGE 2 population-based study of births between 22 and 34 weeks of gestation, we included 578 non-anomalous singleton fetuses with an ultrasound-to-delivery interval <2 days. We used abdominal circumference (AC), head circumference (HC) and femur length (FL) to calculate estimated fetal weight (EFW) with Hadlock's formula and AC and HC to compute the INTERGROWTH's formula. For both formulas, we compared mean percentage errors with standard deviations (sd), and proportions of estimate fetal weight measures within ±10% of birthweight.

Results
Mean (sd) gestational age and birthweight were 29.1 (2.7) weeks and 1219 (489) grams. Mean (sd) percentage errors for Hadlock was closer from zero compared to INTERGROWTH: -0.7 (10.1) and -3.5 (11.6) respectively (P<.001) and more infants were classified within ±10% of their birthweight with Hadlock compared to INTERGROWTH (68.7% vs. 57.8%, P<.001). The INTERGROWTH's formula over-estimated birthweight at 22-23 weeks compared to Hadlock (mean percentage errors of 18.8 (13.6) vs. 5.5 (10.2)) and under-estimated birthweight after 28 weeks: at 29-31 weeks, mean errors were -5.8 (10.9) for INTERGROWTH and -0.6 (10.4) for Hadlock.

Conclusion
Hadlock's EFW formula was more accurate than INTERGROWTH's formula for fetuses between 22 and 34 weeks of gestation. Our results support continued use of Hadlock's formula in France and raise questions about the applicability of INTERGROWTH's intrauterine growth standards.

5.2 | Performance of third trimester ultrasound for the prediction of smallness-for-gestational age: a diagnostic test accuracy meta-analysis

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Objective
To establish the diagnostic performance of ultrasound screening for predicting late smallness for gestational age (SGA).

Method
A systematic search was performed to identify relevant studies published since 2007 in English, Spanish, French, Italian, or German, using the databases PubMed, ISI Web of Science, and SCOPUS. Prospective and retrospective cohort studies in low-risk or non-selected singleton pregnancies with screening ultrasound performed at ≥32 weeks of gestation. The estimated fetal weight (EFW) and fetal abdominal circumference (AC) were assessed as index tests for the prediction of birthweight (BW) <10th. For the meta-analysis, hierarchical summary receiver– operating characteristic curves (hSROCs) were constructed, and quantitative data synthesis was performed using random effects models. The sensitivity of the AC <10th centile and EFW <10th centile for a fixed 10% false positive rate (FPR) was derived from the corresponding hSROCs. A meta-regression procedure was performed to assess the influence of gestational age at ultrasound to the pooled sensitivity.

Results
A total of 21 studies were included. Observed pooled sensitivity of AC and EFW <10th centile for BW <10th centile was 35% (95% confidence interval [CI] 20%-52%) and 38% (95%CI 31%-46%), respectively. Observed pooled specificity were 97% (95%CI 95%-98%) and 95% (95%CI 93%-97%), respectively. Modeled sensitivities of AC and EFW <10th centile for 10% FPR were 78% (95%CI 61%-95%) and 54% (95%CI 46%-52%), respectively. Meta-regression analysis showed a significant increase in sensitivity when ultrasound evaluation was performed later in pregnancy (p=0.001).

Conclusion
Third-trimester AC and EFW perform similar in predicting SGA. However, for a fixed 10% FPR extrapolated sensitivity is higher for AC. There is evidence of better performance when the scan is performed near term and when FGR is the targeted condition.

5.3 | Perinatal outcome of term fetuses born <10th centile: are small for gestational age and growth restricted fetuses different?

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Objective

To evaluate the outcome of term, singleton pregnancies whose birth weight was <10th percentile, according to population-based standards (PbS) and customized birth weight centiles (CbwC).

Method

405 singleton term (≥37 weeks) pregnancies were included: in 122 a diagnosis of FGR (abdominal circumference <10th percentile) was made antenatally. In the other 283 cases, neonatal birthweight was <10th centile without any antenatal evidence of growth restriction (SGA). Data were compared to those obtained in 405 pregnancies with AGA (birthweight 10°- 90° centile) liveborn infants. CbwC for each baby were generated by gestation network centile calculator. Obstetric and perinatal outcomes were collected. Differences among groups were calculated with the unpaired Student t test and with the χ2 test. P <0.05 were considered significant.

Results

Gestational age at delivery, neonatal and placental weight were significantly lower in FGR than in SGA and AGA. 37.7% of FGR mothers had pregnancy complications when compared to 25.4% SGA (p<0.02) and 23.2% AGA (p<0.002). 88.5% FGR had no neonatal pathology when compared to 94.7% SGA (p<0.04) and 97% AGA (p<0.004). The comparison between the PbS and the CbwC showed a centile concordance in 155 (54.8% SGA and 85 (69.7%) FGR (p<0.006): 51/283 (18%) SGA and 10/122 FGR (8%) were classified AGA by CbwC (p<0.01). The CbwC identified among FGR those (classified as <5th) with the worst outcome. On the contrary, we found no differences among SGA according to the CbwC. The comparison between FGR and SGA with CbwC <5th centile confirmed a worst outcome in FGR. Pregnancy complications were increased in FGR (37.7%) when compared to SGA (25.4%; p<0.02) and 23.2% AGA (p<0.002) and this was valid also when analyzing data according to CbwC.

Conclusion

These data show that in a low risk population CbwC are useful in identifying those fetuses with the worst outcome.

5.4 | Effectiveness and cost-effectiveness of routine third trimester ultrasound screening: the IUGR risk selection study (IRIS)

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Objective

IUGR is a major risk factor for perinatal mortality and morbidity. Biometry scans are increasingly used routinely to detect IUGR. However, evidence for its clinical effectiveness is lacking. This nationwide stepped-wedge cluster-randomized trial compares the effectiveness of routine biometry scans in low-risk pregnancies to usual care in reducing perinatal mortality and morbidity.

Method

60 midwifery practices participated, recruiting 13,520 low-risk pregnant women after their standard anomaly scan. All practices offered usual care to monitor fetal growth: serial fundal height measurements with scans only if indicated. Every three months, one third of the practices was randomized for the intervention strategy: a routine biometry scan at 28-30 and at 34-36 weeks added to usual care. Data on the scans were retrieved from sonography and midwifery registries. Perinatal outcomes were retrieved from the Dutch Perinatal Registry. For cases with an indication to have a possible severe perinatal outcome based on Dutch Perinatal Registry, CRF's were filled out by trained research assistants using hospital files. For 389 participants no data on perinatal outcomes could be retrieved.

The primary outcome (n=13,131) was a composite measure of severe perinatal outcomes: perinatal death; Apgar score <4; impaired consciousness; asphyxia; seizures; assisted ventilation; septicaemia; meningitis; BPD; IVH; PVL; or NEC. We performed multilevel logistic regression analyses with midwifery practice, time of crossover from usual care to intervention strategy and obstetric and demographic characteristics as confounders.

Results

The characteristics of the groups of midwifery practices (based on time of crossover) were comparable. From February 2015 to March 2016, 6148 women were included in usual care, 7372 women in the intervention strategy.

During the conference we will present preliminary results regarding both the diagnostic accuracy of routine third trimester biometry scans and the possible effect of these scans on severe adverse perinatal outcome.

PO

5.5 | Combined sequential ultrasound screening at 29 – 32 weeks and 35 – 37 weeks in detection of SGA fetuses

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Objective
The aim of this study was to evaluate the performance of a combined ultrasound screening at 29 – 32 gestation weeks and subsequent examination at 35 - 37 weeks to detect small for gestational age fetuses (SGA) in low-risk singleton pregnancies.

Method
This was a prospective cohort study of low-risk singleton pregnancies undergoing ultrasound assessment at 29 - 32 weeks and subsequently at 35 – 37 weeks. At study inclusion, biometry for estimated fetal weight (EFW) was performed. SGA fetuses were defined as a EWF weight < 10th centiles, using the Hadlock (1991) formula for fetal weight estimation.

Results
A total of 1500 low risk pregnancies were included in the study. Of these, 119 (7,9%) were classified with ultrasound as SGA at 29 – 32 weeks. The remaining 1381 fetuses with normal growth underwent ultrasound screening at 35 -37 weeks and 39 (2,8%) resulted with percentile < 10th. This ultrasound 2 steps screening detected 158 (10,5%) pregnancies complicated by SGA.

Conclusions
In low-risk pregnancies, late ultrasound screening at 35 – 37 weeks' gestation might improve the prediction of SGA so as to detect a greater number of pregnancies that could be subject to adverse perinatal outcomes.

PO

5.6 | Screening for small for gestational age fetuses with universal ultrasonography between 35 – 37 weeks in singleton low risk pregnancies: a prospective cohort study

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Objective
In low risk pregnancies, fetal growth restriction is a major determinant of adverse perinatal outcome. The aim of this study is to evaluate effectiveness of universal ultrasonic fetal biometry for small-for-gestational-age (SGA) fetuses at late third trimester, as a screening test to detect and prevent prenatal risks that could go otherwise undetected and as such could increase perinatal morbidity.

Method
This was a prospective cohort study of low risks singleton pregnancies. We defined SGA fetuses an ultrasonographic estimated fetal weight (EWF) 10th percentile for gestational age (Hadlock, 1991). Italian guidelines require ultrasound screening at 28 – 32 weeks of gestation. According to our research protocol, pregnant women underwent a second late fetal growth screening at 35 – 37 weeks.

Results
Between May 15, 2017, and July 6, 2018, we recruited 3266 women. Patients with previous diagnosis of SGA, fetal anomalies or uncertain dating of pregnancy were excluded. 3205 (98%) were eligible for our study. 112 (3,5%) fetuses were identified with an EWF 10th and in this group in 32 (1%) cases EWF was 5th percentile.

Conclusions
Screening low risks singleton pregnancies with universal third trimester fetal biometry at 35-37 weeks of gestation, could increase the detection of SGA fetuses up to one every 30 cases. The clinical efficacy of such screen positive result should be investigated on a large number of cases.

5.7 | The current management of the SGA fetus in the UK: A survey of practice

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Background
Screening for the small for gestational (SGA) fetus has become an increasingly common feature of antenatal care in the UK. This has principally been driven by a desire to reduce stillbirth in this at-risk group.

Method
We conducted a postal survey of 187 NHS consultant units within the UK to determine what the current practice for the management of the SGA fetus was following the guidance from the Royal College of Obstetricians and Gynaecologists (RCOG) in 2013.

Results
The survey was performed in 3 rounds between 2016 and 2017 with a response rate of 65%. 85% of units assessed risk factors for SGA at booking. 81% of units used a customized SFH chart to screen for SGA with 95% using a

cut off of <10th centile to refer. When ultrasound is used to detect SGA, 80% of units used EFW, with 89% of these using a cut off of <10th centile to diagnose SGA. Only 24% of units had a dedicated fetal growth clinic in which to review patients. 48% of units were able to offer computerised CTG to monitor the SGA fetus.

Conclusions
Overall there is consistency of screening for SGA, aspirin use and identification of SGA (SFH <10th centile, GROW, EFW on USS <10th centile, Umbilical artery monitoring and induction of labour at term). There was a surprisingly low use of computerized CTG to monitor SGA pregnancies despite a recommendation from national guidance to do so and a lower number of specialized fetal growth clinics than might have been expected.

5.8 | GAP: How is it working for us?

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Background
Since the implementation of the Growth Assessment Protocol in 2017, our stillbirth rate has reduced from 5.34/1000 births (n17) in 2016 to 1.96/1000 births (n6) in 2017.

Objectives
Identify the elements of the GAP that are effective in identifying Fetal Growth Restriction (FGR). Compare the recognition rate of FGR before and after the implementation of GAP. Identify areas of improvement to optimise the detection of FGR in the antenatal period.

Method
A cohort of mothers was identified retrospectively whose babies' birth weight were <10th centile. This cohort was examined to identify if FGR was identified in the antenatal period using the GAP. The cohort whose FGR was correctly identified were further analysed to determine the elements of the GAP which led to the detection of FGR.

Results
To date, 245 birth centiles were identified as <10th centile from the period July 2017 to May 2018. 119/245 (48.6%) babies were correctly identified as FGR which is an improvement of 6.7% above our baseline identification rate. In the cohort of identified FGR, 92/119 were categorised as high risk at booking and had serial scans. FGR was identified due to falloff in growth rate (n68), static EFW (n2), incidentally (n7), <10thcentile at 1st serial scan (n42). There were 126/245 (51.4%) not identified as FGR in the antenatal period. Analysis of this group will help identify the elements of the GAP that we need to address in order to optimise the detection of FGR. This data will be available in July 2018 and will be presented at the conference.

Conclusion
The implementation of GAP has improved our detection rates of FGR and has coincided with a significant reduction in perinatal loss. We hope to reduce this further by optimising the application of the Growth Assessment Protocol.

5.9 | GAP SCORE: audit and analysis of SGA babies missed during antenatal surveillance

Sue Turner, Mandy Williams, Oliver Hugh, Jason Gardosi | Perinatal Institute, UK

Objective

Audit of small for gestational age (SGA) birthweights identify that most of these babies are missed antenatally. We wanted to improve our understanding of the reasons for these misses.

Method

GAP-SCORE is a web-based audit tool provided as part of the Growth Assessment Protocol (GAP), designed to assist review of clinical care. It has questions on assessment of risk factors and surveillance of fetal growth during pregnancy, as recommended by RCOG and NHS England guidelines. The tool helps to ascertain reasons for the miss, identify training issues and failures in service provision, and develop action plans for improvement. The study analysed a total of 2488 unselected cases of SGA births not recognised antenatally, which had been entered in 61 NHS hospitals during 2017/18.

Results

As illustrated in the pie chart (Fig), the largest category, 41.4% of missed cases, was in high risk pregnancies where SGA had not been recognised despite serial scanning. A further 14.2% were high risk but had no serial scans (defined as 2 or more in the third trimester). 27.4% were low risk but had one or more scans for various indications (mostly suspected static or slow growth) which nevertheless failed to pick up that the fetus was SGA. A smaller proportion, 17.0%, were low risk cases in which fundal height measurement failed to identify the need for a scan.

The average number of scans in those that were identified high risk at booking was 2.6, with a mean interval between last scan and delivery of 18 days.

Conclusion

The audit highlighted that recommendations for surveillance in high risk pregnancy are not being followed because of the chronic shortages of ultrasound resources in the NHS: fewer third trimester scans are being undertaken (2.5) than recommended (4.5) to monitor pregnancies at high risk of fetal growth restriction. Less than a fifth of cases were due to lack of recognition of SGA by serial fundal height measurement in low risk cases.
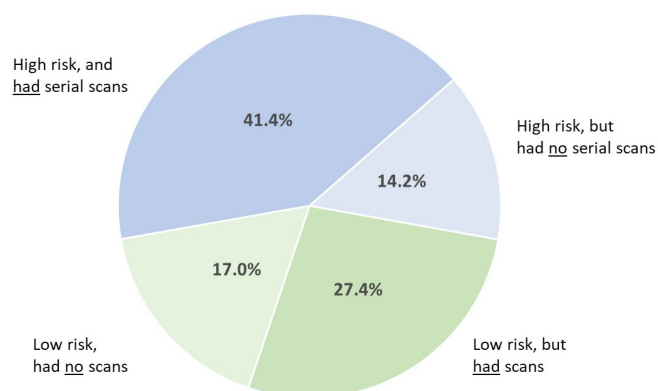
5.10 | Identification of large-for-gestational age fetuses using antenatal customized fetal growth charts: can we improve the prediction of abnormal labor course?

Withdrawn

5.11 | Accuracy of antenatal ultrasound in predicting large-for-gestational age fetuses

Lauren Jade Ewington[1] | Oliver Hugh[2] | Andre Francis[2] | Jason Gardosi[2]

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Objective

The Big Baby Trial is a randomised controlled trial to determine if induction of labour at 38 weeks decreases the incidence of shoulder dystocia in fetuses suspected to be large-for-gestational age (LGA), defined as >90th customised fetal weight centile, between 35+0-38+0 weeks on ultrasound scan (USS). The aim of this study was to determine the accuracy of antenatal USS in detecting LGA at birth, to aid recruitment to the Big Baby Trial.

Methods

The West Midlands PEER database of routinely collected data from 164,000 deliveries between 2009-2012 was reviewed. Women with an LGA fetus >90th customised fetal weight centile on USS (performed for any indication) between 35+0-38+0 were included in the analysis. The outcome was neonatal weight >90th customised centile at birth.

Results

A total of 26,527 women had a scan between 35+0-38+0weeks and of these, 3556 (13.4%) were suspected to have an LGA fetus on scan. 2241 (8.4%) of the cohort were LGA at birth, and 1459 (65.1%) of these were detected by scan. Median gestation at delivery was 276 days (IQR 15.0) and the median interval from scan to delivery was 20 days. Table 1 describes the accuracy of antenatal USS in predicting LGA at birth.

Conclusions

The data obtained from the PEER database show respectable detection rates for fetal LGA from those that have an antenatal USS. Of utility for recruiting participants to the Big Baby Trial is the low false positive rate. However, of concern is the high false negative rate, as these women would not be adequately counselled of the potential risk of shoulder dystocia at delivery.

Sensitivity	65.1%
Specificity	91.4%
Positive Predictive Value	41.0%
Negative Predictive Value	96.6%
False Positive	8.6%
False Negative	34.9%

Table 1 Accuracy of antenatal ultrasound for predicting LGA

5.12 | Validation of a prediction model for fetal overgrowth in pregnancies complicated by diabetes

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Objective

To validate an index that predicts fetal overgrowth in pregnancies complicated by diabetes in a cohort with a different racial and socioeconomic composition and a larger proportion of women with pre-gestational diabetes than the model development cohort.

Methods

Data were derived from a cohort of 308 women with singleton gestations complicated by diabetes who delivered >24 weeks. Prediction model variables (age, history of fetal overgrowth in a prior pregnancy, gestational weight gain, fetal abdominal circumference measurements and fasting glucose values between 24 and 30 weeks) were extracted from medical records and used to calculate each woman's risk of fetal overgrowth. Additional variables for customized birthweight centile calculation were also extracted. A receiver operating characteristic curve was used to assess the predictive ability of the index.

Results

Seventy-nine (26%) pregnancies were complicated by fetal overgrowth. The predictive index had an area under the receiver operating characteristic curve (AUC) of 0.91 (95 % confidence interval [CI] 0.86-0.94) using the recently published Detroit standard and 0.88 (95% CI 0.83-0.92) using the gestation-related optimal weight (GROW) standard that was used to define overgrowth for model development.

Cut-points were selected that identified "high risk" and "low-risk" 5-item index ranges (≥8 and ≥3) that have positive and negative predictive values of 84% (95% CI 70-92%) and 95% (95% CI 90-97%), respectively. The majority of patients in our cohort (n=173, 56%) had a "low risk" index while 16% (n=50) had a "high risk" index. Of the remaining 28% of pregnancies with an "intermediate risk" index, 33% were complicated by fetal overgrowth.

Table (left)

OR odds ratio, aOR adjusted odds ratio, CI confidence interval, AUC area under curve, high fasting glucose ≥100 mg/dL between 24 and 30 weeks, enlarged AC fetal abdominal circumference ≥90th percentile on ultrasound between 24 and 30 weeks, history of overgrowth prior infant birthweight ≥90th customized centile, excessive weight gain in second and third trimesters ≥0.3 lb/ week above Institute of Medicine (BMI-based) goal range.

Conclusion

The published index is predictive of fetal overgrowth despite substantial differences between the development and validation cohorts. The index may serve as a tool for targeting the allocation of healthcare resources and treatment individualization, prior to the period of maximal fetal growth velocity in the third trimester.

Factor	Unadjusted OR (95% CI)	AUC	5-item Fetal Overgrowth Index aOR (95% CI)	Weight
High fasting glucose	24.68 (12.67-48.05)	0.82	24.65 (10.23-59.38)	4
Enlarged AC	25.36 (11.38-56.48)	0.75	20.31 (6.94-59.44)	3
History of overgrowth	7.60 (3.95-15.02)	0.69	4.07 (1.53-10.84)	3
Excessive weight gain	3.06 (1.80-5.19)	0.63	1.43 (0.63-3.22)	3
Age ≤ 30	1.03 (0.62-1.72)	0.50	1.24 (0.55-2.80)	1

Session 6 Fetal Growth Restriction - Early Onset

6.1 | Diagnosis and management of placenta based FGR <32 weeks

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A uniform approach to management of fetal growth restriction (FGR) consistently improves outcome, prevents stillbirth, and allows appropriately timed delivery. By consensus FGR, developing before 32 weeks is considered "early-onset FGR" as it is has a distinct clinical phenotype that is characterized by placental perfusion defects. Accordingly, an estimated fetal weight <10 percentile in an anatomically normal fetus in association with abnormal umbilical artery (UA), middle cerebral artery (MCA), or cerebroplacental Doppler ratio (CPR) is diagnostic of placenta-based FGR in need of fetal surveillance. In these fetuses, progression of UA Doppler abnormality determines the overall rate of clinical deterioration, while abnormal ductus venosus (DV) Doppler precedes deterioration of biophysical variables and stillbirth.

Observational and randomized trials have confirmed that advanced gestational age at delivery is the primary determinant of neonatal survival, making avoidance of iatrogenic prematurity a major management challenge. Infant outcome in early onset FGR is improved if delivery is delayed until late DV Doppler changes are observed. An abnormal biophysical profile, an abnormal computerized cardiotocogram are important safety net criteria for delivery in those fetuses that do not exhibit late DV Doppler findings as part of their clinical deterioration. In patients that do not yet meet these delivery criteria the choice of the surveillance interval is critically important to prevent stillbirth and should be based on umbilical artery and early DV Doppler changes. Intervention trials that evaluated potential treatments to delay clinical progression of early onset FGR have not demonstrated any benefit.

6.2 | Haemodynamics in pregnancies with growth restricted fetuses

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Objective

To compare maternal hemodynamic profile during pregnancy and at 6-12 months post-partum, in women affected by Hypertensive Disorder of Pregnancy (HDP) associated with Intrauterine Growth Restricted fetuses (IUGR), or with normally grown fetuses (AGAf), and in pregnant women affected by intrauterine growth restriction without HDP.

Method

This was a prospective, observational, longitudinal, monocentric study. Consecutive patients we enrolled from 24 weeks of gestation to term, classified as follows: HDP-AGAf, HDP-IUGR, severe IUGR and Controls. Maternal echocardiography was performed during pregnancy at diagnosis and at 6-12 months postpartum.
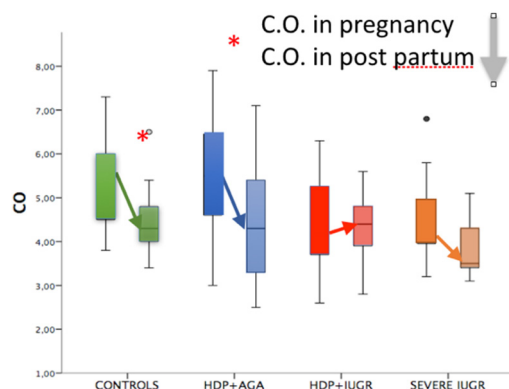
Results

Results Seventy-two patients were eligible for the analysis. In HDP-IUGR and in the severe IUGR groups, maternal cardiac output (CO) was significantly lower and total vascular resistances (TVR) increased, compared with controls. This profile did not change significantly at 6-12 months postpartum. The HDP-AGAf group showed an increased CO, with increased TVR, and increased left ventricular mass (LVM), relative wall thickness (RWT) and a reduced E'/A' ratio. In the post-partum, MAP, TVR and LVM showed normal values in HDP-IUGR but remained significantly higher in HDP-AGAf. In HDP-IUGR and IUGR groups fewer significant longitudinal changes were observed from pregnancy to post-partum.

Conclusion

HDP-IUGR or severe IUGR groups showed very similar poor cardiovascular adaptation to pregnancy metabolic demands. Hemodynamic indices of this group remained unchanged in the post-partum except for the reduction of TVR. This was profoundly different from the increased HR, CO, and lowered TVR observed in normal pregnancies. During pregnancy, the HDP-AGAf group presented similar increased HR, CO, but at the cost of diastolic function impairment, and ventricular remodelling.

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6.3 | Role of maternal haemodynamic evaluation in the definition of fetuses with growth restriction outcome

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Objective
To identify the maternal haemodynamic condition in pregnancies affected by fetal growth restriction (FGR) and to assess the potential correlation with the fetal-maternal outcome.

Method
100 pregnant women underwent a non-invasive cardiovascular assessment and enrolled at the time of definition of fetal growth restriction. According to the fetal ultrasonographic features and to the gestational age at diagnosis, we collected small for gestational age (SGA) (n=50), early fetal growth restriction (eFGR) (n=32) and late fetal growth restriction (lFGR) (n=18) fetuses. Furthermore, we labelled each woman only considering haemodynamic values of total vascular resistance (TVR) at the time of enrolment.

Results
We obtained a group A with low TVR (<1100 dyne-cm- sec-5) (n=58) and a group B with high TVR (>1100 dyne-cm-sec-5) (n=42). Population distribution is represented in Fig.1. Group A is composed by 66% of SGA, 17% of eFGR and 17% of lFGR whereas in group B we had 40% of SGA, 43% of eFGR and 17% lFGR. As regards the complications we noticed an elevated incidence in high TVR group. Focusing on SGA fetuses, we found 14% of incidence of complications in group B and 30% in group A.

Conclusion
We observed an overall increased risk of fetal complications in the group of women with an underlying maternal cardiovascular disorder. This impairment is expressed by a state of hypodynamic circulation with elevated TVR, a decreased preload and a poor capacity of the heart to ensure an appropriate placental perfusion. Although SGA fetuses are not defined as compromised, we have demonstrated that those with an impaired haemodynamics have worse outcome behaving like FGR fetuses. This might suggest a new definition of risk correlated to the maternal cardiovascular condition.

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6.4 | Pravastatin to treat early-onset fetal growth restriction

Manel Mendoza | Raquel Ferer-Oliveras | Hospital Universitari Vall d'Hebron, Barcelona. Spain

Objective
To analyse the sFlt-1/PlGF ratio values and pregnancy outcome in patients with early FGR treated with pravastatin compared with non- treated controls.

Method
Early-onset FGR was defined as EFW ≤3rd centile, before 28+6 gestational weeks, with or without Doppler impairment. After providing a written informed consent, 19 patients accepted to receive 40 mg of pravastatin daily until delivery. Other 19 consecutive pregnancies with early-onset FGR, for which two or more sFlt1/PlGF ratio values were available, were used as controls. One sFlt-1 to PlGF ratio measurement was obtained before introducing Pravastatin (M0) and one more during treatment (M1). Data from another 19 consecutive pregnancies with early- onset FGR, for which two or more sFlt1/PlGF ratio values were available, were used as controls.

Results
Median ratio values at diagnosis (M0) were similar in both groups (105.3 vs 152.2 p=0.544). Gestational age at delivery was inversely correlated with ratio values at M0 in both groups. Ratio values decreased significantly (p<0.001) after Pravastatin (mean M1-M0= -10.12) but rose in controls (mean M1-M0=67.00). Pregnancy duration tended to be longer in cases compared to controls (64.1 vs 47.6 days) but this difference was not statistically significant (p=0.350).

Conclusion
Pravastatin ameliorates angiogenic imbalance and could increase time until elective delivery in early growth- restricted fetuses. This is not a randomised study; therefore, controls may not be comparable to cases. Our results are promising but further research is needed to confirm these findings. correlated to the maternal cardiovascular condition.

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6.5 | Management of very early onset IUGR. Single centre experience 1998-2015

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Objective
To describe the outcome of growth-restricted fetuses with absent or reversed end-diastolic flow (ARED) in the umbilical artery delivered before 30 gestational weeks.

Method
This was a retrospective study of all growth- restricted fetuses (singletons and twins) with ARED flow delivered in Lund during the time period of 1998-2015 (n=142). Control group: all non-IUGR, AGA fetuses delivered <30 gestational weeks during the corresponding time period (n=961). Perinatal mortality, neonatal morbidity, infant mortality and major neurological morbidity of liveborn infants were compared between the two groups.

Results
In the ARED group there were 7 cases of intrauterine death, 2 deaths in the delivery room, and 133 newborns delivered on fetal indication alive by cesarean section. The mean gestational age was 26 gestational weeks in both the ARED and control group, (range 23+3-29+6 and 22+0-29+6, respectively).

There was no significant difference in perinatal mortality between the ARED and control groups (12% vs 15%). ARED fetuses delivered at occurrence of absent end-diastolic flow had a higher survival rate (91%) than those with reversed end-diastolic flow (69%) (p<0.001). The incidence of chronic lung disease was higher in the ARED group than in control group (p<0.001). There were no differences between the groups in the occurrence of necrotizing enterocolitis, retinopathy of prematurity, cerebral hemorrhage or cerebral palsy. Two-year survival was 83% in the ARED group and 87% in the control group (ns). Significantly more children from the ARED group were in need of habilitation services (p=0.02)

Conclusions
Very preterm growth-restricted fetuses with umbilical artery ARED flow delivered on fetal indication showed a high 2-year survival, similar rate of cerebral palsy and higher need for habilitation services compared to non- IUGR very preterm infants.

O

6.6 | Uterine arteries blood flow volume in fetuses with inappropriate growth for gestational age and normal doppler velocimetry

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Objective
To evaluate the blood flow volume (Q) in uterine arteries (UtA) in fetuses with inappropriate growth for gestational age with normal Doppler velocimetry indices.

Method
This is a sub-group analysis of a case-control (1:2) study performed in a single third referral centre, IRCCS Burlo Garofolo, Trieste, Italy. Inclusion criteria for cases were abdominal circumference (AC)<10° centile or reduced growth (AC crossing 50° centiles) with normal Doppler assessment of UtA and umbilical artery (UmbA). Controls were uneventful pregnancies with normal fetal growth and normal Doppler indices (AGA).

QUtA was evaluated by multimodal Doppler (Ferrazzi, 2011), and was also normalized for estimated fetal weight (EFW). Analysis was performed at diagnosis (cases) by logistic regression analysis.

Results
110 cases and 220 controls were recruited. The sub-group analysis was performed on 74 cases and 178 controls. Fetuses with inappropriate growth for gestational age and with normal Doppler indices in UtA and UmbA (green dots) had significantly lower absolute QUtA than AGA (panel a), p<0.0001). When normalized for EFW such significant difference was no longer observed (panel b), p=0.09). Controls are represented by regression line and 95% confidence intervals.

Absolute Q-UtA   Normalized for EFW Q-UtA

a)   b)
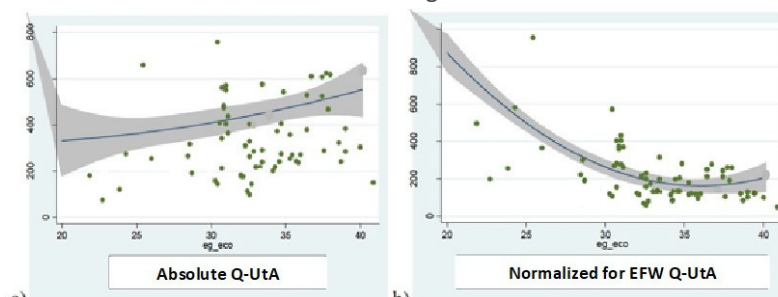
Conclusion
A significant majority of fetuses with AC <10° centile or drop of >50° centiles, with normal Doppler velocimetry of uterine and umbilical arteries, had a significantly lower absolute flow volume in UtA. However, when normalized for EFW, relative flow volume matched the restricted weight achieved by the fetus in utero. These findings are consistent with the criteria that fetuses small for gestational age with normal uterine and umbilical Doppler velocimetry might not just be constitutionally small, but might be in a condition of stunted fetal growth driven by poor nutritional environment.

6.7 | A prediction model for short-term neonatal outcomes in severe early-onset IUGR

A Sharp | **C Cornforth** | **R Jackson** | **J Harrold** | **MA Turner** | **L Kenny** | **PN Baker** | **ED Johnstone** | **A Khali,** | **P von Dadelszen** | **AT Papageorghiou** | **Z Alfirevic** | Department of Women's and Children's Health, University of Liverpool, UK

Objective

Severe early-onset fetal growth restriction (FGR) predisposes to fetal death, neonatal death, neonatal morbidity and neurodisability. The use of placental biomarkers has been proposed for risk stratification in pre-eclampsia, but they could be equally useful in FGR in aiding management.

Method

This is a secondary analysis of the multicentre, placebo-controlled STRIDER UK RCT of singleton pregnancies with severe early-onset FGR. Women with FGR pregnancies between 22+0 and 29+6 weeks of gestation were randomly assigned to receive either sildenafil 25 mg three times daily or placebo until 32+0 weeks' gestation or delivery. We developed prediction models based upon maternal demographics (age, parity, blood pressure, preeclampsia, gestational hypertension), fetal biometric (estimated fetal weight) and Doppler measurements (Middle Cerebral Artery (MCA), Umbilical Artery (UA)) and maternal angiogenic biomarkers [placental growth factor (PlGF), soluble endoglin (sEng), soluble fms-like tyrosine kinase 1 (sFlt-1) and sFlt-1:PlGF ratio).

Results

A complete data set was available for 105 of 135 randomised women. Multivariable regression analysis identified estimated fetal weight (EFW) and sFlt-1:PlGF as independent predictors of livebirth and overall survival. EFW was a consistent predictor for all outcomes other than gestation at delivery. sFlt-1:PlGF ratio was a consistent predictor for all outcomes other than neonatal morbidity.
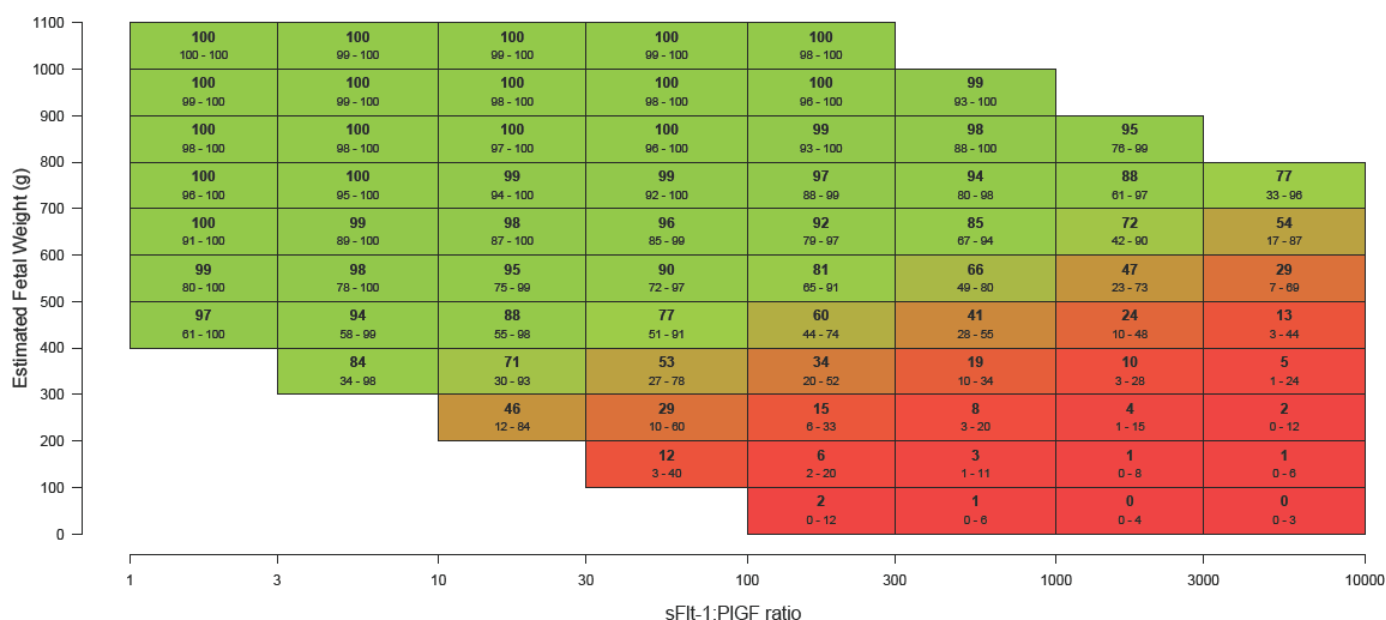
Conclusions

In severe early-onset FGR pregnancies livebirth and overall survival can be predicted using a model involving EFW and sFlt-1:PlGF ratio. This model will allow informed decision making about pregnancy management, especially in cases that may be considered previable.

Session 7 Fetal growth restriction - late onset

K

7.1 | Investigation and management of late onset FGR

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By consensus late fetal growth restriction (FGR) is that diagnosed >32 weeks. This condition is mildly associated to a higher risk of perinatal hypoxic events and suboptimal neurodevelopment. Histologically, it is characterized by the presence of uteroplacental vascular lesions (especially infarcts), although the incidence of such lesions is lower than in preterm FGR. Screening procedures for fetal growth restriction need to identify small babies and then differentiate between those that are healthy and those that are pathologically small. First- or second- trimester screening strategies provide detection rates for late SGA <50% for a 10% of false positives. Compared to clinically indicated ultrasonography in the third trimester, universal screening triples the detection rate of late SGA. As opposed to early third-trimester ultrasound, scanning late in pregnancy (around 37 weeks) increases the detection rate for birthweight below the 3rd centile. Contrary to early FGR, umbilical artery Doppler velocimetry as a standalone does not provide good differentiation between late SGA and FGR. A combination of biometrical parameters (with severe smallness usually defined as and estimated fetal weight or abdominal circumference <3rd centile) with Doppler criteria of placental insufficiency (either in the maternal [uterine Doppler] or fetal [cerebroplacental ratio] compartments) offers a classification tool which correlates with the risk for adverse perinatal outcome. There is no evidence that induction of late FGR at term improves the perinatal outcomes nor it is a cost-effective strategy, and it may increase neonatal admission when performed before 38 weeks.

PO

7.2 | Placental findings in small for gestational age and growth restricted fetuses

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Objective
To compare types and prevalence of placental findings in a cohort of small for gestational age and intrauterine growth restriction with and without Doppler criteria.

Method
A total of 146 placentas from singleton pregnancies were examined. Newborns were classified as small for gestational age (SGA) if birth-weight was below the 10th centile according to local fetal customized standards with normal Doppler (N=36) or intrauterine growth restriction (IUGR) if birth-weight was below the 3rd centile (N=40) or below the 10th centile with abnormal uterine artery Doppler or cerebroplacental ratio (N=70). The following placental findings were evaluated: placental weight less than 10th centile, maternal underperfusion, fetal underperfusion, high grade chronic villitis and massive fibrin deposit.

Results
The prevalence of any placental finding was: 50% for SGA, 52.5% for IUGR with normal Doppler and 70% for IUGR with abnormal Doppler (linear trend p=0.03). Placental weight less than 10th centile was found in 61.8% of SGA, 65% of IUGR with normal Doppler and 64.3% of IUGR with abnormal Doppler (linear trend p=0.78); maternal underperfusion in 38.9%, 42.5% and 58.6 (linear trend p=0.039); fetal underperfusion in 8.3%, 2.5% and 2.9% (linear trend p=0.22); high grade chronic villitis in 5.6%, 10% and 8.7% (linear trend p=0.18); and, massive fibrin deposit in 6.3%, 5% and 10% (linear trend p=0.66), respectively.

Conclusion
Placental abnormalities are more frequent in IUGR with abnormal Doppler than SGA or IUGR with normal Doppler. In these cases, maternal underperfusion is the most frequent placental lesion.

7.3 | Maternal serum levels of PlGF and sFlt-1 in predicting delivery of an SGA newborn

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Objective

The aim of the study was to assess maternal serum levels of sFlt-1, PlGF and the sFlt-1/PlGF ratio in an unselected population of pregnant women and evaluate the cut-off value in predicting delivery of an SGA newborn.

Method

In a prospective cohort study, in a group of 406 unselected pregnant women with singleton pregnancies, maternal serum PlGF and sFlt-1 were assessed using the Thermo Fisher assays on a Kryptor Compact platform. PlGF was assessed three times (at 9–13, 30–32 and 36–37 gestational weeks) and sFlt-1 two times (at 30-33 and 36–37 weeks) and the sFlt-1/PlGF ratio was calculated. Birth weight centiles were evaluated according to INTERGROWTH-21 growth charts. A receiver operating characteristic (ROC) analysis was used to determine the threshold of the levels of PlGF and sFlt-1 and sFlt-1/PlGF ratio in predicting delivery of an SGA newborn.

Results

SGA (birth weight <10th centile) was diagnosed in 7% of the newborns (29/406) and 1% (4/406) had a birth weight <3rd centile. ROC analysis showed that none of the parameters were able to predict delivery of SGA <10th centile, the area under the curve (AUC) was poor for all parameters regardless of gestational age and did not exceed a level of 0.75. In the group SGA <3rd centile, ROC analysis showed an excellent accuracy for PlGF in the 3rd trimester, at 30-33 weeks (AUC = 0.89), and particularly at 36-37 weeks (AUC = 0.91). The optimal PlGF cut-off at 30-33 weeks was 182 with sensitivity 87% and specificity 75% and at 36-37 weeks cut-off 76 with sensitivity 86% and specificity 100%, respectively.

Conclusion

Maternal serum PlGF in the 3rd trimester, particularly at 36-37 week, can predict the delivery of an SGA <3rd centile at term, but not <10th centile, and neither sFlt-1 nor sFlt-1/PlGF ratio improve prediction.

7.4 | Placental growth factor (plGF) as a marker of fetal growth restriction (FGR) caused by placental dysfunction: correlation with uterine arteries doppler and placental histology

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Objective

To evaluate the correlation between ultrasound diagnosed Fetal Growth Restriction (FGR), maternal plasma Placental Growth Factor (PlGF) level, uterine arteries Doppler and placental histology.

Method

This prospective cohort study included women diagnosed with FGR, defined for Abdominal Circumference (AC) < 10th percentile and mean uterine arteries Resistance Index (RI) > 95% percentile, or abnormal umbilical artery Doppler, or growth arrest or CA deflection of 2 quartiles or more in the third trimester. Doppler study of uterine arteries, PlGF and placental histopathological exam were performed on each patient. Maternal blood PlGF was measured within 2 weeks before delivery using ELISA kits. Placentas were analyzed according to Redline classification. The correlations between PlGF level, uterine arteries Doppler study and placental histopathological findings were analyzed.

Results

35 pregnancies complicated by FGR were included in the study. Mean gestational week at diagnosis was 31.6 (20.1- 39.6). Mean gestational age at delivery was 34 weeks (25.5-40.1). 32 women had low PlGF (91.4%), of which 29 (91%) had pathological uterine artery Doppler and 26 (81%) had abnormal histopathological findings. The most common were anomalies of the chorionic villi (87,5%, N=28) especially increased syncytial knots (N = 25, 78.1%) and placental infarcts (N=12, 37.5%). In the 3 women with normal PlGF, placental histology was regular.

Conclusion

The study shows a strong correlation between low plasma PlGF levels, pathological uterine arteries Doppler and histological findings suggestive of placental underperfusion. PlGF could therefore be used as a placental damage severity marker and may be useful in determining the timing of delivery in FGR fetuses.

Table

Maternal plasma PlGF levels	N (%)	Abnormal uterine arteries Doppler	Abnormal placental histology	Small for Gestational Age fetuses	Emergency cesarean section
Normal	3 (9%)	1 (33%)	0 (0%)	2 (67%)	0 (0%)
Pathological	32 (91%)	29 (91%)	26 (81%)	23 (72%)	16 (50%)

7.5 | sFlt-1/PlGF ratio in pregnancies complicated by placental insufficiency

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Objective

An abnormal ratio of proangiogenic (PlGF) and antiangiogenic (sFlt-1) proteins is significantly associated with preeclampsia (PE), HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) and/or intrauterine growth restriction (IUGR). The aim of this study was to evaluate sFlt-1/PlGF ratio in pregnancies complicated by hypertensive disorders (HDP: gestational hypertension, preeclampsia) and/or IUGR.

Method

We recruited 186 patients, from 24 weeks to term: 32 cases of HDP with appropriate for gestational age fetus (HDP- AGAf), 41 cases of HDP with intrauterine growth restriction (HDP-IUGR), 28 early IUGR and 55 late IUGR; 30 controls with uneventful pregnancies were also included. Diagnosis of HDP was made according to the ISSHP criteria. IUGR was defined as abdominal circumference <10thcentile and classified as early or late according to Delphi criteria (Gordjin, 2016). Measurements of sFlt-1 and PlGF were performed on the automated Elecsys system (Roche diagnostic tool) at the time of enrolment.

Results

HDP-IUGR showed the highest sFlt-1/PlGF ratio, significantly more than HDP-AGAf. Early-IUGR also showed a high ratio, not significantly different from HDP-IUGR nor HDP-AGAf (Figure 1).

Conclusion

The sFlt-1/PlGF ratio was significantly higher in all HDP and IUGR phenotypes than controls. Women affected by HDP with IUGR showed the highest ratio, and the smaller variance of observed ratios, as such suggesting the combination of two causes of syncytio- trophoblastic oxidative stress, a small placenta and a possible poor maternal perfusion of the placenta.
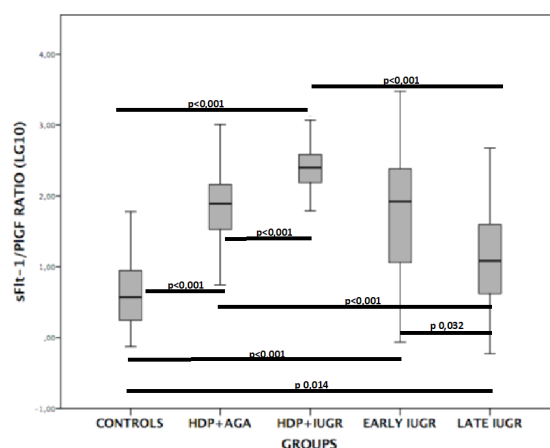

Fig 1. Comparison of sFLT-1/PlGF ratio between the study groups.

7.6 | sFlt-1/PlGF ratio and maternal hemodynamics in pregnancies complicated by placental insufficiency

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Objective

The aim of this study was to evaluate the correlation of angiogenic factors (sFlt-1, PlGF) with maternal hemodynamic profile in pregnancies complicated by gestational hypertension and preeclampsia (HDP), with or without fetal growth restriction.

Method

In this prospective longitudinal study, we enrolled 186 patients, from 24 gestational weeks to term: 32 cases of HDP with appropriate for gestational age fetus (HDP-AGAf), 41 cases of HDP-IUGR, 28 cases of early IUGR and 55 cases of late IUGR; 30 controls with uneventful pregnancies were also included. Diagnosis of HDP was made according to the ISSHP criteria. IUGR was defined as abdominal circumference <10th centile and classified as early or late according to Delphi criteria (Gordijn, 2016). Maternal echocardiography was performed by a dedicated cardiologist, blinded to clinical diagnosis and classification, in order to evaluate hemodynamic parameters (cardiac output CO, total vascular resistances TVR), indexes of systolic function, indexes of diastolic function (E'/A' ratio) and indexes of cardiac remodelling (left ventricular mass LVM). Angiogenic factors were measured at the time of enrolment (Roche Elecsys).

Results

HDP-IUGR showed significantly lower heart rate (HR), lower CO and increased TVR and a reduced LVM, compared to controls. early-IUGR also showed significantly lower HR and CO and increased TVR than controls. Late- IUGR showed the same trend as early-IUGR, without any significant difference from controls. Opposite to this, HDP- AGAf showed increased CO as in controls, and significantly higher TVR; they also presented significantly increased LVM and a reduced E'/A' ratio, indicating an impaired myocardial relaxation. We observed a significant direct correlation between sFlt-1/PlGF ratio and TVR; in contrast, a negative correlation was found between sFlt-1/PlGF ratio and HR and LVM. No correlation emerged with CO and E'/A'.

Conclusion

The sFlt-1/PlGF ratio correlates with maternal hemodynamic parameters, indices of cardiovascular maladaptation in pregnancy.

7.7| The 'no man's land' between late IUGR and AGA fetuses: the constitutionally small fetus

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Objective

Stunted child growth based on biometric assessment of height vs age is a common topic paediatrics as a measure of poor nutrition and unfavourable environment. In prenatal medicine, late IUGR has a similar pivotal role in research and clinical protocols. Unfortunately, confusion still exists on diagnostic criteria. Biometry alone is not considered by some a sufficient criterion to diagnose late IUGR fetuses and functional criteria are required by some or poor neonatal outcomes are advocated by others. We hypothesize that small fetuses with normal functional Doppler indices could in fact be undernourished in utero and, as such, be considered IUGR or stunted fetuses and not "constitutionally small fetuses".

Method

We recruited consecutive cases of fetuses ≥34.6 weeks of gestation with an abdominal circumference (AC) below the 10th centile or with a growth reduction of >40th centiles from mid-trimester biometry, with normal Uterine Doppler PI, normal Umbilical PI, normal Middle Cerebral PI and normal computerized CTG. Patients demographic and perinatal outcome were recorded. Uterine artery and umbilical artery blood flow volume was measured at recruitment on the same occasion of biometric and Doppler velocimetric data.

Results

Fifty-six cases met the inclusion criteria. One case was excluded since birthweight was >10th centile for local standards. Absolute Uterine blood flow volume was highly significantly lower than controls (fig 1). Uterine flow volume per unit fetal weight was 126.7 ml/min/ kg (58.6–145.1) in controls and 81.1 ml/min/kg in SGA fetuses (44.4–115.0) p=0.03. Cesarean section rate was 27.3% among SGA cases. No major neonatal morbidity was recorded. The uterine nutritional supply was significantly reduced in these "constitutionally small fetuses". We could speculate that fetal growth was reduced to adapt to metabolism and growth to a poor nutritional environment, as such not trespassing the zone of fetal stress to meet the criteria of SGA with functional abnormalities or "late IUGR".

Conclusions

The uterine nutritional supply was significantly reduced in these "constitutionally small fetuses". We could speculate that fetal growth was reduced to adapt to metabolism and growth to a poor nutritional environment, as such not trespassing the zone of fetal stress to meet the criteria of SGA with functional abnormalities or "late IUGR".
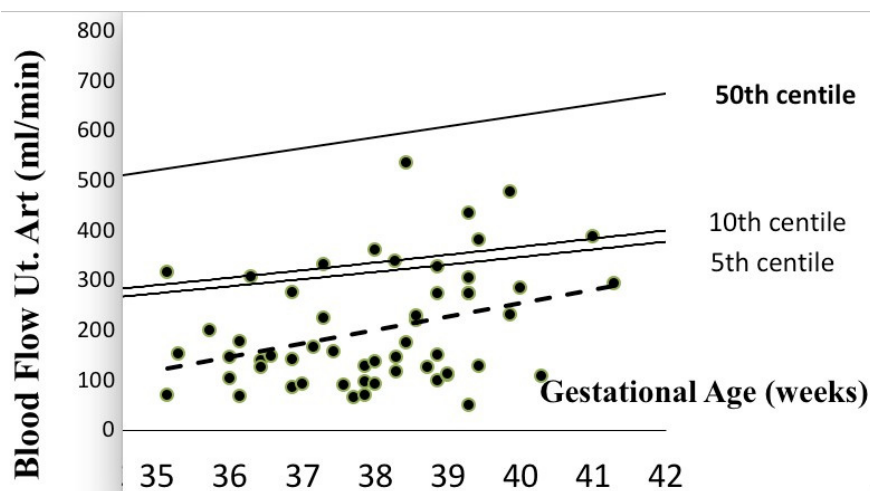
7.8 | Higher-risk of adverse perinatal outcome in adequate-for-gestational age fetuses with abnormal cerebro-placental ratio

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Objective

To assess the risk of adverse perinatal outcome (APO) in adequate-for-gestational-age (AGA) fetuses with an abnormal cerebro-placental ratio (CPR).

Method

We constructed a prospective cohort study of women with singleton pregnancies attending for routine third-trimester screening (>32 weeks). Fetal biometry and fetal-maternal Doppler ultrasound examinations were performed by certified sonographers, where both attending professionals and patients were blinded to the results. The CPR was calculated as a ratio of the middle cerebral artery to the umbilical artery pulsatility indices. APO was defined if occurring any of the following: pH<7.1, admission to the neonatal care unit, hypoglycemia, neonatal death, neonatal intraventricular hemorrhage III or IV, or emergency c-section due to abnormal cardiotocography monitoring. A logistic regression analysis was performed to assess the relationship between APO and CPR <5th centile. Also, a cumulative hazard analysis was performed according to normal (≥p5) and abnormal (<p5) CPR.

Results

A total of 1,463 fetuses were assessed, from these 3% (43/1,463) had a CPR below the 5th centile. APO occurred in 12% (176/1,467) of all pregnancies. The mean gestational age at scan was 34 (SD 1.8) weeks, with a mean estimated fetal weight centile (EFWc) of 63 (SD 23), and a mean CPR centile of 47.6 (SD 29). Unadjusted logistic regression showed an odds ratio of 2.61 (95% CI: 1.29-5.28; p=0.007) for APO in AGA fetuses. After adjusting for gestational age at scan, odds ratio remained significant (OR: 2.57; 95% CI: 1.27-5.21; p=0.008).

Cumulative hazard analysis showed an increased risk for APO in fetuses with abnormal CPR that was remarkably higher at 39 weeks of gestation (0.47; 95% CI: 0.35-0.64; vs. 1.08; 95% CI: 0.40-2.92; p=0.47).

Conclusion

Non-selected third trimester AGA fetuses with abnormal CPR are at higher risk for APO that significantly increases at 39 weeks of gestation.
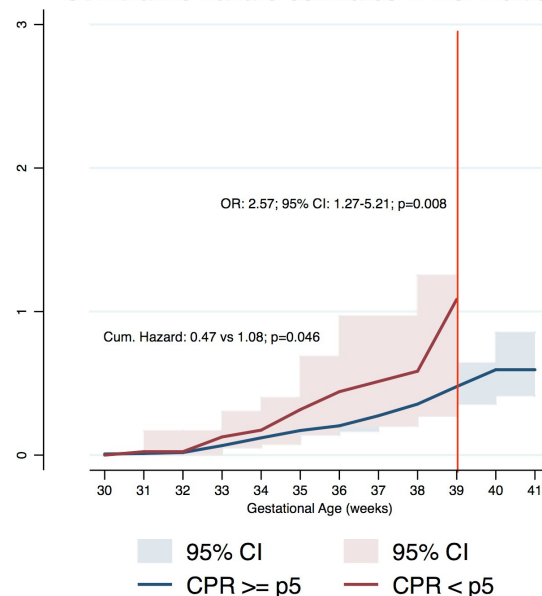

Fig 1. Cumulative hazard estimates in AGA fetuses according to normal and abnormal CPR.

7.9 | Comparison among cerebroplacental ratio, Intergrowth-21st standards, customized growth and local population references for the prediction of fetal compromise. Which is the best approach?

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Objective

To compare the abilities of the cerebroplacental ratio (CPR), intergrowth 21st standards (IG21), customized growth (CG) and local population references (LPR) for the prediction of intrapartum fetal compromise (IFC).

Method

This was a prospective study of 714 fetuses that underwent an ultrasound examination at 34-41 weeks and were delivered within 2 weeks interval. The CPR was converted into multiples of the median (MoM) and the estimated fetal weight (EFW) transformed into CG, IG21 and LPR centiles. IFC was defined as a composite of abnormal cardiotocogram, intrapartum pH requiring caesarean section, 5' Apgar score and admission to paediatric care units.

The accuracies of the CPR and the EFW centiles for the prediction of IFC were evaluated alone and in combination with other gestational characteristics using univariate and multivariate analysis.

Results

Individually, the CPR was the parameter that best predicted the existence of IFC (AUC=0.66). The multivariate analysis showed that the best prediction was again achieved with the CPR, alone or in combination with any of the EFW centiles, (AUC=0.74). No significant differences were seen between the different centile methods.

Conclusion

The best prediction of IFC is obtained with CPR. Evaluation of CPR should be encouraged in term and late-preterm fetuses.

7.10 | Is it possible to predict late antepartum stillbirth by means of cerebroplacental ratio and maternal characteristics?

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Objective

To examine the potential value of fetal ultrasound and maternal characteristics in the prediction of antepartum stillbirth after 32 weeks' gestation.

Method

This was a retrospective multicenter study in Spain. In 29 pregnancies umbilical artery pulsatility index (UA PI), middle cerebral artery pulsatility index (MCA PI), cerebroplacental ratio (CPR), estimated fetal weight (EFW) and maternal characteristics were recorded within 15 days prior to a stillbirth. The values of UA PI, MCA PI and CPR were converted into multiples of the normal median (MoM) for gestational age, and the EFW was expressed as percentile according to a Spanish reference range for gestational age. Data from the 29 pregnancies with stillbirths and 2298 control pregnancies resulting in livebirths were compared and multivariate logistic regression analysis was used to determine significant predictors of stillbirth.

Results

The only significant predictor of stillbirth was CPR (OR= 0.161, 95% confidence interval [CI] 0.035, 0.654; p=0.014); the area under the receiver operating characteristics curve was 0.663 (95% CI 0.545, 0.782) and the detection rate (DR) was 32.14% at a 10% false positive rate (FPR). In addition, when we included MCA and UA PI MoM instead of CPR, only MCA PI MoM was significant (OR= 0.104, 95% confidence interval [CI] 0.013, 0.735; p=0.029), with similar prediction abilities (AUC 0.645, DR 28.6%, FPR 10%).

Conclusion

The CPR and MCA PI are predictors of late stillbirth but the performance of screening is poor.

7.11 | Is labour induction the right choice in term IUGR fetuses?

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Objective

To investigate if labour induction for intrauterine growth restriction (IUGR: estimated fetal weight <5th centile) after 37 weeks improves maternal and neonatal outcomes.

Method

We collected retrospective data obtained from Children's Hospital V. Buzzi, from January 2017 to May 2018. We compared 64 neonates followed during pregnancy and induced for IUGR with 70 small for gestational age infants (SGA: birth weight <5th centile) diagnosed after birth, with spontaneous labour. Exclusion criteria included gestational age less than 37 weeks, breech presentation, stillbirth, maternal diseases and fetal anomaly.

Results

There were no statistically significant differences between the two groups for maternal age, body mass index (BMI), parity and gestational morbidities. Regarding neonatal outcomes, Apgar score < 7 at 1 and 5 min, birth weight (IUGR 2618 ± 525 vs SGA 2609 ± 273 g), NICU admission were comparable between the two groups.

We also compared data on neonatal oxygenation: mean pH (IUGR 7.28 ± 0.07 vs SGA 7.27 ± 0.08), pO2 (IUGR 24.9 ± 4.9 vs SGA 22.4 ± 7.1 mmHg) and pCO2 (IUGR 54.5 ± 8.2 vs SGA 43.7 ± 10.5 mmHg) were similar (p>0.05). The number of cesarean sections (CS) and vacuum extractions (VE) were also similar in the two groups (5 CS and 5 VE in IUGR vs 8 CS and 8 VE in SGA), but medical intervention (episiotomy, CS and VE) for fetal distress (abnormal fetal heart rate) was performed more frequently in fetal IUGR (16/64 = 25% in IUGR vs 15/70 = 21% in SGA).

Conclusion

Planned induction for IUGR after 37 weeks seems to be related with slightly more frequent medical intervention for fetal distress, without an improvement in neonatal outcomes; future randomized trials need to assess effectiveness of induction of delivery for this indication.

7.12 | Perinatal outcomes when electively inducing low fetal weight

PO

E Meler | **L Benitez** | **MF Paz** | **E Eixarch, F Figueras** | Fetal i+D Fetal Medicine Research Center, BCNatal - Barcelona Center for Maternal-Fetal and Neonatal Medicine (Hospital Clínic and Hospital Sant Joan de Deu), IDIBAPS, University of Barcelona, Spain

Objective

To evaluate whether fetal or maternal parameters could predict adverse perinatal outcomes when inducing low birth weight pregnancies.

Method

Retrospective study including all pregnancies with the diagnosis of SGA or IUGR from January 2015 to May 2018. We defined SGA as EFW<10th centile according customized local charts and IUGR when EFW<3rd centile or any abnormality in the Doppler evaluation. Firstly, according protocol, induction was performed with intracervical Foley catheter and 10 mg vaginal Dinoprostone and in a second period of time, with 10 mg vaginal Dinoprostone. In both cases, Oxitocin was initiated later when necessary. We defined adverse perinatal outcome (APO) as 5 min APGAR <7, UA pH <7.10 or neonate sent to ICU.

Results

169 singleton pregnancies were included. 38.5% (n=65) of the patients were multiparous. Among those latter, 27.7% (17/65) had a previous C-section. Mean maternal age was 32.6 years old (SD ± 5.6) and mean maternal BMI was 22.1 kg/m2 (SD ± 4.3) 68% (n=115) of the pregnancies had the diagnosis of IUGR (53 with EFW<3rd centile, 33 with Doppler impairment and 29 with both) and 32% (n=54) of SGA. At the induction, 89.3% of the patients had a Bishop score ≥4. 19.5% (33 out of 169) of all the pregnancies ended up in a C-section: half of the cases because fetal distress and half because failed induction or delivery arrest Any of the APO was present in 10% of the deliveries No statistically differences were found when comparing C-section rate or APO rate between SGA and IUGR groups (3.7% vs 13%, and 16.7% vs 20.9%, respectively). No differences were neither found when comparing the induction method in SGA and IUGR group.

Conclusion

Induction of delivery in low fetal weight is feasible with a 19.5% C-section and 10% of APO. Further analysis need to evaluate what parameters could predict APO or C-section.

Session 8 Fetal Growth in Twins

8.1 | The Italian multicentre study

Tullio Ghi | University of Parma, Italy

Twin gestations are at significantly higher risk of fetal growth restriction in comparison with singletons. Using fetal biometric charts customized for obstetrical and parental characteristics may facilitate accurate assessment of fetal growth. The construction of reference charts for gestation of fetal biometric parameters stratified by chorionicity and customized for obstetrical and parental characteristics has been the objective of a recent multicentric Italian study. For this aim fetal biometric measurements obtained from serial ultrasound examinations in uncomplicated twin pregnancies delivering after 36 weeks of gestation were collected by 19 Italian fetal medicine units under the auspices of the Società Italiana di Ecografia Ostetrica e Ginecologica. The measurements acquired in each fetus at each examination included biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL). Multilevel linear regression models were used to adjust for the serial ultrasonographic measurements obtained and the clustering of each fetus in twin pregnancy. The impact of maternal and paternal characteristics (height, weight, ethnicity), parity, fetal sex and mode of conception were also considered. Models for each parameter were stratified by fetal chorionicity and compared to previously constructed growth curves for singletons. The dataset included 1781 twin pregnancies (dichorionic 1289; monochorionic diamniotic 492) with 8923 ultrasonographic examination with a median of 5 (range 2-8) observations per pregnancy in dichorionic and 6 in (range 2-11) monochorionic pregnancies. Growth curves of twin pregnancies differed from those of singletons, and differences were more marked in monochorionic twins and during the third trimester. A significant influence of parental characteristics was found. In summary the growth of uncomplicated twin fetuses is influenced by parental variables and fetal gender and it is reduced in comparison with singletons starting from 26-28 weeks onwards. This reduction is more evident in monochorionic twins. The reference limits for gestation constructed in this study may provide an useful tool for a more accurate assessment of fetal growth in twin pregnancies.

8.2 | The NICHD fetal growth studies on dichorionic twin pairs

Katherine Laughon Grantz | Epidemiology Branch, Division of Intramural Population Health Research Eunice Kennedy Shriver National Institute of Child Health and Human Development National Institutes of Health, USA

Systematic evaluation and estimation of growth trajectories in twins require ultrasound measurements across gestation, performed in controlled clinical settings. Until recently, there were few such data for contemporary populations. This presentation will review findings from the NICHD Fetal Growth Studies – Twins whose objective was to empirically define the trajectory of fetal growth in dichorionic twins and to compare the fetal growth trajectories for dichorionic twins with those based on a growth standard developed by our group for singletons. The 50th percentile abdominal circumference and estimated fetal weight trajectories of twin fetuses diverged significantly beginning at 32 weeks. There were no differences in head circumference or femur length. The mean head circumference/abdominal circumference ratio was progressively larger for twins compared with singletons beginning at 33 weeks, indicating a comparatively asymmetric growth pattern.

In summary, the comparatively asymmetric growth pattern in twin gestations, initially evident at 32 weeks, is consistent with the concept that the intrauterine environment becomes constrained in its ability to sustain growth in twin fetuses. The clinical challenge is to differentiate small-for-gestational-age (SGA), defined as below the 10th percentile, associated with the normal adaptive process in multiple gestations from fetal growth restriction that is associated with increased morbidity and mortality. Future studies with long term follow up are needed to determine whether dichorionic twin fetuses in otherwise uncomplicated pregnancies that are classified as SGA using a singleton standard are at increased risk for short or long-term morbidity.

8.3 | Twin-specific doppler nomograms in uncomplicated monochorionic twins

M Pellegrino | D Casati | MM Lanna | S Faiola | MA Rustico | I Cetin

ASST Fatebenefratelli Sacco, V. Buzzi Hospital, University of Milan, Via Castelvetro, 32 Milano

PO

Objective
To construct nomograms for fetal Doppler parameters in uncomplicated monochorionic twins from 20 to 36 weeks of gestation.

Methods
Retrospective analysis of a cohort of MC twin pregnancies that underwent prenatal ultrasound surveillance and delivered at a single centre, Buzzi Children's Hospital, University of Milan, from 2010 to 2018. For each twin we longitudinally collected the following Doppler parameters: umbilical artery (UA) pulsatility index (PI), middle cerebral artery (MCA) PI and peak systolic velocity (PSV), cerebroplacental ratio (CPR) and ductus venosus (DV) PI. Ultrasound scans were performed every 2 weeks from the 20th week until delivery. We also recorded neonatal outcome and paediatric follow-up. Only cases with uncomplicated pre- and post-natal course were included.

Figure 1
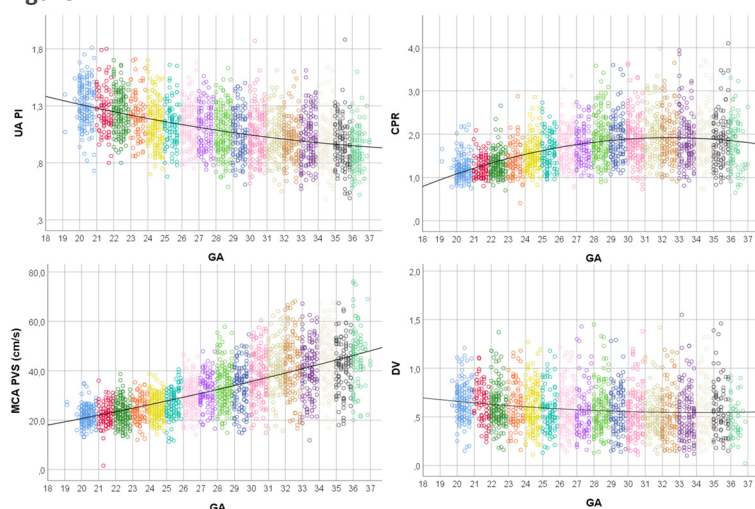
Results
In the study period, 1214 MC twin pregnancies were referred to our centre. We excluded 884 women who delivered in other hospitals and a further 178 cases for pregnancy complications (either fetal or maternal) or being lost at follow-up. We finally selected 152 twin pairs (304 fetuses) with a median of 8 (IQR 7-9) ultrasound scans performed from 20 to 36 weeks and a total of 10269 Doppler parameters analysed. Based on these data, we constructed nomograms for the 5 Doppler parameters under investigation (Fig 1 shows the nomograms for UA PI, CPR, MCA PSV and DV PI).

Conclusions
We present longitudinal reference ranges for UA PI, MCA PI, MCA PSV, CPR and DV PI derived from the largest cohort of strictly selected uncomplicated MC twins currently available to the best of our knowledge. Since the patho-physiology of fetal Doppler velocimetry is different in singleton and MC twin pregnancies, twin-specific reference values are of paramount importance in the surveillance of fetal wellbeing in MC gestations.

8.4 | Perinatal outcomes among twin with severe growth discordance more than 30% in a 7-year retrospective cohort

PO

Carman Wing Sze Lai

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Objective
To examine the association between difference in growth discordance and perinatal outcomes.

Methods
We have retrospectively reviewed all cases of twin pregnancies with growth discordant >=30% from 2012 till May 2018 in our unit.

Results
There were a total of 809 twin pregnancies (1618 individual twins) in the study period. We have excluded 11 cases with single twin demise and fetal reduction, which were not related to discordant growth. There were 272 babies with growth discordance more than 20%. 188 (69%), 60 (22%) and 24 (9%) babies had growth discordance 20-29%, 30-39% and >=40% respectively with their cotwin. Comparing discordant group of 30-39% and >=40%, the smaller twin in >=40% group had significantly higher risk of NICU admission (66.7% vs 91.7%) (p=0.031). There is no significant difference in the risk of discordant anomaly between discordant group of 30-39% and >=40% (20% vs 25%, p=0.637). Comparing types of twins with growth discordance >=30%, significantly more of MCDA twin had Apgar score <7 at 1 minute vs DCDA twin for both smaller cotwin (55.6% vs 30.4%, p=0.007) and bigger cotwin (38.9% vs 13%, p=0.013). There is significant more discordant anomaly in smaller twin in DCDA twin compared to MCDA twin (30.4% vs 5.6%, p=0.043) There are significantly more bigger cotwin of MCDA requiring NICU admission compared to DCDA twin (61.1% vs 21.7%, p=0.026).

Conclusion
Twins with severe discordant growth are associated with high risk of preterm delivery and perinatal complications. More severe growth discordance is associated with higher risk of morbidity of smaller cotwin. Monochorionicity is associated with worse neonatal outcomes compared. For growth discordance >=30%, DCDA twin is associated with a high risk of discordant anomaly. Hence, detailed morphology and discussion of invasive tests to exclude fetal anomaly would be important in such cases.

8.5 | Monochorionic twin pregnancies complicated with twin-twin transfusion syndrome and selective growth restriction of donor twin

Mariano Lanna | Stefano Faiola | Daniela Casati | Alice Turri | Irene Cetin | Maria Angela Rustico |
Fetal Therapy Unit "U. Nicolini" Ospedale Vittore Buzzi- ASST FBF Sacco, Università di Milano, MI Italy

Objective

To evaluate perinatal outcome of monochorionic (MC) twin pregnancies complicated with twin-twin transfusion syndrome (TTTS) and selective growth restriction (sIUGR) of the donor twin in a large series treated at a single center.

Methods

Retrospective analysis (2004-2017) of a consecutive series of MC twin pregnancies complicated both with TTTS and sIUGR of the donor twin, and treated with endoscopic laser coagulation of placental vessels performed with selective or Solomon technique. TTTS was diagnosed according to Quintero stages. The diagnosis of donor IUGR was made when the estimated fetal weight (EFW) was < 10th percentile, or when the EFW difference was ≥ 25%. Subsequent to laser treatment, ultrasound scan was performed after 24 and 48 hours, followed by weekly surveillance until delivery By cesarean section. For each case, obstetrical and perinatal outcome were recorded.

Results

A total of 444 TTTS cases were treated during the study period, and 112 (25%), donor twins had a growth restriction. Overall, intrauterine demise (IUFD) of the donor twin occurred within one week of the procedure in 86/444 cases (19%). The IUFD rate in non-IUGR donor twins was 9% (30/332), lower than in IUGR donors, where the IUFD rate was 50% (56/112 cases) , p 0,005. The neonatal death (NND) rate was 7% with an overall survival rate of 70%; however, in the IUGR donor sub-group, the NND rate was 10% (11/112 cases), with an overall survival rate of 40%, p 0,005.

Conclusion

Laser treatment for TTTS has a higher risk of adverse outcome when the donor twin also has growth restriction.

8.6 | Perinatal outcome in monochorionic twin pregnancies complicated with selective intrauterine growth restriction

Mariano Lanna | Stefano Faiola | Daniela Casati | Marcella Pellegrino | Irene Cetin | Maria Angela Rustico |
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Objective

To analyze perinatal outcome of a consecutive series of monochorionic (MC) twin pregnancies complicated with selective intrauterine growth restriction (sIUGR).

Methods

Retrospective analysis of all MC pregnancies complicated with sIUGR (2007-2017). Each pregnancy was managed with weekly ultrasound. Pregnancies were divided into groups according to umbilical artery (UA) Doppler pattern at first examination: Type I (flow persistently positive), type IIA (flow persistently absent) or IIR (persistently reversed), or type III (intermittent pattern). Changes in UA Doppler pattern were recorded. In cases with signs of imminent death before viability, feticide of sIUGR twin by bipolar cord coagulation (BCC) was an option. Data on obstetrical and perinatal outcome as neonatal death (NND) were collected.

Results

Outcome	Type I n= 156	Type IIA n= 57	Type 2R n= 30	Type 3 n= 57	Total n=300	p
Double IUFD	4 (2)	7 (12)	5 (17)	1 (2)	17 (6)	0,001
IUGR IUFD	2 (1)	5 (9)	4 (13)	2 (3)	13 (4)	0,001
BCC of IUGR	3 (2)	11 (19)	8 (26)	2 (3)	24 (8)	< 0,001
Large twin loss after BCC	0 (0)	4 (7)	0 (0)	0 (0)	4 (1)	
TOP	2 (1)	3 (5)	0 (0)	1 (2)	6 (2)	
Miscarriage	2 (1)	0 (0)	0 (0)	0 (0)	2 (1)	
GA at delivery	33 (31-36)	30(27-33)	30 (27-33)	32 (29-34)	32 (27-36)	
NND Large twin	4 (2)	3 (5)	2 (6)	4 (7)	13 (4)	0,05
NND IUGR twin	12 (8)	6 (10)	7 (34)	5 (9)	30 (10)	0,01
Overall survival Large twin	144 (92)	40 (70)	23 (77)	51 (89)	258 (86)	< 0,001
Overall survival IUGR twin	131 (84)	25 (44)	6 (20)	46 (81)	208 (69)	<0,001
Intact survival Large twin	141 (90)	40 (70)	23 (77)	50 (88)	254 (85)	0,003
Intact survival IUGR twin	125 (80)	23 (40)	5 (17)	43 (75)	196 (65)	< 0,001

Conclusion

The analysis of this large cohort from a single center confirms that Type I sIUGR has a good prognosis, and that Type IIR cases have the highest risk of adverse outcome. Unlike in the original series, in this series Type III cases showed a good perinatal survival rate, with no significant incidence of cerebral injury in either the large or the IUGR twin.

Session 10 Therapies for placental insufficiency - The EVERREST Studies

10.1 | Scientific rationale and aims of the consortium

Anna David | Institute for Women's Health, University College London, UK

Fetal growth restriction (FGR) is a major global obstetric problem affecting up to 8% of all pregnancies. Reduced uterine blood flow plays a central pathophysiological role. Using normal sheep pregnancy, we previously demonstrated that local VEGF gene transfer to the uteroplacental circulation using adenovirus (Ad) vectors increases uterine blood flow, attenuates uterine artery constriction and increases angiogenesis. Maternal or fetal haemodynamics were unchanged; the vector did not spread to the fetus. In FGR sheep where reduced uterine blood flow mid-gestation correlates with smaller fetal size, maternal uterine artery Ad.VEGF gene transfer improves fetal growth velocity compared to control treated or untreated FGR ewes. Treated fetuses have reduced "brain-sparing". These results have been replicated in the FGR pregnant guinea pig. This is proof of principle that VEGF local gene therapy can safely improve fetal growth in severe FGR. The EVERREST consortium is an EC FP7 funded Innovation for Health project that aimed to carry out the first trial of maternal growth factor therapy in pregnant women affected by severe early onset FGR, using interventional radiology to delivery Ad.VEGF into the uterine artery. During the project, the Ad.VEGF vector has been optimised and manufactured to GMP. Reproductive toxicology studies have been conducted in the human placenta ex vivo and in the pregnant rabbit. The consortium considered bioethical, legal and regulatory issues of a maternal gene therapy trial in discussion with stakeholders and patients. We have conducted an observational study of severe early onset FGR from maternal diagnosis through to two year neonatal outcomes, leading us to develop predictive tests of prognosis, and to refine our clinical trial inclusion and exclusion criteria. The consortium achieved orphan disease designation for placental insufficiency and is about to apply for ethical and regulatory approval for the definitive clinical trial.

10.2 | Ethical issues in a trial of maternal gene therapy

Rebecca Spencer | Institute for Women's Health, University College London, UK

Objective
To evaluate the ethical and social acceptability of a phase I trial of maternal uterine artery vascular endothelial growth factor gene therapy to treat severe early-onset fetal growth restriction (FGR) in pregnant women.

Method
We conducted a literature review on the ethical and legal issues of highly experimental treatments in pregnant women. Semi-structured and qualitative interviews were conducted in European countries with key stakeholders (disability groups, professional bodies and groups supporting families affected by pregnancy loss and FGR, n=34) and with women/couples who have experienced pregnancies affected by severe early-onset FGR (n=24). Input was also provided by our Independent Ethical Advisory Committee (IEAC) and a Patient and Public Involvement Advisory Group (PPIAG).

Results
Key issues raised by the literature review and discussed in the interviews were whether it is ethical to treat a pregnant woman with a potentially risky intervention from which the fetus rather than the woman will benefit, and whether it is ethical to treat this condition of the unborn who may otherwise have died but with the treatment may survive with a serious disability. Important ethical considerations raised by the IEAC and PPIAG for the conduct of the trial included informed consent and therapeutic misconception. The literature review concluded that there was no ethical or legal objection to the intervention nor to a trial of this intervention. Overall, stakeholders and women/couples viewed the proposed trial in positive terms. Women were generally interested in participating in clinical trials where these conferred a potential benefit to their unborn child. The risk of disability of the premature child was a concern but not considered a bar to conducting a clinical trial.

Conclusion
Maternal gene therapy to treat severe early-onset FGR appears to be ethically and socially acceptable but ethical considerations must be central to trial design.

Understanding early onset FGR: The EVERREST Prospective study

10.3 | Outcomes of early onset FGR: the fetus

SO

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Objective
The EVERREST prospective study is aiming to define the clinical and biological characteristics of pregnancies affected by severe early onset fetal growth restriction (FGR) so as to refine the inclusion and exclusion criteria for a clinical trial of a novel maternal adenovirus gene therapy.

Method
The study is conducted in four Fetal Medicine centres in Europe. Women were recruited whose fetus had an estimated fetal weight (EFW) < 3rd centile and <600g between 20+0 and 26+6 weeks gestation.

Results
From March 2014 to August 2018 we have recruit-ed 114 participants, and analysed pregnancy and outcome data of 93 women. In 26 cases (28%) there was a perinatal loss, of which in 21 cases (23%) the fetus died in utero before reaching an EFW of around 500g at which delivery could be considered. Median gestational age at intrauterine death was 25+4 weeks (22+2 - 29+0 weeks). 5 partici- pants decided to terminate the pregnancy. We had 67 live deliveries, 47 (70%) of those delivered before 34 weeks of gestation. Indications to expedite delivery were fetal in 48 (72%) cases, mainly due to worsening Doppler studies. Most babies (76%) were delivered via caesarean section.

Conclusions
In our case series, we observed a high rate of perinatal loss and preterm birth. Worsening fetal Doppler studies and/or pre-eclampsia indicated a need for preterm delivery. Despite the early diagnosis of FGR, a few women in our cohort delivered at term, as their fetus continued to grow and did not develop abnormal ultrasound features.

10.4 | Early onset FGR - baseline medical & obstetric characteristics: 6 year prospective study

SO

Francesc Figueras | Martinez RJ | Spencer R | Maksym K | Dyer J David A | on behalf of the EVERREST consortium
BCNatal, Hospital Clinic and Hospital Sant Joan de Deu, University of Barcelona, CIBERER & IDIBAPS, Barcelona, Spain. Institute for Women's Health, University College London, London, UK. Department of Clinical Sciences Lund, Obstetrics and Gynecology, Skane University Hospital, Lund University, Lund, Sweden. University Medical Centre Hamburg-Eppendorf, Hamburg, Germany.

Objective
To assess the baseline medical and obstetric history of pregnant women complicated with a severe early-onset growth-restricted fetus (eFGR).

Method
We conducted a multicenter six-year prospective cohort study which included women with a singleton fetus and an estimated fetal weight <600 grs and <3rd centile for gestational age as defined by local criteria, between 20 and 20+6 weeks based on ultrasound and/or last menstrual period. Women under 18 years, abnormal karyotype, fetal structural abnormalities, indication for immediate delivery, maternal HIV, hepatitis B or C infection, or premature-preterm rupture of membranes, were excluded. A descriptive analysis was conducted and results were presented as tables and graphs.

Results
A total of 112 fetuses were diagnosed with severe early-onset fetal growth restriction and therefore were included in this study. Seventy-two percent of the participants were enrolled at University college London, thirteen percent were from Hospital Clinic of Barcelona, while nine percent were from Hamburg-Eppendorf University, and eight percent came from Lund University. The mean maternal age was 33.8 (SD 6.5) years. Mean maternal weight was 72 (SD 18.7) kg, and mean height was 164 (SD 7) cm. From the 112 enrolled patients, 61% (68/112) were of white-European ethnicity, followed by a 9% (10/112) of black people. Smoking was present in 6% (7/112) of the total population. Forty-six women (41%) had a relevant medical history.

Of these, the most common condition was hypothyroidism accounting for a 24% (11/46) of this population, followed by 22% (10/46) of women with chronic hypertension requiring medication. Of the family history, the two most common features were: having sibling with chronic hypertension (11%; 5/46), and family history of diabetes (9%; 4/46). Forty-nine women (44%) were parous. From these, 59% (29/49) had at least one live birth, 31% (15/49) had a previous miscarriage, 12% (6/49) had at least one small-for-gestational-age baby, and 10% (5/49) had a fetal-growth-restricted baby. Only one woman had a previous stillbirth (2%), and two were diagnosed with severe preeclampsia in any previous pregnancy (4%).

Conclusions
Nulliparity, hypothyroidism, and chronic hypertension are the most common relevant medical antecedents affecting women diagnosed as eFGR, while family history of chronic hypertension if the most common family background.

Figure 1
Characteristics of women included in the study.
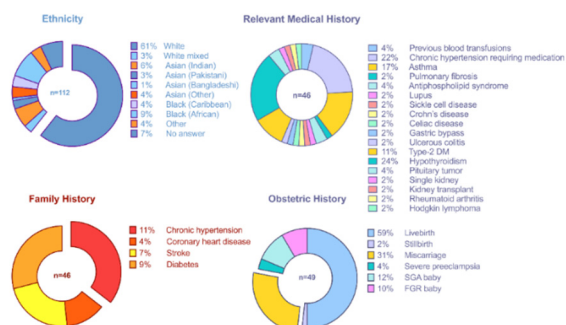
10.5 | Outcomes of early onset FGR: the neonate at 12 months

Ingran Lingam | Okell J | Buquis G | Spencer R | Maksym K | Peebles DM | Marlow N | David AL | Huertas-Ceballos A
University College London, United Kingdom

Objective

To characterise short-term outcomes of preterm infants born following pregnancies complicated by severe early-onset fetal growth restriction (FGR).

Method

Pregnant women with severe early FGR (EFW< 3rd centile and < 600g, 20+0-26+6 gestational age, GA) were recruited in the EVERREST study at University College London Hospital (NCT02097667). Short-term outcomes of surviving infants born < 34 weeks of GA (n=22) were compared to control infants with birthweight appropriate for GA (n=44), matched 1:2 for GA, gender and hospital of birth. Infants with congenital abnormalities, twin deliveries and those born outside the UCLH neonatal unit were excluded.

Results

Infants exposed to FGR had a more prolonged hospital stay (p=0.007), protracted invasive and non-invasive ventilatory requirement (p=0.01) and longer time to establish full enteral feeds (p<0.001). There was also a trend towards increased severity of chronic lung disease (p=0.06) among the FGR cohort. There was no significant difference in survival, necrotizing enterocolitis or culture-proven sepsis between study groups.

Conclusion

Fetal growth restriction conveys significant risks of prolonged respiratory support, difficulties in establishing feeds and longer hospital admission compared to age and gender matched control preterm infants. These findings may better inform the antenatal counselling of pregnancies complicated by FGR.

10.6 | Pregnant women's experiences and perceptions of study participation

Anna David | Merryl E Harvey[1], Jade Dyer[2], Rebecca Spencer[2] | [1]. Faculty of Health, Education and Life Sciences, Birmingham City University, Birmingham; [2] Institute for Women's Health, University College London, London, UK

Objective

The EVERREST Prospective Study is a multicentre observational cohort study of pregnancies affected by severe early-onset fetal growth restriction (FGR): estimated fetal weight <3rd centile, <600g, 20+0-26+6 weeks of pregnancy, no known chromosomal, structural or infective cause. We explored the experiences and perceptions of pregnant women participating in research during a pregnancy affected by severe early onset FGR.

Method

This was a retrospective descriptive qualitative interview study of women participating in the EVERREST Prospective Study. Audio-recorded semi-structured telephone interviews were conducted with a purposive sample of 12 women, >1 year after delivery of their baby. Two pregnancies had ended in stillbirth and one in neonatal death, reflecting the EVERREST outcomes. Participants gave informed consent, were 16 years or older and were interviewed in English using a topic guide to ensure a consistent approach. Questions focused on pregnancy experiences, involvement with the EVERREST study and potential involvement in future research. Recordings were transcribed verbatim for thematic analysis using NVivo10.

Results

Four broad themes were identified; 'before joining the EVERREST Prospective Study', 'participating in research', 'information and support' and 'looking back and looking forwards'. Each broad theme incorporated several subthemes. All participants recalled their reaction to being told their baby was smaller than expected. The way this news was given had a lasting impact. A range of benefits of participation in the EVERREST Prospective Study were described and the participants were positive about the way it was conducted. As a consequence, they were receptive to participating in future research. However, the findings suggest that research teams should be sensitive when approaching families at a difficult time or when they are already participating in other research.

Conclusion

This study highlights the willingness of pregnant women to participate in research and identifies strategies for researchers to engage participants.4444

10.7 | Challenges in recruitment in studies of FGR

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Clinical researchers recruiting patients for studies on early-onset fetal growth restriction (FGR) face various challenges that can limit the number of enrolled cases. Severe FGR in extremely preterm pregnancy is a rare disease and the physicians primarily providing antenatal care to the pregnant women might recognize the FGR late or they might wait to refer the patient to the perinatal center first when they deem the fetus viable. Such late referrals might lead to a collision between the study protocol and the clinical management guidelines that suggest immediate delivery either on maternal or fetal indication. Furthermore, there might be factors fulfilling exclusion criteria or the enrollment can be prevented by practical problems. We will exemplify the challenges in recruitment by presenting the experience from two EVERREST consortium members participating in the EVERREST Prospective Study – Department of Obstetrics and Gynecology at Lund University, Sweden and Department of Obstetrics and Fetal Medicine, Hamburg-Eppendorf, Germany.

Both departments are tertiary perinatal referral centers with expertise in management of early-onset FGR. During 3 years of the study, the Lund and Hamburg centers registered 28 and 27 patients, respectively, that fulfilled the inclusion criteria (live singleton fetus, estimated fetal weight <600g and <3rd centile for gestational age; gestational age at diagnosis 20+0-26+6 weeks). In Lund, 8 (29%) patients were recruited. The corresponding figure for Hamburg was 9 (33%). The reasons for exclusion were similar in the two centers and included immediate delivery on fetal or maternal indication, fetal abnormal karyotype or structural malformation, or maternal infection. Other causes of non-enrollment were lack of capacity to give informed consent, language barrier, or that the patient declined to participate. Some of the problems might have been overcome by better staffing, access to interpreters or by improved information. Nevertheless, recruitment to studies on early-onset FGR, especially to randomized trials, will remain a challenge.

10.8 | Reproductive toxicology studies: human placenta and pre-clinical rabbit

Heikura T [2] **| Dauzat C** [1] **| Bansard C** [1] **| Nguyen A** [1] **| Bentz S** [1] **| Rossi CA** [2,3] **| Spezia F** [1] **| Forster R** [1] **| Lees M** [3] **| Ylä-Herttuala Y** [2] **| David AL** [3] **on behalf of the EVERREST consortium** | [1]CiToxLAB, 27005 Evreux, France | [2]University of Eastern Finland, Kuopio, Finland | [3]UCL Institute for Women's Health, London, UK

Objective
The EVERREST consortium is translating uterine artery (UtA) injection of Adenovirus vector (Ad) encoding the pre-processed Vascular Endothelial Growth Factor-D isoform (Ad.VEGF-DΔNΔC) into the clinic to treat severe early onset fetal growth restriction. Using the pregnant rabbit which has a similar placentation to third trimester human placenta, we studied the effect of high and low dose administration of Ad.VEGF-DΔNΔC into the UtAs of dams and their offspring via interventional radiology.

Methods
Time-mated female primigravid New Zealand white rabbits underwent X-ray guided serial catheteri- sation and injection of both UtAs under general anaesthesia on day 19 postconception. Dams re- ceived an intravascular injection (0.8mL) of either Ad.VEGF-DΔNΔC vector (high or low dose n=26 per group) or formulation buffer (n=24).Dams and fetuses underwent post-mortem analysis at 3 or 10 days post-op (n=4 per time point, per group) to study fetal survival and biodistribution.

The remaining dams were allowed to deliver and at either 28 days post-op (day 16 postnatal) or day 90 post-op (day 79 postnatal) the pups underwent post-mortem analysis for toxicity, pup survival and biodistribution.

Results
Dam post-op survival was good; mortality of 5 dams was incidental (during or following surgery; miscarriages). The livebirth and weaning indices were similar in the 3 groups. There was no vector detectable by RT-PCR in a broad range of fetal or pup tissues at any time point. As expect- ed, vector was detected in falling concentrations in a few maternal tissues as post-op days advanced.

Conclusions
UtA injection of high or low dose Ad.VEGF-DΔNΔC vector using interventional radiology techniques does not appear to adversely affect rabbit dam or pup survival. There is no evidence of vector spread across the placenta to the pups. These results are encouraging for clinical translation.

Developing and Planning the EVERREST clinical trial

SO

10.9 | Developing the ATIMP (Advanced Therapy Investigational Medicinal Product) for EVERREST

Tommi Heikura | David AL, Ylä-Herttuala S, on behalf of the EVERREST consortium

Objective
The development of the Adenovirus vector (Ad) encoding the pre-processed Vascular Endothelial Growth Factor-D isoform (Ad.VEGF-DΔNΔC) for EVERREST consortium to be translated for uterine artery (UtA) injection into the clinic to treat severe early onset fetal growth restriction.

Method
DNA sequence encoding VEGF-DΔNΔC gene was cloned in the shuttle vector and co-transfected with adenovirus backbone vector to produce recombinant adenovirus by homologous recombination. Positive plaques were isolated, tested by PCR and expanded in the HEK293 cells. Recombinant viruses went through series of release assays before tested for functionality in vitro and in vivo.

Results
Produced vectors were tested to be sterile, free of replication competent adenoviruses (RCA), and they produced VEGF-DΔNΔC protein in high quantities in both cell culture and animal models, as measured from cell culture media and animal serum, respectively. In addition, various methods showed the functionality of the produced protein.

Conclusions
Ad.VEGF-DΔNΔC vector increased endothelial cell proliferation, blood vessel dilatation and perfusion in transdused tissues. These results were encouraging for further testing in preclinical models and clinical translation.

SO

10.10 | Manufacturing the EVERREST IMP (Investigational Medicinal Product)

Robert Shaw | Minna Pollen, Anna-Kaisa Lehtivarjo, Minna Karhinen | Trizell Ltd, UK

Objective
The EVERREST Advanced Therapy Investigational Medicinal Product (ATIMP) is an Adenovirus vector (Ad) encoding the pre-processed Vascular Endothelial Growth Factor-D isoform (Ad.VEGF-DΔNΔC). It is being specifically manufactured for the consortium reproductive toxicology studies and the clinical trial, as scientific advice from the UK Regulator (Medicines and Healthcare Products Regulatory Authority, MHRA) has advised minor modifications to the originally developed ATIMP to enable clinical translation. The ATIMP will be used in pregnant women for the first time to treat severe early onset fetal growth restriction (FGR). Optimal manufacture and testing of the materials is critical to the success of the programme.

Method
The preparation of the pre-clinical and clinical material for the EVERREST studies has been undertaken in the commercial premises of FinVector Oy, a world leader in the research and development of viral-based gene therapy products, with state-of-the-art facilities and a highly experienced scientific team working in the gene therapy market. The company are authorised under the European Medicines Agency (EMA) for the production of gene therapy products for clinical and commercial supply. The process includes thawing and expansion of HEK293 master cell bank, infection of expanded cells with master viral seed stock (MVSS), preparation of bulk harvest, cell lysis and preparation of Crude Viral Lysate (CVL), further purification and formulation of a purified CVL to prepare purified sub-batch, followed by pooling and filling, inspection, labelling and secondary packaging.

Results & Conclusion
The EVERREST Drug Product has been produced according to GMP manufacturing guidelines and is ready for submission for clinical trial application.

SO 10.11 | FGR as an orphan disease

Anna David | **R Spencer[1]** | **C Rossi[1]** | **M Lees[1]** | **D Peebles[1]** | **J Martin[1]** | **P Brocklehurst[2]** | **S R. Hansson[4]** | **K Hecher[5]** | **K Marsal[4]** | **F Figueras[6]** | **E Gratacos[6]** | [1]. University College London, UK. [2]. University of Birmingham, UK. [4]. Lund University and Skane University Hospital, Lund, Sweden. [5]. University Medical Centre Hamburg-Eppendorf, Germany [6]. University of Barcelona, Spain

Objective
Orphan drug legislation aims to encourage the development of medicines for rare conditions that might otherwise be financially unviable. For orphan designation the disease must be life-threatening or chronically debilitating, the prevalence of the condition in the European Union must be not more than 5 in 10,000 and the medicine under development must be of significant benefit to those affected by the condition. We determined whether a novel therapy for placental insufficiency could achieve orphan drug status as part of an application for European Medicines Agency (EMA) orphan designation.

Method
We estimated the annual incidence of placental insufficiency, defined as an estimated fetal weight below the 10th centile in the presence of abnormal umbilical artery Doppler velocimetry, per 10,000 European Union (EU) population. We used incidence estimation based on literature review and published national and EU statistics. Data were drawn from published literature, including national and international guidelines, international consensus statements, cohort studies and randomised controlled trials, and published national and EU statistics, including birth rates and stillbirth rates. Rare disease databases were also searched.

Results
The proportion of affected pregnancies was estimated as 3.17% (95% CI 2.93% to 3.43%), using a weighted average of the results from two cohort studies. Using birth rates from 2012 and adjusting for a pregnancy loss rate of 1/100 gave an estimated annual incidence of 3.33 per 10,000 EU population (95% CI 3.07 to 3.60 per 10,000 EU population).

Conclusions
Maternal vascular endothelial growth factor gene therapy for placental insufficiency leading to fetal growth restriction was granted EMA orphan status in 2015 after we demonstrated that it is a rare, life-threatening or chronically debilitating and currently untreatable disease.

SO 10.12 | Inclusion and exclusion criteria and predicting outcome of early onset FGR

Rebecca Spencer | Institute for Women's Health, University College London, UK

Objective
To identify pregnancies with a sufficient risk of fetal and neonatal death to justify inclusion in a phase I trial of maternal growth factor gene therapy for early-onset fetal growth restriction (FGR).

Method
A prospective multicentre study of pregnancies with an estimated fetal weight <3rd centile and <600g between 20+0 and 26+6 weeks' gestation without a structural, chromosomal, or infective cause. Univariate and multivariable associations with fetal or neonatal death were explored using logistic regression and Area Under the Receiver Operating Characteristic Curve (AUC) for: umbilical (UmA) and uterine artery (UtA) pulsatility index (PI); abnormal fetal growth trajectory (AFGT: >10% worsening of weight deviation over 2 weeks); maternal serum concentration of placental growth factor (PlGF). Secondary outcomes included gestational age of livebirth or diagnosis of intrauterine fetal death (IUFD) and placental Maternal Vascular Malperfusion (MVM).

Results
Of 65 participants, 21 pregnancies (32%) ended in fetal or neonatal death. UmAPI >2SD above the mean, AFGT and PlGF showed capacity for predicting fetal or neonatal death (Table). Combining potential inclusion criteria increased specificity but at the expense of sensitivity and number of potentially eligible participants. Maternal serum PlGF concentration (natural log) showed a strong positive correlation with gestational age of livebirth or IUFD (r=0.82, p<0.00005) and was a better predictor of MVM than UmAPI z score (AUC 0.84, 95%CI 0.69-0.98 vs. AUC 0.57, 95%CI 0.36-0.78). UmAPI >2SD above the mean and UtAPI >95th centile were chosen as inclusion criteria. Pregnancies meeting these criteria ended in livebirth or IUFD at a median of 26+6 weeks' gestation (range 22+4-36+0) with 65% of liveborn babies suffering severe neonatal morbidity or neonatal death.

Conclusions
While ultrasound inclusion criteria can identify suitable participants for a phase I trial, maternal serum concentration of PlGF may have utility in trials of potential FGR therapies with proven safety profiles.

Table: Univariate prediction of fetal or neonatal death, expressed as Area Under the Receiver Operating Characteristic Curve (AUC), sensitivity and specificity. CI=confidence interval, PlGF=placental growth factor, SD=standard deviation, UmA=umbilical artery pulsatility index, UtAPI=uterine artery pulsatility index. Doppler velocimetry reference ranges = Schaffer & Staudach. 1997. *Doppler-Referenzkurven*

		Total (n=65)	Fetal or neonatal death (n=21)	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
UmAPI >2SD above mean	Yes	33	16 (48%)	0.69 (0.57 to 0.81)	76% (53 to 92%)	61% (46 to 76%)
	No	32	5 (16%)			
		(n=63)	(n=20)			
UtAPI >95th centile	Yes	50	17 (34%)	0.54 (0.44 to 0.64)	85% (62 to 97%)	23% (12 to 38%)
	No	13	3 (23%)			
		(n=57)	(n=16)			
Abnormal fetal growth trajectory	Yes	27	12 (44%)	0.69 (0.56 to 0.82)	75% (48 to 93%)	63% (47 to 78%)
	No	30	4 (13%)			
		(n=63)	(n=21)			
Maternal serum PlGF <35 pg/ml	Yes	31	16 (52%)	0.70 (0.58 to 0.82)	76% (53 to 92%)	64% (48 to 78%)
	No	32	5 (16%)			

10.13 | Developing standard maternal and fetal adverse event criteria for FGR clinical trials

Rebecca Spencer | Institute for Women's Health, University College London, UK

Objective

Clinical trials of maternal and fetal therapies face many research governance challenges. Adverse event (AE) monitoring is important for trial safety. Standard severity grading criteria are in place for hundreds of non-obstetric AEs, but AEs and their grading are poorly developed for clinical trials in pregnant women and their fetuses. We convened an international group of fetal therapy, obstetric, neonatal, and industry experts to develop maternal and fetal AE severity grading criteria.

Method

Existing severity grading criteria, national and international guidelines, and consensus statements were searched to identify definitions of key events and indicators of 'severe' and 'life-threatening' conditions relevant to maternal and fetal clinical trials. New AE definitions were defined through discussion and iterative review.

Results

Current severity grading criteria were inconsistent for maternal events and largely lacking for fetal events. Draft sets of maternal and fetal AE severity grading criteria were developed. To provide the clearest clinical trial safety data the consensus was that AE severity should be graded independently for the pregnant woman and the fetus. In addition, fetal AEs were defined as being diagnosable in utero with the potential to cause a detrimental effect in the fetus. Fetal AE terms were further modified through discussion with the Medical Dictionary for Regulatory Activities (MedDRA) and accepted to their terms list. The proposed maternal and fetal AE grading criteria were modified in light of feedback from patient support groups and are now undergoing an online Delphi process to achieve broader consensus.

Conclusions

Systematic and consistent maternal and fetal AE grading criteria will provide more meaningful understanding of safety and allow safety comparisons between trials.

10.14 | Regulatory Process – MHRA

Jade Dyer | EG Gemma Jones [1],Rebecca Spencer[2], Anna L David[2] |
[1]. Comprehensive Clinical Trials Unit, University College London. [2]. Institute for Women's Health, University College London, UK.

Objective

EVERREST is a complex first in woman trial using an adenovirus vector Advanced Therapy Investigational Medicinal Product (ATIMP) for pregnant women to treat severe early onset fetal growth restriction (FGR), which is a world first. Submission of a clinical trial application to the UK Regulator (Medicines and Healthcare Products Regulatory Authority, MHRA) is required for the EVERREST Clinical Trial.

Method

The team have approached the MHRA and European Medicines Agency (EMA) to seek advice at stages of the trial development in preparation for the clinical trial application. In addition to the complexity of this type of application, there are also challenges related to the target population (pregnant women) and the administration method of the ATIMP (interventional radiology guided intrauterine artery injection).

Results

Both the MHRA and the EMA have been supportive in their responses to the EVERREST team requests for advice. In the most recent advice (July 2018), the MHRA suggested how the team could adapt the trial design to account for the amount of Drug Product available. In addition, the MHRA provided constructive feedback to refine the trial inclusion criteria, and advice on clinical trials application, which the consortium are hoping to submit by December 2018. Due to the complex nature of the trial, the MHRA advised that the application will need additional review by the Clinical Trials, Biologicals and. Vaccines Expert Advisory Group of the Commission on Human Medicines.

Conclusions

The application for EVERREST clinical trial authorisation is a complex process. Keeping an open dialogue with the regulator throughout the design of the clinical trial and problems encountered regarding the Drug Product has helped the team to ensure that steps are not missed in the final application. It has also provided reassurance that such an application would not be out-right rejected by the UK Regulatory authority.

Session 11 Debate

O 11.1 Are we placing too much emphasis on fetal size?

Wessel Ganzevoort – Amsterdam UMC, NL**; Jason Gardosi -** Perinatal Institute, UK

Fetal growth restriction is an indicator of placental insufficiency and is strongly associated with adverse perinatal outcome. This debate is about whether too much emphasis is being placed on 'size' when developing strategies for risk assessment and prevention.

WG argues that the recent dominance in the medical literature about which reference charts to use, and dichotomization of fetal size at the 10th percentile, overlooks the fact there is not a single cut-off in any growth chart that acts as an absolute divider between high and low risk for adverse outcome. Thus, the collective goal of all researchers to identify, monitor and effectively manage growth-restricted fetuses is better served by replacing dichotomisation of normal versus abnormal fetal growth at the 10th percentile by interpretation of fetal size in context with other known parameters of fetal risk - all as continuous parameters. The use of prospective comprehensive datasets should facilitate better risk assessment for the individual fetus, to help direct effective and appropriate interventions.

JG's counter argument is that the debate about which growth standard to use was necessary and has been settled through evidence that size, and therefore growth, need customized limits to allow adjustment for constitutional variation, and to help distinguish between normal and abnormal growth. Implementation of a more precise standard has led to better detection of fetuses that are at risk due to growth restriction, improved application of additional investigations, enhanced clinical confidence in management including timely delivery, and ultimately increased prevention of adverse outcomes.

Session 12 Policies & Protocols: do they reflect the evidence?

K 12.1 Overview of international guidelines on fetal growth

Lesley McCowan | University of Auckland, Auckland, New Zealand

Objective
To summarise consensus and controversy between recently published National Guidelines on SGA or FGR.

Methods
Seven national guidelines were identified that were available in English.

Results
SGA is defined as birthweight <10th centile and the most common definition of FGR on ultrasound is estimated fetal weight (EFW) <10th centile (3 recommend population and 4 customised EFW). There is agreement about the importance of risk selection (7/7) and low dose aspirin for those with major risk factors (6/7). All recommend fundal height measurement in the third trimester, three recommend a customized chart, two McDonald's rule and one suggests anatomic landmarks or measurement. The majority (6/7) do not recommend routine third trimester ultrasound. Umbilical artery Doppler is universally advised in suspected SGA. There is inconsistency in the recommended frequency for scans after diagnosis of SGA/FGR (2-4 weekly) and 5/7 comment on the importance of including reduced growth velocity in assessment of FGR.

In late onset FGR (≥32 weeks') 4/7 recommend use of cerebral Doppler studies; recommended timing of delivery varies from 37-40 weeks'. There is universal agreement that corticosteroids should be administered before birth at <34 weeks, and general consensus on the use of magnesium sulphate for neuroprotection in early onset FGR <32 weeks. Most recommend using computerized CTG to time delivery in FGR <32 weeks. Gestation at delivery for FGR with absent and reversed end- diastolic velocity varies - 32 to ≥34 weeks and 30 to ≥34 weeks respectively.

Conclusion
Further convergence between guidelines could be achieved by incorporation of existing evidence and consensus statements. The utility of late third trimester ultrasound to prevent morbidity/mortality is a research priority. Prospective studies are needed to compare new international population ultrasound standards with those in current use.

3.1 | Are our SGA babies slipping through the net?

Fida Ali | Pallavi Karkhanis | Shalini Patni | University Hospitals Birmingham, Birmingham Heartlands Hospital. UK

Objective
Early antenatal detection and correct management of small for gestational age (SGA) fetuses during pregnancy helps improve perinatal outcomes and reduce stillbirth rates. The aim of this study was to determine antenatal detection rates of SGA fetuses at our unit with a focus on missed cases to improve detection and outcomes.

Methods
This was a retrospective study in a large NHS trust (10,000 deliveries/year). All SGA babies (birth weight <10th centile), over a three month period, were included. We use customised GROW charts and our protocol includes 2 scans at 28 and 34 weeks for all high risk pregnancies.

Results
198 SGA babies were identified (7.7% incidence). All cases were offered scans as per protocol. Our antenatal detection rate for SGA was 39%. Despite 2/3 having had at least two growth scans, 61% were not detected. 55% of missed cases had their last growth scan <36 weeks with an average interval to delivery of 22 days. 14% of undetected cases were low risk. 21% delivered preterm with an induction rate of 48%. 2/3 delivered vaginally. 39% required a neonatal unit admission due to prematurity, respiratory distress, suspected sepsis and jaundice. We had no cases of neonatal deaths or stillbirths in normally formed babies.

Conclusion
Our detection rates were well below national average (55.6%). The main reasons noted for 'missed' SGA cases was insufficient provision of growth scans and despite the challenges, we have recently established further funding for serial growth scans until delivery. We also advised further assessment of scan image quality for 'missed' cases as a possible contributor and performing continuous audits with dashboard display of detection rates.

3.2 | Screening Programme for Fetal Growth Restriction in Low Risk Population

JM Arraez, | E Mazarico | M Cantallops | M Serra | MD Gómez Roig | F Figueras
Hospital Sant Joan de Déu, BCNatal, Barcelona, Spain.

Objective
To determine the detection rate of a screening programme for fetal growth restriction in a low risk population.

Methods
A retrospective cohort was created of 14,816 consecutive babies born between 2013-2017, that had a routine third trimester ultrasound performed between 32-34 weeks. Newborns were classified as small for gestational age (SGA) if the birthweight was below the 10th centile according to local fetal customized standards.

Results
2008 babies were identified as SGA (13.55%). The detection rate of SGA was 36% (95%CI 33.9%-38.1%). While the detection rate for SGA born <37 weeks was 61% (95%CI 55.5%-66.3%), it was 31% (95%CI 28.9%-33.4%) for SGA born >37 weeks.

Conclusions
In unselected pregnancies, detection rate for SGA of 32-34 weeks scan is low, especially in newborns born after 37 weeks. Other strategies could be considered to increase the detection rate and it is needed the implementation of quality audits of ultrasound measurements.

3.3 | To evaluate GROW customised charts in the classification of term birthweight infants <2.5kg and their predictive value for neonatal care unit admission

S Delavari | J Aquilina | Royal London Hospital, NHS, London, UK

Objective
To evaluate customised birth weight centiles in term Low Birth Weight Pregnancies.

Methods
A retrospective cohort analysis of 572-singleton pregnancies, with infants' birth weight ≤2500 grams, without congenital malformations that were delivered between 37-42 weeks of gestational age from 01-Jan- 2013 to 31-Dec-2015 at Royal London Hospital were included. The LMS and GROW customised methods were used to construct birth weight centiles. Birth weight centiles in different ethnicities were compared. Sensitivity, specificity, PPV and NPV for both methods in prediction of NICU admission were calculated. The number of NICU admission was 30 (5.24%). LMS had a higher sensitivity in prediction of NICU admission in SGA (100% vs 86%) and severe SGA infants (90% vs 66%). GROW customised had a higher specificity in the prediction of NICU admission in SGA (22% vs 1%) and severe SGA infants (15% vs 58%). The probability of NICU admission in SGA infants identified by either of methods was similar. ROC curve indicated that neither GROW customised centile nor LMS could predict NICU admission in SGA infants (p<0.05).

Results
417 of the population was Asian (72.9%), of whom 379 (66.3%) were of Bangladeshi descent. By using LMS method, 100% of Caucasian infants and 99% of Asian infants were classified <10th centile. When GROW customisation was used 27.3% of Asian, 5.6% of African- Caribbean and 6% of Caucasian were reclassified ≥10th centile.

Conclusion
Using GROW customised charts significantly reduces the proportion of SGA infants primarily in the Asian population. Use of ethnicity and maternal characteristics to classify birth weight centiles would allow better detection of true SGA infants. Neither GROW customised charts nor LMS methods are effective in predicting NICU admission. If the infants were not SGA by either method, they were less likely to need NICU admission.

3.4 | Perinatal outcome and morbidity in small for gestational age newborns with and without prenatal diagnosis

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Fetal Medicine Unit, Obstetrics Service, Hospital Universitario Austral, Buenos Aires, Argentina.

Objective
To assess the influence of prenatal diagnosis (PD) on perinatal outcomes in a cohort of small for gestational age (SGA) newborns.

Methods
Retrospective study of SGA newborns from simple pregnancies, between October 2009 and February 2018 who had an ultrasound in the third trimester. We separated them in two groups. Group 1 (G1) with PD, and Group 2 (G2) without PD. Perinatal morbidity was assessed through a morbidity score, which included: Apgar at 5 minutes, NICU admission, neonatal complications, need for mechanical ventilation and parenteral nutrition.

Results
236 SGA newborns were included. 51.7% (n=122) were detected prenatally and 48.3% (n=114) were not. From G1, 22.1% (n=27) were born before 34w, and from the G2 4.4% (n=5). The gestational age (GA) at diagnosis was 28.0w (+ 0.87).The GA at birth was significantly lower in G1 (36.7w + 0.634 vs 38.4w +/- 0.36, p<0.01).

The last ultrasound evaluation was at 34.1w (+ 0.5) (G1: 33.8 + 0.7, G2: 34.7 + 0.5, p 0.124). The PI of the uterine arteries in the last evaluation was higher in G1 (1.04 +/-0.1 vs 0.88 +/- 0.7 p0.013). There were no significant differences in the cerebroplacental ratio (1.88 (+/- 0.1) vs 1.94 (+/- 0.1) p0.234). BW was significantly lower in G1 (2387g vs 2564g (p<0.001)) and this was correlated with higher NICU admission (42% G1 vs 14% G2 p<0.001) and higher perinatal morbidity (23% vs 7%, p<0.001).

Conclusion
Those fetuses in whom PD was possible, seem to constitute a subgroup of worse prognosis, although in this group the influence of gestational age as a risk factor for perinatal complications should be considered.

3.5 | Retrospective analysis of small for gestational age (SGA) babies at our health board following implementation of the Growth Assessment Protocol (GAP)

Nandini Halder | Manju Nair | Susan Jose | Dawn Apsee | Donna Evans | Margaret Birch |
Department of Obstetrics and Gynaecology, Abertawe Bro Morgannwg University Health Board, Wales, UK

Introduction
The Perinatal Institute for Maternal and Child Health in the United Kingdom has recommended the use of GAP to enable early identification and appropriate management of IUGR babies and thereby aim to reduce stillbirth. 125 out of 157 UK Health Boards that is 80% have implemented it as of 1st July 2018. Our Health Board which comprises of 2 consultant-led units and a stand-alone midwife-led-unit with a delivery of 5918 in 2015, implemented the GAP from July 2016 onwards.

Objective
We present a retrospective cohort study of SGA babies to determine if their management were compliant with GAP.

Method
We identified 93 SGA babies with birth weight less than the 10% centile born between February 2018 to March 2018 in our Health Board of whom 44 babies (39 term and 5 preterm born below 37 weeks gestation) have been reviewed and presented below.

Results
12 out of 44 SGA babies were identified by use of antenatal customised growth chart suggesting 27.27% true positives. Screening was done by SFH (symphysio- fundal height) alone in 18 cases. SFH and EFW (estimated fetal weight) were not accurately plotted in 14 cases of which 6 cases (13.6%) would have warranted a further growth scan had they been plotted correctly. All were livebirths in this cohort.

Conclusion
Small numbers in this study is a limitation but initial reduction in stillbirth rates from 4.67/1000 in 2015 to 3.5 /1000 births in 2016 suggests an initial improvement. Further training of practitioners including measurement of SFH and correct plotting is required given the findings of inaccurate plotting. A prospective study of use of customised growth chart is required to assess the sensitivity and specificity of the protocol.

3.6 | Screening for small-for-gestational-age fetuses in Denmark

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Objective
Small-for-gestational-age (SGA) fetuses have higher risk of adverse perinatal outcome and long-term consequences. Antenatal identification of SGA improves the outcome. Unfortunately, false diagnosis of SGA increases the risk of unnecessary obstetric interventions. In Denmark, the national screening program for SGA includes ultrasound estimates of foetal weight (EFW) on clinical indication only. If EFW ≤ -15% of expected for the gestational age, the fetus will be considered at risk of SGA. The aim of this study was to investigate the prevalence of SGA and the performance of the screening programme for SGA in Denmark.

Method
We included 2954 singleton pregnancies with date of delivery in 2015 based on CRL measurements at the 1st trimester ultrasound scan (US) performed at Aalborg University Hospital. SGA at birth was defined by BW ≤-22% (Marsal et.al., 1996). Pregnancies at risk of SGA were defined by EFW ≤-15%.

Results
At birth, the prevalence of SGA was 3.3 %. Of the 2954 pregnant women, 63.3 % had at least one ultrasound EFW. The sensitivity of SGA in the total population was 69.4 %, and the false-positive rate was 9.3 %. 21.4 % of the SGA babies never had an ultrasound EFW.

Conclusion
This study demonstrates a rather low performance of the Danish antenatal screening for SGA. The main limitations of the screening program are:
1. Inappropriate selection of women for ultrasound EFW
2. Inaccurate ultrasound estimates of fetal weight

3.7 | The rising number of growth scans and audit of screening for SGA in women with low PAPP-A

Blair Wilson[1] | Isobel Clegg[2] | Graham Tydeman[3] | [1]University of Edinburgh, Scotland, UK | [2,3]NHS Fife, Scotland, UK.

Background

Normal pregnant women in Scotland should be offered 2 scans: booking and Anomaly Scan. Increasing recommendations for scans may not be accompanied by extra resources. Low PAPP-A is one of the growing list of indications.

Objective

Using prospectively collected data over 14yrs, demonstrate trends in demands on scan department and compare with perinatal mortality figures in NHS Fife. Audit RCOG guidance for women with a low PAPP-A

Method

Total numbers, scans/ booker and indication for scan were compared with perinatal mortality data. Women with PAPP-A <0.4MoM over 1yr were audited against scans performed and success in identifying SGA.

Results

Since 2003, there was a rise from 3.5 to 4.5 scans/ booker representing an extra 3500 scans/yr with no reduction in perinatal mortality. Over 1yr, 99 women had PAPP-A <0.4. Of the recommended 3 growth scans, 78 had a 28 week; 92 a 32 week and 85 a 36 week scan. In none of these women, using AC or EFW, was fetal SGA identified, defined as <10th centile with customised EFW charts. However, there were 8 babies born with birthweights less than the 10th centile. The mean value of PAPP-A did not differ between groups subsequently found to be SGA or not (0.28 vs 0.32 MoM p=0.062)

Conclusions

Even 15yrs ago, the average number of scans/ women exceeded two but in that time scans for fetal growth have more than doubled with no change in perinatal mortality although, of course, a crude indicator of health. RCOG guidelines are largely being followed however the extra 255 scans for low PAPP-A failed to identify any of 8 SGA fetuses. The association of SGA with PAPP-A is not doubted but before implementation, guidance perhaps needs to consider the impact on departments and research undertaken to demonstrate that following guidance achieves its aims.
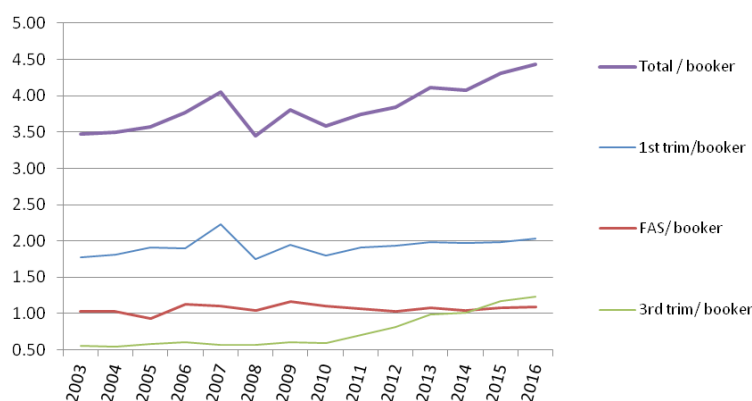

Figure 1. The rising demands on scan departments.

3.8 | Accuracy of the symphysis-fundal height as a screening test for small-for- gestational age fetuses at birth within a low risk population

Andrea Dall'Asta | Tullio Ghi, Enrica Roletti | Fosca Peveri | Martina Gnetti | Tiziana Frusca |
Department of Medicine and Surgery, Obstetrics and Gynecology Unit, University of Parma, Italy.

Objective

To evaluate the accuracy of the symphysis-fundal height as a screening test for small-for-gestational age (SGA) neonates within a low risk population close to term.

Methods

Prospective observational study conducted at a single Tertiary Unit over a 2-year period. Women with uncomplicated singleton pregnancies between 35 and 37 weeks of gestation were submitted to symphysis- fundal height measurement, which was performed using standardized methods and Calvert reference curves. Data collected included symphysis-fundal height percentile and birthweight percentile corrected for gestational age, neonatal gender and parity according to Italian reference neonatal charts by Bertino et al. in order to identify small- (SGA), appropriate- (AGA) and large-for- gestational age (LGA) neonates.

Results

1501 cases were included, among whom 116 (7.7%) were postnatally diagnosed as SGA, 1219 (81.2%) AGA and 166 (11.1%) LGA. Symphysis-fundal height <10th percentile was found in 231 cases (15.4%) of whom only 43 were postnatally confirmed as SGA, thus yielding an overall sensitivity of 37% and PPV of 18.6%. On the other hand, symphysis-fundal height was >10th percentile in 73/1385 (5.3%) neonates who were eventually diagnosed as SGA. Symphysis-fundal height between >10th percentile showed a 100% sensitivity and a 94.2% PPV for AGA or LGA fetuses.

Conclusions

Within a population at low risk of obstetric complications the symphysis-fundal height standard charts represent a poor screening test for SGA. Our findings suggest that a different screening method consisting in customized curves and gestation-adjusted-projection is worth to be evaluated.

3.9 | Prediction of small for gestational age neonates and adverse outcomes in late onset fetal growth restriction: a comparison of standard and Intergrowth charts

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Department of Medicine and Surgery, Obstetrics and Gynecology Unit, University of Parma, Italy.

Objective
To compare the performance of two different growth charts in the prediction of small for gestational age (SGA) neonates and adverse perinatal outcomes in late onset fetal growth restriction (FGR).

Methods
Consecutive series of non-anomalous singleton pregnancies followed at a single Tertiary Centre between 2014 and 2018. Fetuses were defined as late FGR based on ultrasound finding at 32+0-36+6 weeks of estimated fetal weight (EFW) <10th percentile of the Yudkin curve. Within this cohort we applied the Integrowth-21 charts in order to compare the performance of both curves in the prediction of SGA neonates and adverse perinatal outcomes.

Results
275 cases were included, of whom only 133 (48.4%) had EFW <10th percentile according to the Integrowth-21 curves. Postnatal confirmation of SGA occurred significantly more frequently in fetuses with EFW <10th percentile according to the Integrowth-21 curves (104/133, 78.2% vs 177/275, 64.4%, p 0.006), which were also associated with significantly lower birthweight (2275±465 vs 2453±447, p <0.001) and birthweight percentile (7.1±11.8 vs 10.5±11.9, p 0.007) and higher rate of admission to neonatal intensive care unit (NICU) (38/133, 31.9%, vs 54/275, 21%, p 0.03). When evaluating fetuses with EFW >10th percentile according to the Integrowth-21 charts, postnatal confirmation of SGA occurred in 73/142 (51.4%). In this group, 16 neonates (11.6%) were admitted to NICU and 16 (11.6%) had composite adverse outcome.

Conclusion
Within a selected cohort of late FGR fetuses identified by standard curves the Intergrowth-21 charts show good prediction of SGA and identify a subpopulation of late FGR fetuses with significantly lower birthweight and a significantly higher risk of NICU admission, albeit showing an over 50% false negative rate for SGA. A further comparison with customized antenatal growth charts is under investigation.

3.10 | Identification of fetal growth restriction in a population of stillbirths: a comparison of three different growth curves

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Objective
To investigate the accuracy of three different growth curves in diagnosing growth restriction in a population of stillbirths.

Methods
Patients with a singleton pregnancy and intrauterine fetal death (IUFD) ≥ 28 weeks of gestation, without chromosomopathy or major anatomical malformations, diagnosed and delivered at our university center from 2010 to 2017. Growth centiles according to birthweight at delivery and to estimated fetal weight (EFW) at last available ultrasound scan were assessed by means of three growth curves: INES neonatal curves or Hadlock's fetal curves (reference curves as per our Institutional protocol), Intergrowth-21 curves (IG-21), and customized curves (GROW). Histopathological analysis of the placenta was performed in all IUFD cases by one pathologist specialized in placental evaluation. Placental lesions were diagnosed according to Amsterdam Placental Workshop Group Consensus 2016.

Results
93 cases of stillbirth ≥ 22 weeks' gestation were identified, 29 (31.2%) of whom met the inclusion criteria. Analyses were performed in 28/29 cases (1 excluded due to lack of data). Comparison of birthweight centiles according to INES, IG-21, and GROW showed different rates of growth restriction, defined as birthweight <10th percentile: 3/28 cases as per INES, 4/28 cases as per IG-21, and 11/28 cases as per GROW.

Ultrasound data at last evaluation were available in 9/11 IUFD cases with growth restriction at birth according to GROW. An EFW <10th percentile was identified in 4/9 fetuses as per Hadlock, 1/9 fetuses as per IG-21, and 7/9 fetuses as per GROW. Placental histology revealed vascular damage of thrombotic nature on both maternal and fetal plate in 20/28 IUFD cases.

Conclusion
The use of customized fetal and neonatal curves could improve identification of growth restriction. This could help preventing occurrence of IUFD and, alongside with expert-driven placental histological analysis, ameliorating case classification.

POPULATION CHARACTERISTICS (n=28)	
Ethnic Group	
• East European	5/28 (18%)
• South European	16/28 (57%)
• North African	2/28 (7%)
• West African	2/28 (7%)
• Middle Eastern	1/28 (4%)
• Pakistani	2/28 (7%)
Maternal age (years)	32,07 ± 4,84
GA IUFD (week)	36,1 ± 4
BMI at booking	25,00 ± 6,4
Nulliparity	16 (57%)
Smoke	2/28 (7%)

3.11 | Stillbirth risk and SGA rate in subgroups according to maternal size: comparison of GROW, WHO and IG21 fetal growth standards

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Objective
Fetal growth restriction is linked to stillbirth and other adverse pregnancy outcomes and use of the correct standard is essential for accurate assessment of growth status and perinatal risk. We wanted to assess the performance of three international fetal weight standards in their ability to correlate small for gestational age (SGA) and stillbirth risk in pregnancies of mothers with normal body mass index (BMI) but different height and weight groups.

Method
The cohort was a multi-ethnic dataset of 2.02 million term pregnancies from 10 countries (Bhutan, China, Germany, India, Ireland, Netherlands, Slovenia, Sweden, UK and USA). We selected mothers with normal BMI (range 18.5-25.0 kg/m2) from each constituent dataset's main ethnic group, which left 1.25 million cases with complete data for analysis. This cohort was divided into 4 equal size groups, with increasing maternal weight and height pairs to maintain normal BMI (Group 1: weight <57kg, mean height 162cm; Group 2: 57-62kg, 166cm; Group 3: 62-67kg, 169cm; Group 4: >67kg, 173cm). The three standards (Intergrowth 21st -IG; WHO; and GROW) were applied according to their respective methods and formulae to determine SGA rates.

Results
The term stillbirth rate (per thousand) was similar across the 4 size groups, varying from 1.07 to 1.20. The SGA rate according to GROW was also similar across the maternal size spectrum, ranging from 9.7-10.2%, and followed the stillbirth curve closely. In contrast, both uncustomised standards (IG and WHO) showed significantly different SGA trends from that of the stillbirth curve, with low SGA rates in large mothers and high SGA rate in small mothers: WHO SGA rates ranged from 8.8% to 21.8% (2.5 fold increase) and Intergrowth SGA rates ranged from 2.2 to 6.8 (3.1 fold increase) (see Figure).

	1	2	3	4
SB	1.20	1.14	1.07	1.16
SGA GROW	10.2	9.9	9.7	9.8
SGA IG	6.8	4.2	3.1	2.2
SGA WHO	21.8	15.1	11.8	8.8

Fig 1 Stillbirth and SGA rates according to IG, WHO and GROW

Conclusion
Adjustment of the fetal growth standard according to maternal size improves the association between SGA and stillbirth risk, while both WHO and IG standards failed to represent the stillbirth rates within maternal subgroups.
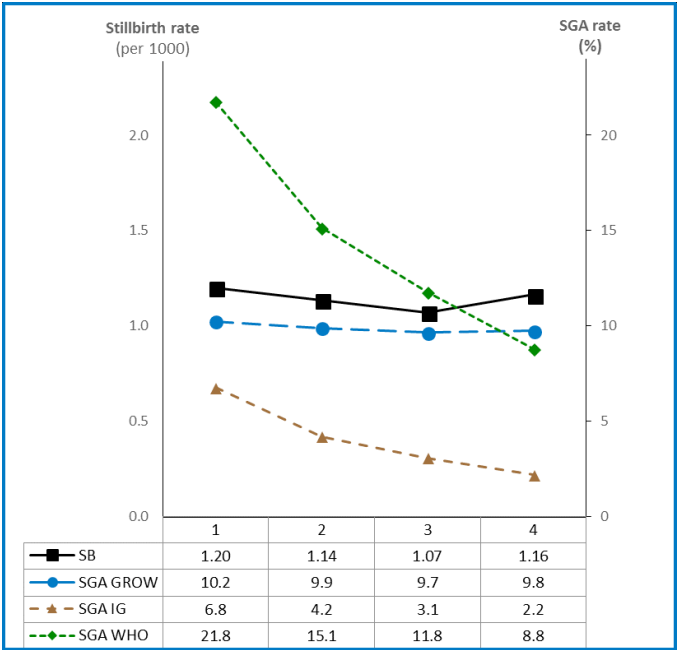
3.12 | The effect of maternal going-to-sleep position on birthweight: a secondary analysis of an individual participant data meta-analysis of going-to-sleep position and the risk of late stillbirth

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Objective
Supine maternal position in late pregnancy is associated with vena caval compression and reduced maternal cardiac output, with the likely consequence of decreased placental perfusion. We hypothesised that women who reported going-to-sleep supine, after 36 weeks of pregnancy, would have babies with lower birthweight and birthweight centiles compared with women who did not go to sleep supine.

Method
Control participants >36 weeks' gestation from four international case-control studies contributing to the Collaborative Individual Participant Data meta-analysis of Sleep and Stillbirth, comprised the study population. The independent effect of going-to-sleep position on birthweight, customised and INTERGROWTH 21st birthweight centiles was assessed using multivariable analysis, accounting for known confounders of fetal growth.

Results
Of 1149 participants, 524 (45.6%) reported going-to- sleep on their left side, 278 (24.2%) on their right side, 32 (2.8%) supine and 315 (27.4%) in another position. Adjusted mean birthweight among supine sleepers was 166g less (95% CI -19g to -313g) than non-supine sleepers (3343g vs 3509g, p=0.03). Among supine sleepers there was a trend toward decreased adjusted mean customised birthweight centile (supine 39.6, non-supine 49.4, p=0.07), and increased adjusted odds (aOR) of birthweight <50th customised centile (aOR 2.11 95% CI 0.98-4.56). There was a significant decrease in adjusted mean INTERGROWTH 21st centile (supine 49.1, non-supine 59.6, p=0.03) and increased aOR of birthweight <50th INTERGROWTH 21st centile (aOR 2.43 95% CI 1.09-5.46) among supine sleepers.

Conclusion
Supine going-to-sleep position in late pregnancy is independently associated with a reduction in mean birthweight and INTERGROWTH 21st centiles. This association is biologically plausible and suggests that maternal supine going-to-sleep position may be associated with reduced fetal growth.

9.1 | Definitions of fetal growth restriction in existing literature over time: A systematic review

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Objective
To list existing definitions of fetal growth restriction in published studies, and how this has changed over time. As fetal growth restriction has no uniform definition in existing literature and is usually ill-defined as small for gestational age.

Method
A review was performed in Pubmed, MEDLINE/EMBASE and all studies describing a cohort of patients with fetal growth restriction in three different years in the last two decades (1994, 2004 & 2014) were included.

Results
The literature search resulted in 118, 191 and 307 records in the years 1994, 2004 and 2014, respectively. Over these years 30, 31 and 44 different definitions for fetal growth restriction were used. The preferred definition among all years was a postpartum definition: birth weight below the 10th percentile. Increasing over time, definitions with antepartum parameters were used. There was also a big heterogeneity in used growth centiles, population based were most frequently used.
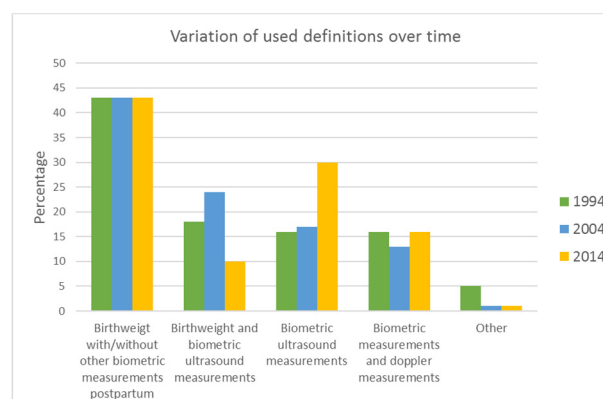

Figure: distribution of used definitions over time.

Conclusion
This review reflects the existing major heterogeneity in defining fetal growth restriction among studies that focus on the subject. This hinders adequate and reliable comparison of different cohorts. The different definitions need to be tested for their applicability and ability to identify the true fetus at risk of adverse outcomes. Uniformity of defining and used growth charts is necessary for future research and clinical practice.

9.2 | Consensus based definitions of fetal growth restriction

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Objective
To develop consensus definitions of fetal growth restriction (FGR) diagnosed during singleton/twin pregnancy and in the newborn, to be used clinically to identify fetuses/newborns at risk for adverse outcome and in research to harmonize reporting and definition in the absence of a gold standard.

Method
Electronic-Delphi surveys were performed among three international expert panels with standardized methods and predefined consensus rules. Each panel consisted of leading experts in that particular field. Responses were fed back at group-level and a list of participants was provided. Non-responders were excluded from subsequent rounds. In the first round, variables were scored on a 5-point Likert scale; in subsequent rounds, inclusion of variables and cut-offs were determined with a 70% level of agreement. In the final round participants selected the ultimate algorithm.

Results
In the three separate procedures ≥79% of the participants completed the total procedure. Consensus was reached on definitions for early- and late FGR in singleton pregnancies, for (selective) FGR in monochorionic and dichorionic twins, and for growth restriction in the newborn. In all definitions, functional parameters as well as biometric parameters were included. In all procedures the consensus reflected that growth restriction could be present in fetuses without a biometric parameter below the 10th percentile.

Conclusion
The new definitions recognize that small for gestational age fetuses/babies are not necessarily growth restricted, and that fetuses/babies appropriate for gestational age can be growth restricted. These definitions will help to focus on subjects at risk for placental insufficiency related adverse outcome, both in clinical practice and trials. Furthermore, uniformity in defining FGR will aid comparison in cohorts and therefore will help to improve knowledge and future management of FGR. With new evidence for additional items in the future, the procedures should be repeated. Prospective studies are needed to validate these definitions.

9.3 | Subtle cardiovascular changes in SGA fetuses may be associated with neonatal morbidity

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Objective

To assess the presence of subclinical cardiac changes in fetuses in early stages of placental insufficiency and whether this is related to increased neonatal morbidity.

Method

Retrospective case-control study between September 2016 and October 2016. We analyzed 3 groups: G1: Controls (EFW 10-90 centile) G2: small for gestational age (SGA), defined as EFW 3-10 centile without Doppler changes and G3 Early stage growth restriction, defined by EFW below 3rd centile, or 3-10 percentile with altered Doppler but positive umbilical end-diastolic flow). We evaluated the following echocardiographic variables: LSI, RSI, TAPSE, MAPSE, IVRT, MPI and a Cardiovascular Score (CS) published by Cruz Lemini. Perinatal morbidity was assessed through a composite score, which included neonatal complications, need for mechanical ventilation and nutrition.

Results

84 patients were included, G1=30, G2=28, and G3=26. The gestational age (GA) of the echocardiogram was similar in the three groups (p=0.650). We observed a slight trend to a lower left and right SI in G2 and G3 (p=0.466, p=0.163). TAPSE and MAPSE were significantly lower in G2 and G3 (p=0.007 and p<0.001). IRT was higher in G2 and G3 (p=0.034) and MPI was lower in G3 (p=0.034). All patients in G1 had normal CS, whereas G2 and G3 had higher scores (p<0,001). Patients with perinatal morbidity and those requiring NICU had significantly higher SC (-2,17 vs 0,18, p<0,001; -2,97 vs 0,048, p<0.001), respectively.

Conclusion

Fetuses in early stages of placental insufficiency appear to have subclinical morphometric y functional cardiac changes when compared their well-grown counterparts. The CS could be a useful tool for discriminating those fetuses with a higher risk neonatal complications and complex care.

9.4 | Cardiac function and doppler indices before and after administration of steroid in fetuses with growth restriction

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Objective

To determine the effects of corticosteroids on the cardiovascular function and Doppler parameters, in fetuses with growth restriction.

Method

This was a prospective cohort study conducted at a tertiary hospital between, April 2017 to December 2017. Fetal cardiovascular function in fetuses with intrauterine growth restriction (IUGR) was assessed immediately before and 6 hours after the second dose of betamethasone, which has been administered in the routine management of fetuses with pre-term IUGR. Fetal arterial and venous Dopplers were assessed.

Fetal cardiac function before and after the steroid administration, which included left and right ventricular function was measured by calculating myocardial performance index (MPI) and E: A ratios.

Results

Fifty patients were included at a mean gestational age of 36.6 ± 1.73 weeks. Eight fetuses were below the 3th percentile and all had no interval growth during a 2-week period. There was a significant decrease of mean right MPI from 0.654 to 0.639 (p=0.017), left MPI from 0.658 to 0.551 (p<0.001) after corticosteroid exposure. There was no significant change in left or right ventricular E/A ratios and no difference was detected in umbilical artery, middle cerebral artery or ductus venosus pulsatility index following administration of corticosteroids.

Conclusion

Corticosteroids improved global cardiac function as evidenced by improvement in left and right sided MPI. However there was no change in the fetal arterial and venous doppler resistance flow indices. Large prospective studies with a larger sample size are needed to confirm the finding of improvement in cardiac function.

9.5 | A Pilot study of fetal growth, maternal hemodynamics and plasma and placental expression of epidermal growth factor

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Objective
Fetal growth restriction (FGR) is mainly caused by placental insufficiency. Therapy with nitric oxide donors (NO donors) is gaining interest, as NO is an important regulator of basal vascular tone and myometrial relaxation. Epidermal Growth Factor Like Domain 7 (EGFL7) has a critical role in placental and fetal growth. This study aimed to investigate maternal cardiovascular system organization and fetal growth and EGFL7 plasmatic and placental modulation in response to the treatment with NO-donors in FGR pregnancies.

Methods
10 pregnant women with a diagnosis of FGR, treated or not with NO donors and oral fluids, were enrolled and subjected to blood sampling and placenta collection, together with fetal obstetric ultrasound and maternal hemodynamic evaluation using USCOM (UltraSonic Cardiac Output Monitor). All patients underwent elective caesarean section. Placental distribution and mRNA levels of EGFL7 and the pan-endothelial marker CD31 were studied by immune-fluorescence and qRT-PCR analysis, respectively. EGFL7 plasma concentration was evaluated by ELISA.

Results
Immunofluorescence analysis of placental samples confirmed that EGFL7 was expressed by both endothelial and trophoblast cells, as previously demonstrated, and qRT-PCR showed that, in the maternal side of the placenta of NO-treated patients, EGFL7 mRNA expression was significantly increased by about 3.5-fold, even more than CD31, compared to untreated IUGR pregnancies, matched for gestational age. Circulating levels of EGFL7 were not affected by NO-treatment. After 2 weeks of treatment our data demonstrated that FGR fetuses with high TVR showed an improvement of maternal haemodynamic parameters. Moreover, fetal growth has been increased in those who had NO donors treatment.

Conclusion
Treatment with NO donors improves maternal hemodynamic and fetal growth, by restoring placental vascular structure, especially on maternal compartment, by increasing the expression of the pro- angiogenic protein EGFL7, which is critical for placental vascularization and embryonic growth.

9.6 | Physiopathology of adrenal sparing: ultrasound and functional evaluation of fetal adrenal glands in relation to fetal growth restriction and pre-eclampsia

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Objective
To correlate in vivo the morphological and functional aspects of adrenal sparing in fetuses with intrauterine growth restriction (FGR) and to investigate the role of fetal adrenal hormones in the development of maternal gestational hypertension.

Methods
Prospective study at the 2U obstetrics sector (Sant'Anna hospital, Turin) between January 2014 and May 2017: 67 single pregnancies undergoing a morphological study of the foetal adrenal glands by evaluation of the average adrenal diameter and of the adrenal glands/abdominal circumference ratio; 21 cases undergoing a functional study by catecholamine and cortisol dosage on funicular and maternal blood taken at delivery (only if caesarean section out of labor to reduce confounding effect). The results were analysed by comparing the FGR group from hypertensive mothers and the FGR group from normotensive mothers with a control group (AGA in normotensive mothers).

Results
The adrenal glands/AC ratio is higher in the groups FGR of both hypertensive and non-hypertensive mothers than in the control group; the funicular levels of noradrenaline are higher in the groups FGR than in the control group; maternal noradrenaline values are lower in the groups FGR than in the control group.

Conclusion
First study to demonstrate in vivo the correlation between adrenal dimensional increase and activation in FGR fetuses. High levels of NA in FGR fetuses are an expression of compensation (adrenal-sparing) but they may be correlated with long-term metabolic risks. The finding of low NA values in the hypertensive mothers of FGR, in contrast to the literature reporting increased NA values in gestational hypertension, can be explained by the selection of pre-eclampsia cases of placental vs maternal origin.

9.7 | Inter- and Intra-observer variability in ductus venosus blood flow measurement

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Objective
Change of flow of the ductus venosus appears to be associated with adverse neonatal outcomes. While good repeatability of the ductus venosus pulsatility index for veins (DV PIV) is of importance for use in a clinical setting, the test characteristics and robustness of the DV PIV have been inadequately described. The aim of this study is to investigate inter- and intra-observer variability of the ductus venosus.

Methods
Women with a gestational age between 26 and 32 weeks were eligible for inclusion. Doppler sonographic fetal assessment was performed by two independent highly trained obstetric gynecologists. Each sonographer alternately performed three measurements in each participant. The inter- and intra-observer variability of the DV PIV measurement was assessed using the Bland– Altman method with ANOVA.

Results
A total of 114 DV measurements was taken from 19 participants with a median age of 31 years (IQR 26-34) and BMI of 25.4 (IQR 21.3-29.1).Both sonographers were able to assess the DV PIV in all participants. Overall the difference in means between both sonographers was very low with a mean of 0.0072 (SD 0.10), corresponding to limits of agreement between -0.195 and 0.209. The precision and 95% CI of the bias and lower and upper limits of agreement were respectively 0.0072 (-0.041;0.056), -0.195 (-0.279;-0.110), and 0.209 (0.125;0.293). The relative difference was 1.8%, with limits of agreement (LoA) -27% to 31%. There was no statistically significant difference between measurements in either of the sonographers (p = 0.42, and p = 0.53).

Conclusion
There was reasonable agreement between sonographers as indicated by a small mean difference in PIV. DV measurements showed to be consistent within sonographers indicating good inter-observer variability. Based on these results we believe the reproducibility of the DV PIV Doppler is good and justifies clinical use.

9.8 | Elevated numbers of placental macrophages in pregnancies complicated with fetal growth restriction

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Objective
Fetal growth restriction (FGR) is the strongest single risk factor for stillbirth in high income countries [1]. Placental dysfunction is present in cases of both FGR and stillbirth, and in pregnancies with reduced fetal movements (RFM). There is evidence for placental inflammation in pregnancies where the infant is stillborn or at high risk of stillbirth, with elevated numbers of placental macrophages (Hofbauer cells)[2]. We aimed to investigate the number of Hofbauer cells in infants with fetal growth restriction (FGR).

Methods
Two groups of FGR pregnancies were studied. In group 1, FGR was defined as individualised birthweight centile (IBC) ≤3rd centile (n=8) and uncomplicated pregnancies (n=8). In group 2, FGR was defined as a decrease of ≥25 centiles between third trimester estimated fetal weight and IBC (n=24), in women presenting with RFM. Controls were pregnancies with RFM with normal growth rates (n=12) and uncomplicated pregnancies (n=12), matched for maternal demographics. Placentas were randomly sampled and Hofbauer cells quantified using immunohistochemistry for CD163 and unbiased image- analysis.

Results
There was no difference in Hofbauer cell number between FGR infants (≤3rd centile) and controls. In contrast, there was an increase in Hofbauer cells from RFM pregnancies complicated with FGR compared to both control groups (p≤0.005). There was no difference in Hofbauer cell number between RFM controls and healthy controls.

Conclusion
There is heightened immune activation in the placenta, with elevated Hofbauer cells in pregnancies where there is a fall in fetal growth trajectory in the third trimester. This was not seen in pregnancies where the infant was ≤3rd centile at delivery, potentially due to these infants being constitutively small. These data extend previous observations linking inflammation to placental dysfunction and adverse fetal outcomes.

References
1 Flenady V et al 2011, Lancet, 377(9774):1331–40.
2 Derricott H et al 2016, AJP, 186(4), 952:961

9.9 | Umbilical vein blood flow volume in fetuses with inappropriate growth for gestational age and normal doppler velocimetry

Tamara Stampalija[1] | **Leila Lo Bello[1]** | **Lorenzo Monasta[2]** | **Ilaria Fantasia[1]** | **Mariachiara Quadrifoglio[1]** | **Chiara Ottaviani [1 3]** | **Maria Bernardon[1]** | **Caterina Businelli[1]** | **Enrico Ferrazzi[4]** | [1]Unit of Fetal Medicine and Prenatal Diagnosis, Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy; [2]Unit of Clinical Epidemiology, Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy; [3]School of Medicine, University of Trieste, Italy; [4]Unit of Obstetrics, IRCCS Fondazione Cà Granda Policlinic of Milan, University of Milan, Italy

Objective

To evaluate the blood flow volume (Q) in umbilical vein (UmbV) in fetuses with inappropriate growth for gestational age with normal Doppler velocimetry indices.

Method

This is a case-control (1:2) study performed in a single third referral centre, IRCCS Burlo Garofolo, Trieste, Italy. The inclusion criteria were fetal abdominal circumference (AC)<10° centile or reduced growth (AC crossing 50° centiles). Doppler assessment of uterine arteries (UtA), umbilical artery (UmbA) and middle cerebral artery (MCA) was performed. Controls were uncomplicated pregnancies with normal fetal growth and without any Doppler alteration (AGA). Q-UmbV was evaluated on a free umbilical cord loop and was normalized for estimated fetal weight (EFW) (Barbera-2009). Analysis was performed at diagnosis by logistic regression.

Results

110 cases and 220 controls were recruited. The analysis was performed on 106 cases and 178 controls due to missing outcome data or onset of complication in controls. Fetuses with inappropriate growth for gestational age were analysed according to: at least one abnormal Doppler finding in UtA, UmbA or MCA (orange dots, n=41), or all normal Doppler findings (green dots, n=65). Fetuses with inappropriate growth for gestational age, with or without Doppler alterations in UtA, UmbA or MCA, had significantly lower Q-UmbV, both absolute and normalized for EFW, than AGA. The figure represents: a) absolute Q-UmbV (both p<0.0001); and b) normalized for EFW Q-UmbV (p<0.0001 for fetuses with and p=0.01 for fetuses without Doppler alteration, respectively). The controls are represented by quadratic regression line and 95% confidence intervals.
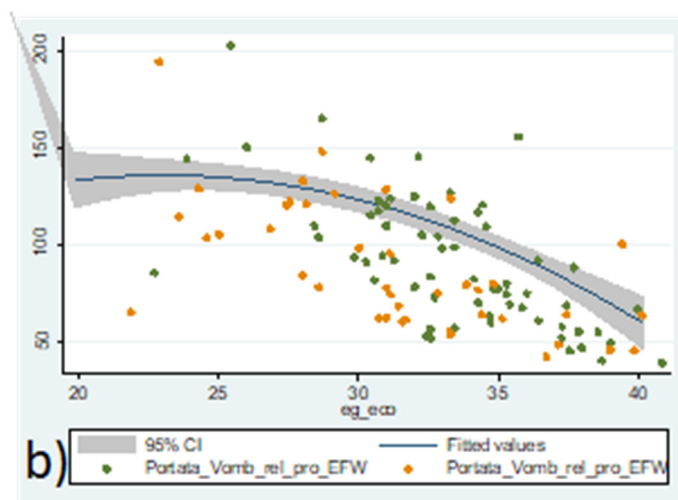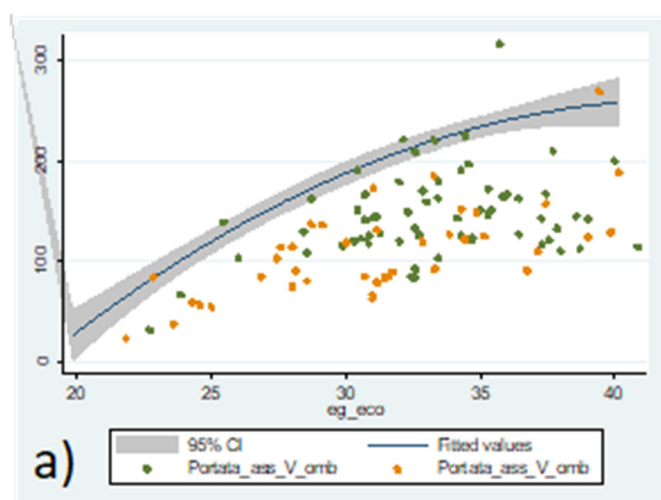
Conclusion

In fetuses with AC<10° centile or drop of >50° centiles, with otherwise normal Doppler velocimetry indices commonly assessed, the Q-UmbV is lower than in AGA. This finding suggests that fetuses considered to be "small for gestational age" or "constitutionally small" could, however, suffer some degree of imbalance between placental blood supply and metabolic demand.

9.10 | Uterine and umbilical vein blood flow volume in fetuses detected antenatally as inappropriate for gestational age but with normal birthweight

Tamara Stampalija[1] | **Leila Lo Bello[1]** | **Lorenzo Monasta[2]** | **Ilaria Fantasia[1]** | **Mariachiara Quadrifoglio[1]** | **Chiara Ottaviani[1 3]** | **Maria Bernardon[1]** | **Caterina Businelli[1]** | **Enrico Ferrazzi[4]** | [1]Unit of Fetal Medicine & Prenatal Diagnosis, Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy; [2]Unit of Clinical Epidemiology, Institute for Maternal & Child Health, IRCCS Burlo Garofolo, Trieste; [3]School of Medicine, University of Trieste; [4]Unit of Obstetrics, IRCCS Fondazione Cà Granda Policlinic of Milan, University of Milan, Italy

Objective

Systematic discrepancies occur between diagnosis of fetal growth restriction and postnatal evaluation based on birthweight. We wanted to analyse blood flow volume (Q) in uterine arteries (UtA) and umbilical vein (UmbV) in fetuses detected antenatally as growth restricted with weight at birth within normal reference ranges.
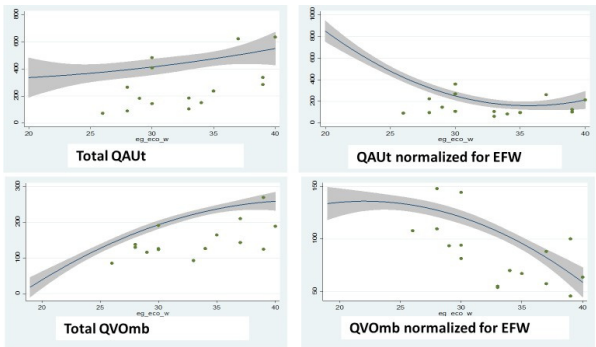
Methods

This is a case-control (1:2) study performed in a single referral centre, IRCCS Burlo Garofolo, Trieste, Italy. The inclusion criteria for cases were: fetal abdominal circumference (AC)<10° centile or reduced growth (AC crossing 50° centiles). Birthweight was evaluated according to neonatal Italian weight-charts adjusted for parity and gender (Bertino, 2010). Controls were uneventful pregnancies with normal fetal growth and normal birthweight. Q-UtA was evaluated according to published Doppler multimodal methodology (Ferrazzi, 2011); Q-UmbV was assessed on a free umbilical cord loop (Barbera, 1999). Absolute flow volume was also normalized for estimated fetal weight (EFW). Analysis was performed on values obtained at diagnosis by logistic regression.

Results

110 cases and 220 controls were recruited. The analysis was performed on 106 cases and 178 controls due to missing data or onset of complications in control group. In 16 cases (green dots) there was a discrepancy between antenatal diagnosis, 14 cases with AC<10° centile and 2 with AC drop >50° centiles, and postnatal classification of birthweight >10° centile. Cases presented a significantly lower Q-UtA and Q-UmbV (both absolute flow volume and normalized flow for EFW) than controls (absolute Q-UtA p=0.0005, normalized Q-UtA p=0.04; total Q-UmbV p<0.0001; and normalized Q-UmbV p=0.04, respectively). Controls data are represented by quadratic regression line and 95% confidence intervals.

Total QAUt | QAUt normalized for EFW
Total QVOmb | QVOmb normalized for EFW

Conclusion

Prenatal assessment by ultrasound biometry and Doppler flow volume of uterine arteries and umbilical vein allows for better identification of fetuses that fail to reach their growth potential than newborns' weight charts even when based on local standards.

9.11 | Fetal dopplers at term in pregnancies affected by gestational diabetes: role in prediction of perinatal outcomes

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Objective

Timing of delivery for women affected by Gestational Diabetes (GDM) is still controversial: the good clinical practice often suggests to offer induction of labour at term in order to reduce the complications associated with this condition while recent evidences support the expectant management. Fetal Dopplers represent a validated tool to test fetal wellbeing at term and can select pregnancies that need increased surveillance. The aim of the present study is to evaluate the role of fetal Dopplers at term for prediction of pregnancy outcomes in patients affected by GDM.

Methods

Prospective cohort study in a single center. Evaluation of Umbilical Artery (UA) PI, Middle Cerebral Artery (MCA) PI, Cerebro-Placental Ratio (CPR) and Umbilical to cerebral ratio (UCR) at > 37 weeks' gestation in singleton, morphologically normal pregnancies affected by GDM, has been performed in order to estimate the association between ultrasound measurements at term and perinatal outcome. Regression linear analysis was used to estimate the association between fetal Dopplers and neonatal pH, neonatal Apgar score, neonatal weight and a composite adverse outcome. Receiver Operating Characteristic (ROC) Curve was used to estimate the possible predictive value of the above association.

Results

Our results on 130 women showed MCA PI to be the best predictor of perinatal outcomes in terms of low Apgar score at the 1st minute, pH and composite adverse outcome (p<0.05). UCR showed a significant correlation with neonatal pH (p<0.05). No significant correlations for UA PI and CPR MoMs have been demonstrated in our population. However, the small sample size is a limitation of the study.

	Composite adverse outcome	1st min Apgar	5th min Apgar	pH
UA PI MoMs	0.37	0.97	0.86	0.11
MCA PI MoMs	0.05*	0.00*	0.08	0.02*
CPR MoMs	0.16	0.25	0.17	0.24
UCR MoMs	0.07	0.06	0.28	0.02*

Results of the linear regression. P value. *significant as <0.05

Conclusion

Evaluation of MCA Doppler and eventually UCR at term can be a useful tool to discriminate pregnancies affected by GDM that can benefit from IOL before 41 weeks in order to reduce complications related to this condition.

9.12 | Evaluation of the quality and reliability of middle cerebral artery (MCA) and umbilical artery (UA) doppler images in a randomized controlled trial

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Objective
To evaluate the quality and the inter-rater reproducibility of the middle cerebral artery and umbilical artery Doppler measurements performed in a multicenter randomized controlled trial "Ratio37: Revealed versus concealed criteria for placental insufficiency in unselected obstetric population in late pregnancy"

Methods
20 patients were randomly selected (2 images per patient, umbilical artery and middle cerebral artery) from each of the 6 participating centres. A total of 240 images were evaluated by six different experts and scored on an objective scale of six items (anatomical site, image magnification, angle of insonation, waveform, speed, velocity scale), using pre-defined quality criteria. (S. Ruiz- Martinez, G. Volpe, S. Vannuccini, A. Cavallaro, L. Impey & C. Ioannou (2018) The Journal of Maternal-Fetal & Neonatal Medicine). Images scoring more than 4 points were defined as of good quality. The agreement between experts was assessed using inter-class correlation coefficient.

Results
According to each rater more than 92% of the images were objectively classified as good images. For the UA over 92% of the images scored 4 points or more. For the MCA, more than 94% of the images were classified as good-quality. The inter-rater reproducibility reached 80% for both the UA and MCA (95% CI, 53 to 94%), 64% (95% CI, 23% to 89%) for the UA alone, and 79% for the MCA alone (CI 95%, 52% to 94%), which is good.

Conclusion
The quality of the measurements was good in more than 95% of the cases. The inter- observer reliability was found acceptable.
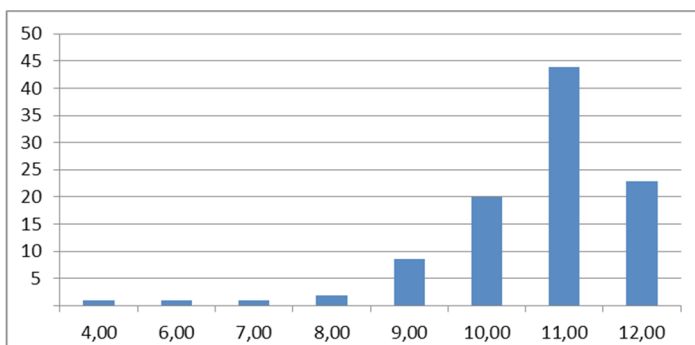
9.13 | Birthweight/placenta weight ratio in clinically unexpected stillbirth

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Objective
To investigate the role of the birthweight placenta weight (BWPW)-ratio in the association of placental insufficiency (PI) and stillbirths.

Methods
A retrospective cohort study of stillbirths between January 2000 and December 2017. Based on clinical information, the stillbirth cohort was divided into three groups: known placental insufficiency (1), any other condition diagnosed prior to stillbirth (2) and unexpected (3). The proportion of (absolute) low birthweight, placenta weight (<p10) and the BWPW-ratio was calculated.

Results
295 Cases of stillbirths occurred of whom 109 cases (37%) were assigned to group 1 (placental cause), 57 cases (19%) were assigned to group 2 (other causes) and the biggest group was that of the unexpected stillbirth with 129 of the cases (44%). Of the latter, 71% had an abnormal BWPW-ratio (high BWPW-ratio in 69% and low BWPW-ratio in 2%). These proportions were similar in the group of placental causes of stillbirth and significantly lower in the stillbirths caused by other conditions. Low birthweight was present in 41.1% of the unexpected stillbirths, this was not significantly different from the other causes-group (47.4%) but significantly higher in the placental causes- group (91.7%). Low placenta weight was seen in 69.8% of the unexpected stillbirths, this was even higher in the placental causes group (91.7%), but significantly lower in the other causes-group (42.1%).

Conclusion
The majority of unexpected stillbirths had a high BWPW-ratio and a low placental weight. These proportions were similar or higher in the stillbirths due to known PI but significantly lower in the stillbirths due to other causes. This study demonstrates that high BWPW-ratio is significantly associated with clinically unexpected stillbirths. This suggests that an undetected PI contributes to a large proportion of the unexpected stillbirths. Our results underline the necessity of further research in placental investigations and biomarkers of PI to potentially prevent stillbirth.

9.14 | Umbilical artery intima-media thickness: A predictor of poor perinatal outcome in fetal growth restriction

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Objective
To correlate umbilical artery intima-media thickness (uIMT) to perinatal outcome in pregnancies complicated by fetal growth restriction (FGR).

Methods
This prospective cohort study was performed in Suez Canal University Hospitals between July 2015 and June 2017. It included singleton, non-malformed pregnancies complicated by FGR, defined as severe growth lagging [estimated fetal weight (EFW) <3rd centile] or milder lagging (<10th centile) combined with abnormal maternal/fetal Doppler. Ultrasound examinations included fetal biometry, Doppler studies of umbilical and middle cerebral arteries, and uIMT measurement. The relationship between various antenatal variables (EFW, Doppler, gestational age at delivery, and uIMT) and a composite adverse perinatal outcome was examined by logistic regression. Receiver operating characteristic (ROC) curve was used to analyse uIMT individually as a predictor of composite adverse perinatal outcome.

Results
This cohort (n=60) included 14 patients (23%) with early-onset (EO) FGR <32 weeks and 46 (77%) with late-onset (LO) FGR ≥ 32 weeks gestation. The mean uIMT was significantly higher in the EO group (0.63 mm) compared to the LO group (0.55 mm; p-value <0.001). Within the LO-FGR group, higher uIMT measurements were significantly associated with poorer neonatal outcomes, including lower birthweight centiles, lower 5-minutes Apgar scores, need for NICU admission and higher neonatal morbidities. Pregnancies that resulted in perinatal mortality showed thicker uIMT measurements, but this difference was significant only in the EO group. Umbilical artery IMT was one of the significant predictors of adverse perinatal outcome (P value 0.009). A cut-off uIMT thickness ≥ 0.565 mm achieved the best prediction of adverse perinatal outcome (sensitivity 82%, specificity 78%, AUC 0.79, 95% CI 0.66-0.93, P value <0.001)

Conclusion
uIMT is significantly higher in EO compared to LO-FGR and is a significant independent risk factor for adverse perinatal outcome in FGR pregnancies. Further larger- scale research is required to confirm these findings.

9.15 | Free thiols in maternal serum and urine for the detection of fetal growth restriction

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Objective
Oxidative stress is a feature of both fetal growth restriction (FGR) and pre-eclampsia (PE). The extent of oxidative stress is reflected by the level of free thiols as they are readily oxidized when exposed to reactive species. As FGR often remains undetected before birth, the aim of this pilot-study is to assess the utility of urinary and serum free thiols as a clinical reflection of placental oxidative stress in a case-control study.

Methods
Twenty-four patients with a singleton pregnancy between 24-36 weeks of gestation were divided into three groups: isolated FGR (n=9), FGR with PE (n=11) or uncomplicated controls (n=14), based on their sequential fetal biometry, abnormal Doppler patterns and the presence of gestational hypertension with proteinuria. Free thiols were determined in first morning urine, 24-hour urine and serum. Placentas were pathologic examined for features of placental insufficiency.

Results
Serum free thiols were significantly lower in patients with FGR and PE when compared to patients with isolated FGR (p=0.001) and healthy pregnancies (p=0.001). Serum free thiols did not differ between the latter groups. No significant differences were demonstrated in first morning- and 24-hour urine among all groups. The incidence of placental pathology like accelerated maturation (p=0.005), microscopic infarction (p=0.003), distal villous hypoplasia (p=0.001) and hypoxia (p=0.05) were more common in patients with FGR and PE than in isolated FGR and control placentas.

Conclusion
Urinary and serum free thiols do not change in isolated FGR. However, pregnancies complicated by FGR combined with PE were associated with lower serum free thiols (reflecting increased oxidative stress) and more placental abnormalities compared to isolated FGR. This suggests that the placental pathogenic mechanism of FGR in pre-eclamptic women is different from FGR in absence of PE. Whether modification of free thiols improves outcome warrants further exploration.

P1 | Early growth velocity and mode of conception in the prediction of SGA

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Objective

The aim of the study is to produce a predictive model of birthweight including early growth velocity (vCRL), maternal characteristics, type of conception, uterine Doppler, and biochemistry (PAPP-A and bhcg) . We were also interested in the differences between growth velocity according to type of conception.

Method

This is a cohort study of a single center including all pregnancies with an early scan at 8-9 wks and the 12 wks scan. The vCRL was calculated substracting the CRL 12-CRL 8 divided by days (mm/d). The other variables included in the algorithm were MOM uterine Doppler, MOM PAPP-A, MOM bhcg, maternal weight and height, smoking habit. The type of conception was classified as: spontaneous, IVF, frozen embryo cryotransfer, and egg donation. A logistic regression model including all the variables was used to create the prediction algorithm of the birthweight. Also the detection rate of SGA at term and preterm was calculated.

Results

5079 singleton pregnancies were included, 86,7 % (4947) spontaneous and 13.3 % (762) Assisted Reproductive Techniques (ART) . The mean vCRL was 1.66 mm/d in the spontaneous and 1.68 mm/d in the ART group(p 0.003). This statistical significance was lost when we compared the zcore of birthweight among the two groups. (p 0,09). Comparing the different types of conception was significant the difference between the frozen cryotransfer groups with higher vCRL compared to the other groups. Regarding the predictive model the significant variables were: smoking, maternal weight and height, uterine Doppler, Papp-A and bhcg and vCRL , The more significant variables in the model were smoking and uterine Doppler with a negative impact and vCRL as positive. The ROC curve of the entire model has an AUC of 0.68 (0,66-0,70). The detection rate of the model for a 10% false positive for any SGA was 31%, for SGA below 37 wks was 38,5% and below 35 wks 46.7%.

Conclusion

Adding the vCRL to a model with maternal characteristics and placental function permits to detect half of the SGA below 35 weeks. There is no relevant impact according to the type of conception in the final model.

P2 | Anogenital distance in male and female fetuses at 26 to 30 weeks gestation

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Objective

In recent years, anogenital distance (AGD) across development has become of interest for researchers and clinicians. Of particular interest is the potential to predict later infant and adults outcomes (i.e. male reproductive potential, Eisenberg et al, 2011). Previous studies have correlated it with androgen secretion, in particular fetal testosterone, and this has been suggested to be a driver of AGD. This study aims to further explore the potential of measuring AGD during late second-, early third trimester of pregnancy, and make an early assessment of population specific impacts on reference ranges.

Method

206 typically developing singleton pregnant mothers (99 male, 107 female fetuses) were invited for an ultrasound between 26-30 weeks pregnancy. Women were recruited prospectively at the Rosie Maternity Hospital in Cambridge, UK and 3D ultrasound scans were performed using a GE 8 Expert Ultrasound system. AGD was measured from the centre of the anus to the base of the scrotum in males, and to the posterior convergence of the fourchette in females. Replicating previous research measuring fetal AGD in Sheba Hospital, Israel (Gilboa et al, 2014).

Results

Results show significant sexual dimorphism in fetal AGD, replicating previous results. However significant differences were also observed in reference ranges produced from the Israeli and UK samples.

Conclusion

Our result is consistent with AGD measurement in utero being feasible and supports previous suggestions that AGD is influenced by fetal androgen secretion. In addition, we also show that similarly to fetal biometry charts, AGD lengths differ between populations, therefore personalised population charts need to be created.

P4 | A study of STV calculation algorithms – comparison of two applications for computerized CTG analysis

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Objective
Computerized analysis of fetal cardiotocogram was designed to overcome the inter-observer variability of visual assessment. Currently, the most used software is FetalCare (Huntleigh Healthcare Ltd, Cardiff, UK). Limitations of this software are that exact description is not freely available, assessment is limited to one hour and batch processing is not possible. For this reason, we designed new software, STVcalc. The aim of this study was to compare STVcalc with FetalCare version 2, using a population of severe early-onset fetal growth restriction with a high proportion of abnormal CTG's.

Method
STVcalc was developed based on the FetalCare system. All women who delivered between 24 and 31 weeks by cesarean section for fetal distress with a small for gestational age fetus or had fetal death and had at least two CTG's recorded, were selected. The same CTG tracings were analyzed by the two programs. Short-term variability (STV), decelerations and accelerations were compared by non-parametric statistics.

Results
491 CTG's were analyzed. STV by FetalCare was non- clinically significant higher than by STVcalc (proportional difference 0.02 ms; IQR -0.01 to 0.05 ms). Agreement for a cut-off of 3.5 ms below 29 weeks and 4.0 ms thereafter was 95% (95% CI 93% - 97%). For a cut-off at respectively 2.6 ms and 3.0 ms the agreement was 99% (95% CI 98% to 100%). FetalCare was less sensitive, but more specific than STVcalc for the detection of decelerations and excluded outliers less effective. As decelerations and outliers are excluded from STV calculation this explains the small difference of STV between both applications. Acceleration counts were similar.

Conclusion
Only slight differences were observed between both applications. STVcalc may have advantage for clinical practice as well as research, as it allows analysis for more than one hour, has the feature of batch processing and is available as freeware.

P5 | Is low cerebro-placental ratio (CPR), as a placental disfunction marker, a limitant to reach the optimal weight in dichorionic pregnancies?

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Objective
To evaluate the correlation between CPR and birthweight in dichorionic and simple pregnancies in diferents percentile groups, afther 32 weeks of gestation.

Methods
retrospective comparative cohort study of data obtained in a single tertiary referral centre in a period from 2009 to 2018. We analysed the CPR within 15 days before birth in dichorionic twins born after 32 weeks, and we correlated this with birthweight. Afterwards we compared the results with a cohort of simple pregnancies. Doppler indices were converted to multiples of the median. And we compared both pregnancies between different percentile groups.

Results
The study included 310 fetuses, 166 in the twin group, and 144 in the simple pregnancy group. There was a significant difference between the media of birthweight, CPR MoM, and birthweight percentile from dichorionic and simple pregnancies (p < 0,001). There was a significant correlation between MoM CPR and birthweigt in twins (p<0,001). When comparing with simple pregnancies, the percentage of twins in the 50-90 percentile group with low CPR was significantly higher (21% vs 4.4%). (p=0,037).

Conclusion
Our results show a positive corrrelation between placental function, evaluated by CPR, and birthweight after 32 weeks in dichorionic pregnancies. The percentage of fetuses with MoM CPR <PC 5 was higher in all groups of dichorionic pregnancies. A statistically significant difference was observed in the group of "eutrofhic fetuses" birthweight (Pc 10-90) and particularly in the higher group (PC 50-90). This finding may suggest a greater difficulty for twins in reaching highest birthweight percentiles, and placental function could be one of the limitation for reaching the genetic potential. In addition, both the umbilical IP correlation and the CPR MoM with birth weight were significant.

P6 | Partial molar pregnancy coexisting with a live diploid fetus, complicated by intrauterine growth restriction and eclampsia

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Introduction

Molar pregnancies with viable fetus occur up to 1 in 20,000 gestations. Only 5 cases of triploid partial mole with diploid fetus have been reported up to date. We present such a case, complicated by intrauterine growth restriction (IUGR) and eclampsia.

Case

During the first trimester ultrasound scan in 25 years old woman, gravida 2, para 1, no fetal abnormalities were detected and calculated risk of trisomy was low. The ultrasound scan at 19 weeks revealed a single female fetus with no anatomical anomalies. Abnormal "jelly like placenta" with numerous cysts was observed. Moreover, at 25 weeks IUGR with abnormal Doppler was diagnosed and patient was admitted to hospital. During hospitalization the patient's blood pressure was normal. Deterioration in Doppler scan was observed so the patient was administered intramuscular betamethasone. At 27 weeks a cardiotocograph revealed an imminent fetal asphyxia and female newborn weighting 740 grams was delivered via caesarean section.

Early postoperative period was complicated by hypertension of 200/100 mmHg and two eclampsia attacks. The patient received hypotensive and anticonvulsive treatment. She was transferred to Neurological Intensive Care Unit, where she was diagnosed with posterior reversible encephalopathy syndrome (PRES). Maternal postpartum serum βHCG concentration was not elevated (5 mIU/mL). Due to abnormal image of the placenta, representative samples of tissues were processed to the microscopic slides. The findings were compatible with a partial molar pregnancy. The placenta karyotype was triploid (69 XXY), while the newborn karyotype was diploid (46 XX). Now, at the age of 18 months the infant is phenotypically and developmentally normal.

Conclusion

It is, so far, sixth described case a triploid partial molar pregnancy resulting in diploid normal karyotype live-born infant. Molar pregnancy is associated with high risk of fetal and maternal complications.

P7 | The association between expression of microrna-21 and microrna-141 with the occurrence of intrauterine growth restriction

Magdalena Zgliczynska[1] | **Katarzyna Kosińska-Kaczyńska[1]** | **Mateusz Gielata[2]** | **Eliza Kobryń[1]** | **Agata Majewska[1]** |
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[2]Laboratory of Molecular Biology of Cancer, Centre of New Technologies, University of Warsaw, Poland

Objective

MicroRNAs (miRNAs) are small RNA molecules that regulate expression of genes. Decreased miR-21 and increased miR-141 concentrations in the placenta correlate with lower birth weight of fetuses, and the reverse dependence was found in placenta of women with fetal macrosomia. It suggests that miR-21 and 141 are involved in processes related to intrauterine growth. The aim of the study is to determine if abnormal expression of microRNA-21 (miR-21) and microRNA-141 (miR-141) occurs in intrauterine fetal growth restriction (IUGR).

Method

The study group consisted of 10 women in single pregnancies complicated by IUGR and the control group was made up of 10 women in healthy pregnancies. From each patient samples of blood and placenta were collected. Total RNA was extracted and diluted in diethylpyrocarbonate water to a final concentration of 450 ng/μL. Total RNA was used in a reverse transcription reaction. The product was subjected to amplification. The expression levels of chosen miRNA were normalized by using endogenous control RNU6B. $2^{\wedge}$-ΔCp values were used to detect differences in the expression. Kruskall- Wallis test for non-parametric distribution was used to compare the expression among groups. Other applies tests were: T-student test and chi2-test. Differences with a p-value < 0.05 were considered as statistically significant.

Results

MiR-141 had significantly higher expression in samples of placenta derived from women in pregnancies complicated by IUGR (p=0.02) than in control group (Figure 1). Moreover, in control group, significantly more samples had detectable expression of miR-21 in placenta than in study group (p=0.006).

Figure 1

Conclusion

Overexpression of miR-141 and lower expression of mir-21 might be a part of IUGR pathogenesis. Exploration of epigenetic mechanisms of IUGR may help to understand mechanisms of the disease and identify possible maternal predictive factors as well as possible gene therapy targets in IUGR treatment.
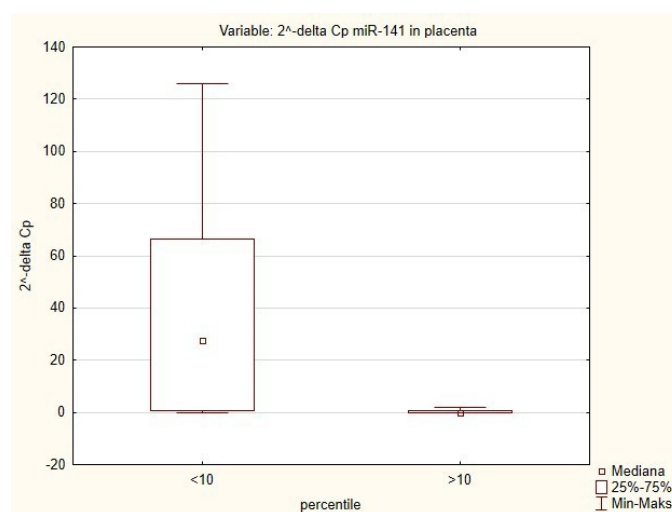
P8 | Fundal height measurements - size does matter

Edel Clare | Premila Thampi | Milton Keynes University Hospital, UK

Objective

To assess the diagnostic test accuracy of "Fundal Height Measurement" in detecting abnormalities of fetal growth.

Method

A scoping review of published research articles specifically to pregnant women who have under gone a form of fetal measurements through fundal height measurements (FHM) and estimated fetal weight (EFW).

Patients: Singleton pregnancies in low risk population

Index Test: FHM performed with a standard measuring tape

Comparator/reference standard: Ultrasonic measurements of abdominal circumferences

Outcome/target condition: Fetuses that are small for gestational age (SGA) and or have fetal growth restrictions (FGR).

Results

The probability of finding a difference between FHM and gestational age of 3 cm or more using blank tapes was 55% in obese women and 67% in extremely obese women, indicating serious bias. Sensitivity and specificity will vary depending on BMI. In these cases USS would be the gold standard.

Conclusion

Detection of abnormal fetal growth historically is very poor. Standardised training and the implementation of protocols has shown to increase the detection of SGA/FGR and is fundamental in the reduction of stillbirths. FHM could be a very useful diagnostic test for assessing fetal growth only when the reliability and validity can be ensured by providing continuity and uniformity of technique. To avoid adverse effects every clinician caring for pregnant women and their fetuses need to familiarise themselves with the growth assessment protocol (GAP) and practice accordingly in order to improve patient safety in maternity units. Each unit has a duty of care to ensure that women using the service are receiving evidence based care.

P9 | Clinical evaluation of the effectiveness of low PAPP-A in the identification of small-for-gestational-age babies: A GDH audit

A Collister | O Ajibola-Taylor | Amanda Staffer | R Myagerimath | Wirral University Teaching Hospital

Objective

In light of the RCOG considering low pregnancy associated plasma protein A (PAPP-A) <0.415MoM in the 1st trimester as a major risk factor for small for gestational age (SGA), recommending serial growth scans for all affected, we have undertaken an audit to establish the risk for SGA within our local population of women with low PAPP-A levels prior to introducing this risk factor within our local guidelines.

Method

Retrospective review of all pregnant women 2015 and 2016 with low PAPP-A levels, detected as part of their first trimester screening.

Results

Total of 137 patients were included in the audit (2015 - 65 patients, 2016- 72 patients).

- 41% low PAPP-A patients had serial growth scan for other reasons; 23% (n=13) were expected SGA, 9% (n=5) unexpected SGA.
- Low PAPP-A as the only risk factor; 2% (n=2) expected SGA, 11% (n=9) were unexpected SGA Most SGA cases had additional risk factors
- One off scan is unlikely to detect SGA Similar number of missed SGA cases in both groups (9% versus 11%)

	Serial growth scans 56(41%)	Not for serial growth scans 81(59%)
Normal growth	38(68%)	70(86%)
Expected SGA	13(23%)	2(2%)
Unexpected SGA	5(9%)	9(11%)

Conclusion

Within our unit of more than 3000 deliveries a year 9.3% of infants are SGA, mostly born to women classed as 'high risk'. Within our 'low risk' group (PAPP-A not tested) our SGA proportion is only 3.8%. This is much lower than the 13% of SGA cases within our 'low risk low PAPP-A level' group. At present within our unit we are treating women with low PAPP-A levels and no other risk factors for SGA as 'low risk', this audit has identified these women are indeed at higher risk than those with normal PAPP-A levels supporting its introduction as a risk factor into our local SGA guidelines.

P10 | Fundal height measurement accuracy pre-and post training

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Objective
Serial measurement of fundal height is the method of antenatal surveillance of fetal growth in primary care. We wanted to assess the effect of standardised training on the accuracy of measurement.

Method
The multidisciplinary workshops were part of the New Zealand GAP programme and included 50 maternity staff, consisting of senior and junior obstetricians (n=32) and midwives (n=18). The method was according to the Perinatal Institute's recommendations
[1] and included semi-recumbent positioning, bimanual palpation to determine the fundus, and measurement with non-elastic tape to the symphysis pubis along
the longitudinal axis of the fetus. Readings were undertaken by all participants before and after the training.

Results
Each trainee took one measurement at the beginning and another at the end of the training workshop. The results are plotted on the histogram (Fig 1). The range of fundal height measurements before training was +10 to -5 cm compared to the actual reading. After training, the range was reduced to +3 to -1 cm, and resulted in 92% of readings being +/- 1cam from the actual reading.
This study highlighted the importance of training to ensure that all maternity care providers can measure fundal height in a standardised way, thereby improving the accuracy and reliability of antenatal surveillance of fetal growth.

P11 | Audit: Was there adequate utilisation of the customised growth chart and its principles in the detection of all growth restricted babies below the 10th centile, delivered in a small DGH

K Verma | Aseela Dassanayake | Scarborough General Hospital (York Teaching Hospitals), UK

Customised Growth Charts (CGC) have been known to confidentially detect all babies developing growth restriction during the ante-natal period. Its use in ante-natal care aims to reduce perinatal morbidity and mortality rate by ensuring timey detection and delivery of these babies. CGC were introduced in this unit to ensure adequate and appropriate surveillance and a safe and timely delivery. Scarborough hospital is a small district hospital delivering approximately 1700 women annually. This hospital however drains a population with several risk factors leading to growth restriction in utero

Objective
1. To detect the percentage of growth restricted babies under the 10th Centile delivered at Scarborough Hospital over an 8-month period.
2. To estimate the percentage detected successfully during the ante-natal period using customised growth charts
3. To see if customised growth charts are being used to their best advantage.
4. To detect the percentage of growth restricted babies missed during the ante-natal period and the to determine the reasons thereof.

Method
A retrospective analysis of case records between January 2017 to August 2017.

Results
Majority of the babies with growth restriction were detected successfully with a good outcome. Peri-natal morbidity and mortality remained at a low level as compared with the other trusts within the country. In a negligibly small percentage of women where growth
restriction was only detected after the birth of the baby, minor risk factors which could lead to growth restriction were ignored and serial scans and early induction was not offered.

Conclusion
When arranging serial scans and follow up, major risk factors leading to growth restriction were mainly taken into consideration. Minor risk factors should also from a significant contributing factor when arranging serial growth scans for women at a risk of having a baby with growth restriction.

P12 | Is it better to be big or small? - Adverse perinatal outcomes comparison

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Objective
Both ends of the growth spectrum are related to adverse perinatal outcomes. Although different etiologies and complications are connected with SGA and LGA both can lead to unfavorable outcome. Aim of this study is to compare both extreme ends of growth spectrum to answer the question if they are equally dangerous for fetus and neonate.

Methods
This is a secondary analysis Warsaw Singleton Cohort, consisting of all 39905 singleton births from years 2010-2017. All neonates <10th birthweight percentile where considered SGA, >90th birthweight percentile LGA, between 10-90th percentile AGA. Incidence of perinatal mortality and composite neonatal outcome were calculated for each group.

Results
Among preterm neonates being LGA was a protective factor for all analyzed outcomes. For term neonates LGA become a risk factor for intrapartum complications. Being SGA was a risk factor for all analyzed outcomes. Preterm LGA babies had better outcome than AGA, but that was not true for term LGA.

Conclusion
Being SGA is a risk factor for pregnancy and birth complications throughout the whole pregnancy, while LGA may be a protective factor for preterm and risk factor for term infants.

P13 | Accuracy of antenatal ultrasound estimation of fetal weight within South-Eastern Health & Social Care Trust (SEHSCT)

Ryan Lavery | Caroline Bryson | Ulster Hospital Dundonald, South-Eastern Health & Social Care Trust

Objectives
- To objectively assess the accuracy of ultrasound estimation of fetal weight within SEHSCT
- To identify factors which may contribute to increasing or decreasing accuracy
- To make recommendations which will increase accuracy of growth scanning and ultimately improve outcomes
- To enable us to give patients the most accurate assessment of the estimated weight of their baby and put in place the most appropriate plan of care for each woman

Methods
- 100 singleton pregnancies sampled between December 2017 and February 2018
- Data collected from maternity hand-held notes in Delivery Suite, maternity ward and our alongside midwife-led unit using dedicated proforma
- Patients must have been scanned within 14 days of delivery
- Multiple pregnancies excluded
- Validated Perinatal Institute tool used to calculate percentage error between estimated and actual birth weight – allows for time since scan and known expected growth velocity depending on exact gestation

Conclusion
- Overall scan accuracy compares favourably to the previous multicentre study by the Perinatal Institute
- Estimated fetal weight less accurate in women with a higher BMI and using Hadlock 2 Hadlock 4
- calculation more accurate with all scans across all margins of error in our unit

Limitations
- Small numbers of patients within some subgroups led to underpowered study e.g. midwife scans & BMI ≥ 35
- Unable to take into account other cofounding factors affecting scan accuracy e.g. deeply engaged vertex, direct OA position

Results:

% error		+/-10%	+/-15%	+/-20%
Perinatal Institute (<37 weeks)		69.6%	85.6%	91.9%
Perinatal Institute (37+ weeks)		72.8%	89.6%	95.9%
SEHSCT (overall)	n=100	64.0%	85.0%	93.0%
BMI < 35	n=91	64.8%	85.7%	93.4%
BMI ≥ 35	n=9	55.6%	77.8%	88.9%
Consultant	n=26	46.2%	76.9%	92.3%
ST3-7/SpR	n=54	68.5%	87.0%	94.4%
ST1-2	n=14	71.4%	85.7%	85.7%
Midwife	n=6	83.3%	100%	100%
Hadlock 2 (BPD/AC)	n=71	62.0%	81.7%	90.1%
Hadlock 4 (BPD/AC/HC/FL)	n=29	69.0%	93.1%	100%

References
Francis A, Tonks A, Gardosi J; Accuracy of ultrasound estimation of fetal weight at term. Arch Dis Child Fet Neo Ed 2011; 96: Fa61
Hadlock FP, Harrist RB, Martinez-Poyer J; In-utero analysis of fetal growth: A sonographic weight standard. Radiology 1991; 181: 129-133

P14 | Student midwives' perception of the growth assessment protocol (GAP): Preparation for clinical practice

Rebecca Lawes | The University of Plymouth, Devon, UK

Fetal growth restriction (FGR) defined as a fetus who does not reach their predicted growth potential; therefore is a major complication of pregnancy and puts the fetus at increased risk of stillbirth (SB). FGR can be late in gestational onset and can present in an otherwise low risk pregnancy. Surveillance, detection and onward referral of these pregnancies is often the responsibility of the midwife in a community based clinic.

In preparing student midwives for clinical practice, clinical skills sessions are aligned to what constitutes an antenatal appointment. Symphysis fundal height (SFH) is a clinical skill with a rationale for assessing fetal growth and wellbeing.

The GAP protocol has been implemented in all the hospitals in the South West region where Plymouth University students are clinically placed; although there are local Trust variations and interpretations of the protocol. Plymouth University has taught the GAP protocol to all 1st year student midwives since Feb 2016.

Aim
To explore 2nd year student midwives perceptions of the GAP training and its impact on their clinical practice.

Objective(s):
To examine understanding of SGA, increased risks of SB and the importance of the detection and surveillance of a SGA pregnancy, in the context of clinical practice.

Method
semi-structured interviews of five 2nd year student midwives who had received the GAP training in their 1st year and were now in clinical practice. Qualitative methodology using an interpretative phenomenological approach (IPA) to seek to understand the student's experiences.

Conclusion
The findings suggest that the training was 'authentic'. The students felt prepared with the clinical SFH, documentation and plotting skills; the associated terminology for example SGA and the rationale for GAP in preventing avoidable SB. There was however, a level of 'clarity' and 'confusion' in practice with regards to adhering to the GAP protocol.

P15 | Accuracy of fetal weight by ultrasound

F Michelotti | E Romano | M Pureti | Stockport NHS Trust, England.

Objective
Scanning at risk pregnancies for estimated fetal weight (EFW) is now an integral component of strategies to prevent stillbirth and neonatal morbidity.

Recommendations regarding timing and mode of birth are based on EFW plotted on customised growth charts, assuming a level of accuracy in weight estimations by ultrasound. We should be able to inform women of
the accuracy of scanning in their local unit. We aimed to undertake a retrospective audit of growth scans to assess accuracy.

Method
No national standard for assessing the quality of growth scans was identified. Francis (2011) suggested that 72.8% of EFW should be within 10%, 89.6% within
15% and 95.9% within 20% of actual birth weight. Women having a growth scan within 10 days of delivery were identified. 57 patient records were reviewed for demographic factors, delivery details, estimated weight and birth weight.

Results
Average gestation at delivery was 38+2 weeks, with 4.9 days between scan and delivery. 70% of EFW fell within a +/- 10% margin of error. Of scans with a greater than 10% error, 80% were over estimated, average error being 478g. We analysed a subgroup estimated over the 90th centile. Of these, 90% were overestimated with 30% greater than 10%. 11% of babies in this group were over the 90th centile at birth. Average birth centile being 74, and weight 3696g. 75% of these women were electively delivered.

Conclusion
Regular audit of the accuracy of EFW is essential to give women accurate information. We should be able to provide information regarding margins of error
direction of error. Where EFW is above the 90th centile, improvements need to be made in the accuracy of estimation in order for women to benefit from a policy of intervention to reduce risk, as 89% of babies in this group had normal birth weight.

P16 | Identification and management of antenatal risk factors for growth restricted babies in a district general hospital

H Mistry | H Sheehan |E Guyett | Doncaster and Bassetlaw NHS Foundation Trust, South Yorkshire, United Kingdom

Introduction

There is evidence to suggest that fetal growth restriction (FGR) is strongly associated with stillbirth, perinatal morbidity and neonatal death. Confidential enquiries into stillbirths reports 'a third of term, normally formed, antepartum stillbirths are related abnormal fetal growth'. Antenatal detection of FGR varies across England with small for gestational age (SGA) detection rates poorly calculated.

Current RCOG guidance and NHS "Saving Babies Lives" care bundle recommend risk assessment to aid classification of risk and guide surveillance for FGR.

Objective

The aim of this study was to ensure the risk of FGR has been assessed in all pregnancies and surveillance has been carried out appropriately, in compliance with national guidelines. We also identified SGA babies not detected antenatally, aiming to improve future detection rates.

Method

A retrospective audit of electronic records on all women booking in pregnancy during January 2016 at a District Hospital. Exclusion criteria included twin pregnancies and second trimester miscarriage or termination.

Results

A total of 355 patients were included in the study. There were no risk factors for FGR in 142 of these patients, however, 70% had growth scans. Of the babies born, 16.3% (n=58) were SGA (birthweight less than 10th centile on customised growth chart). Antenatal risk factors were identified in 70.6% of these pregnancies (n=41), and 29.4% babies were 'unexpectedly' SGA- ie no risk factors were identified in the antenatal period. 'Major' risk factors were identified in 29% and 'minor' risks were identified in 4.8% of the patients.

Conclusion

Many stillbirths are preceded by FGR and are potentially avoidable through improved antenatal recognition. Correctly identifying risk factors for FGR is complex and risks evolve as pregnancy progresses. Further consensus on risk factors for referral and 'scan schedule' may allow for better allocation of scanning resources.

P17 - withdrawn

P18 | Experience of GROW programme in Causeway Hospital, Northern Ireland

R O'Flaherty | R Hamilton | Causeway Hospital, Coleraine, Northern Ireland

Objective
To complete a review of the maternity notes of all cases of Small for Gestational Age (SGA) babies born in Causeway Hospital during the period of one year and examine the antenatal care provided as well as peripartum outcomes.

Method
We retrospectively reviewed the maternity notes of all the babies delivered between April 2017 and March 2018 who had a birthweight under the 10th centile, identifying the cases from the delivery suite register. Areas examined included the insertion in the maternity notes of a customised growth chart, identification at booking of risk factors for SGA and appropriate care, i.e. serial scans or serial symphysiofundal heights, arranged and the circumstances and mode of delivery.63 cases of SGA were identified during the study period of which the notes of 53 of these were available to review.

Results
All charts had a personalised growth chart present with the correct estimated date of delivery. In 96% of the cases with risk factors present these were identified correctly and the patients were selected for serial growth scans however the majority of cases where SGA was present had no risk factors at booking and were therefore followed with symphysiofundal heights. Where SGA was present and identified, patients were appropriately reviewed and delivered at a suitable time.

Conclusion
Although there have been improvements in detection of SGA as well as broadening the scope of serial growth scans to include a simplified risk stratification tool there is still work to be done in the education of midwives and doctors alike, especially in regards to accurate plotting and measurements. Northern Ireland is unique in the United Kingdom with the majority of scanning being carried out by doctors in routine antenatal clinics and this has come under scrutiny with the ultrasound scanning review focussing on adequate training of junior doctors and accuracy of scanning.

P19 | Screening, detection and management of small for gestational age fetuses at the Liverpool Women's Hospital

C Perry | A Sharp | U Agarwal | Z Alfirevic | Liverpool Women's Hospital NHS Foundation Trust, UK

Background
The UK stillbirth rate is slowly declining at 3.93 per 1000 births. The introduction of Gestation Related Optimal Weight (GROW) charts has helped to reduce this, however despite this the UK is still struggling with some of the highest stillbirth rates in industrialised countries. When a fetus is small for gestational age (SGA) there is an increased likelihood of stillbirth. Identification of those pregnancies at risk of SGA, and the subsequent management of this condition may improve perinatal outcomes.

Method
At the Liverpool Women's Hospital we have developed and introduced four pathways to aid with the screening, detection and management of SGA fetuses in order to standardise the approach to SGA detection with the aim of reducing stillbirth.

LWH SEVERE EARLY-ONSET IUGR MANAGEMENT ALGORITHM

	DV normal	DV PI>95	Absent/reversed DV a-wave
Umb Art PI>95	FU 7 days	FU 3 days	Daily scan, deliver if absent a-wave persists
Umb Art absent	FU 3 days	FU 3 days	Daily scan, deliver if absent a-wave persists
Umb Art reversed	FU 3 days	FU daily	Daily scan, deliver if absent a-wave persists

Generally outpatient management with 2 x week cCTG prior to FMU scan
60 min cCTG at each visit (even if meets sooner)

Indications for delivery
STV <2.6ms less than 29+0, or <3.0ms at 29+0 onwards
Or Persistent Deep Decelerations

If steroids given within 72 hours cCTG criteria should be interpreted with caution

Results
We describe an integrated pathway of SGA screening and management that includes risk factor based screening at booking followed by a risk based ultrasound led SGA detection pathway. Those women with a prior history of early onset SGA (<34 weeks) have serial fetal medicine unit (FMU) scans combined with uterine artery dopplers, whilst those with previous later onset (>34/40) SGA undergo serial growth scans with sonographers. We also detail a structured approach to the management of severe early-onset fetal growth restriction using a combination of fetal Dopplers and cardiotocograph developed during our recent STRIDER trial

Discussion
We describe a standardised approach to the screening, detection and management of the SGA fetus identified at all gestations. By adopting such an approach we anticipate that we will be able to assess the impact upon stillbirth and other complications of SGA.

P20 | Circumvallate placenta and early onset intrauterine growth restriction

Mini Poothavelil | Joanna Patrickson | Sally McCullock | Cumberland Infirmary, North Cumbria University Hospitals NHS Trust, United Kingdom

Objective
Circumvallate placenta has an incidence of 1-2%, and is associated with placental abruption, IUGR, preterm birth and pre-term rupture of membranes. It is difficult to diagnose on antenatal ultrasound. We present a two cases of a severe growth restriction associated with a circumvallate placenta.

Method
Case series

Results
Circumvallate placenta was noted on anatomy scans of both patients in terms of thickened leading edge of the placenta. In the second patient, we noted the membranes were lifted off the edge of the placenta. The first patient had a 28-weeks growth scan which

confirmed early onset IUGR and a posterior placed placenta appeared abnormal and highly vascular. The patient had a Grade 2 caesarean section due to abnormal CTG at 30 weeks gestation. The placental
histology confirmed a small circumvallate placenta and uteroplacental malperfusion. The second patient also had a growth restricted fetus at 28 weeks. She had a Grade 2 caesarean section due to placental abruption at 30 weeks' gestation.

Conclusion
In circumvallate placenta, the chorionic plate is smaller than the basal plate, reducing the functional placental mass and resultant IUGR; sonography is of limited value for its detection and requires focus on placenta contour. We were able to achieve this and plan care for both patients.

P21 | A case of Non-Hodgkin's lymphoma in pregnancy

Fadimatu Aliya Umaru | Shrabani Mukherjee | Queen Alexandra Hospital, Portsmouth, UK

Objective
Non-Hodgkin's lymphoma is rarely diagnosed during pregnancy. Lymphomas occurring in pregnant women are usually of high-grade and tend to involve multiple organs. Despite the usual late diagnosis and aggressive nature of the disease, in most cases the pregnancy could be allowed to continue till term with a positive outcome. Sometimes, the course of lymphoma might accelerate after delivery with rapid deterioration of the condition of the mother.

Method
This is a case review of a 33 year old lady who was diagnosed with Non- Hodgkin's lymphoma whilst she was having her first pregnancy. During the early part of her pregnancy she presented with night sweats, dyspnoea and back pain. She was investigated extensively including ECG, CT pulmonary angiogram, echocardiogram and directed biopsy of the mediastinal mass detected on imaging. She was subsequently diagnosed as having high grade B cell lymphoma consistent with primary mediastinal large B cell (non- Hodgkin's) lymphoma.

Results
Her pregnancy and lymphoma have been successfully managed with a curative intent and involved a multidisciplinary team including Obstetricians, Oncologists and Cardiologists. She was treated with a total of six cycles of R-CHOP chemotherapy (Rituximab, Cyclophosphamide, Hydroxydaunomycin, Vincristine, Prednisolone) with excellent symptomatic response and the improvement was also confirmed by repeat CT scan. She has been offered a Caesarean Section at 34 weeks of gestation in order to commence radiotherapy to the mediastinal mass postnatally.

Conclusion
This case illustrates the importance of the role of a multidisciplinary team in the management of such rare conditions. B cell lymphoma has an incidence of 4% of total cancer cases in the UK and mostly affects people aged between 80 to 84 years. Hodgkin's lymphoma is the most frequent haematological malignancy during pregnancy while non-Hodgkin's lymphoma is quite rare during this period and has an estimated annual incidence of 0.8 per 100,000 women.

P22 | Outcome of large for gestational age fetus in an unselected population in non- diabetic mothers who delivered before 40 weeks' gestation

Tamal Datta, <u>Radhika Viswanatha</u> | Epsom and St Helier University Hospital NHS Trust, United Kingdom

Objective
To assess the birth outcomes in large for gestational age (LGA) in non-diabetic mothers.

Method
Retrospective analysis of 100 LGA cases delivered before 40 weeks' gestation.

Results
Of these 100 deliveries 38 were primigravid and 62 were multigravid mothers. 56% of these mothers were body mass index (BMI) less than 25; 26% were 25-30; 7% were 30.1- 35; 9 % were BMI >35. 79% had growth scan after 35 weeks' gestation and 33% of these scans predicted a fetus greater than 90th centile.
28% had induction of labour. 33% had spontaneous vaginal birth; 15 % delivered by instrumental delivery;

18 % by category 1 and 2 caesarean; 34 % by category 3 & 4 caesarean section. 9 % of these mothers experienced a major obstetric haemorrhage of greater than 1.5L blood loss. 3% experienced 3rd degree perineal tear. 4% of these babies suffered shoulder dystocia.

Conclusion
Our data shows that 82% of mothers were BMI below 30. 52% of these babies were delivered by caesarean section. LGA is associated with of increased risk of maternal and fetal morbidity, however there is no clear guideline regarding management of suspected LGA. Further research on expectant management
versus planned induction of labour could provide more information regarding management options in view of reduction in maternal and fetal morbidity.

P23 | Effect of diabetes mellitus in pregnancy on fetal liver length measurements

<u>**Amira Younis**</u>**, Khaled Alnahas, Waleed Foad, Tamer Yehya |** Suez Canal University, Faculty of Medicine, Egypt

Objectives
This study aimed at detecting the effect of diabetes mellitus in pregnancy on fetal liver length measurements in diabetic pregnant women as an indicator of fetal macrosomia.

Method
80 pregnant women, visiting Suez Canal university hospital's antenatal care clinics. They were divided into two equal groups; diabetic (Study) group and non- diabetic (Control) group. Regular fetal biometry and Fetal liver length were measured sonographically at 28 and 37 weeks of gestation. At each visit, diabetic control was investigated through measuring fasting blood sugar, two hour postprandial blood sugar and HbA1C.

Results
Fetal liver length measurements at 28 weeks were noted to be higher in the diabetic group ranging from 40.4mm to 55mm (mean ± SD = 48.9±3.4) compared to a range from 34.5mm to 49.2mm (mean ± SD = 41.7±3.3) in the non-diabetic group. At 37 weeks, the difference between the two groups was again statistically significant, ranging from 41.6 to 57.8 in the non-diabetic group (mean ± SD = 53.1 ± 3.3) compared to 54.6 to 70.8 (mean ± SD = 63.3 ± 4.5) in the diabetic group.

Conclusion
Fetal liver length measurement during pregnancy could be used to detect the degree of glycaemic control, the need to start medical treatment or adjustment of doses and for the prediction of fetal macrosomia and its possible complications. Further studies are required to create population charts.

P24 | Longitudinal assessment of interventricular septum thickness in monochorionic biamniotic twins complicated by TTTS and treated with laser coagulation of placental anastomoses

Stefano Faiola | **Giulia Pavone** | **Daniela Casati** | **Marcella Pellegrino** | **Mariano Lanna** | **Maria Angela Rustico** | **Irene Cetin** |
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Objective
To investigate the impact of fetal laser surgery (FLS) of placental anastomoses on interventricular septum (IVS) thickness in a cohort of monochorionic (MC) twins complicated with twin-to-twin transfusion syndrome (TTTS).

Method
We made a prospective evaluation of IVS thickness in both donor and recipient twins of MC pregnancies with TTTS, treated at our Institution from 2011 to 2014. We longitudinally measured IVS thickness by M-mode during diastolic phase and converted into zeta score. Ultrasound scan was scheduled 24 hours prior to FLS, then one week and four weeks later, and in the postnatal period. A comparison was made between donor and recipient twins.
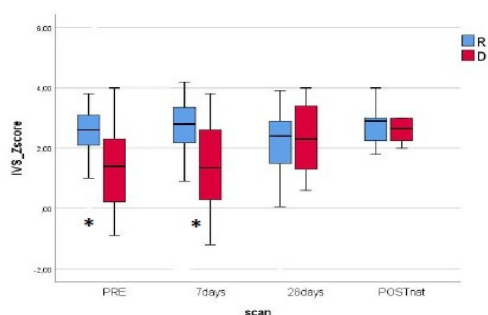
R: Recipient Twin; D:Donor Twin; IVS :interventricular septum

PRE: Before laser coagulation of anastomosis; POSTnat:Postanatal assessement ; * = P<0.005

Results
In the study period, 76 MC pairs complicated by TTTS underwent FLS. IVS thickness measurements were obtained prenatally in both twins of 20 (26%) of these pregnancies by the same operator. In 16 of these 20 cases (80%), IVS thickness was also measured in the postnatal period (5-7 years old, median 6). None of the cases examined had post-operative complications. Before FLS, IVS thickness was significantly greater in the recipient than in the donor twin (p<0.005), with a median Z score above 2. There was no significant change in IVS thickness among recipient twins at prenatal follow-up after FLS, whereas an increase in IVS thickness was observed among the donors. At 4 weeks post-FLS, the median Z score in the donors resulted above 2, as it was for recipients. No difference between the twins was found in postnatal life, but the median Z score was greater than 2 for both twins.

Conclusions
Our data show that recipient myocardial hypertrophy does not resolve in recipient twins subsequent to FLS, whereas there is increasing IVS hypertrophy in the donor. This might be due to cardiac overload in donor twins resulting from laser coagulation of placental anastomoses.

P25 | A possible role of placental growth factor (PlGF) in the management of fetal growth restriction (FGR) with abnormal umbilical artery doppler velocimetry

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Objectives
To evaluate the clinical utility of Placental Growth Factor (PlGF) in the management of Fetal Growth Restriction (FGR) with abnormal Umbilical Artery (UA) Doppler velocimetry.

Method
This prospective cohort study included women with a preconceptional or current risk of placental dysfunction. Our analysis focused on women with FGR and abnormal UA Doppler velocimetry (Pulsatility Index > 95th percentile, absent or reversed end-diastolic flow) between 24 and 34 weeks. FGR fetuses were defined for Abdominal Circumference (AC) < 10th percentile and a mean uterine arteries RI > 95th percentile or growth deflection of two quartiles or more in the third trimester. PlGF was determined in maternal blood at the time of hospitalization for abnormal UA Doppler, using commercially available ELISA kits and analyzed according to pregnancy outcome.

Results
75 singleton pregnancies were included in the study. 40 were complicated by FGR. 11 patients had a pathological Doppler study, namely: 4 women exhibited pathological uterine Doppler, 6 had an absent flow and 1 showed a reversed end-diastolic flow. The level of PlGF was abnormal in all women. 7 out of 8 patients with significantly low plasma PlGF levels (<12pg/mL) had the worst obstetric outcomes: 4 developed preeclampsia, complicated in 1 case by stillbirth; 4 developed cardiotocography anomalies (1 had placental abruption). Cesarean sections were performed in all cases, except in that complicated by stillbirth (6 urgent, 1 elective for absent flow).

Conclusion
Our study shows a correlation between low PlGF levels and Doppler study. A maternal PlGF concentration < 12 pg/mL may be an indicator for low placental reserve. Including PlGF dosage in the surveillance of FGR with abnormal umbilical flow may be useful to define the timing of delivery, especially in the third trimester.

P26 | Preterm infants outcomes: Is more important the weight or the gestational age?

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Gynecology and Obstetrics 2U Sant'Anna Hospital, University of Turin, Italy

Objectives

To define how the intrauterine growth pattern modifies the risk associated with preterm birth.

Method

Retrospective analysis of 535 single pregnancies with preterm delivery <37 weeks at Gynecology and Obstetrics 2U Sant'Anna Hospital in Turin between January 2011 and December 2014. The cases were stratified for gestational age at delivery (<30, 30 + 0 - 31 + 6 , 32 + 0 - 33 + 6, 34 + 0 - 36 + 6) and for growth pattern (IUGR with pathological umbilical dopplerflussimetry, IUGR with normal umbilical and pathological uterine dopplerflussimetry, SGA with normal uterine and umbilical dopplerflussimetry, AGA). The incidence of an adverse composite outcome (at least one of the following: patent ductus arteriosus, acute necrotizing enterocolitis (NEC), food intolerance (FI), intraventricular haemorrhage, preterm retinopathy) and its components to different gestational age and in the different growth patterns were assessed.

Results

Incidence of adverse composite outcome: <34 weeks similar in IUGR vs. AGA, >34 weeks increased in IUGR. Higher incidence of FI in IUGR vs AGA, significant> 30 weeks.

Conclusion

The pejorative effect of IUGR on the adverse composite outcome is evident only in the late preterm. <30 weeks the neonatal prognosis depends on the low gestational age and not on the intrauterine growth pattern. Between 30-36 + 6 weeks the diagnosis of IUGR allows to identify infants at risk of FI so as to be able to start a proper nutritional management and improve the prognosis (incidence of NEC 2.14% vs 7% in the literature).

P27 | Birth weight and nutritional indices prediction using fractional limb volume and estimated fetal weight

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Hospital Sant Joan de Déu, BCNatal, Barcelona, Spain.

Objectives

To determine if Fractional Limb Volume (FLV) has higher precision in predicting birth weight and nutricional indices than estimated fetal weight (EFW).

Method

A prospective cohort was created of 100 singleton fetuses from unselected pregnancies at routine third trimester scan (32-37 weeks). The following biometrical measurements were obtained at each scan, adhering to standardized recommendations: biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL).

EFW was calculated from these four parameters using the Hadlock formula. Additionally, a 3D volume set of the thigh was obtained. Fractional tight volume measurements were manually traced afterwards around the central portion of the femur diaphysis (4D View, GE Healthcare Ultrasound). After delivery, birth weight and the following nutricional indices were obtained: ponderal index, subscapular fold and tricipital fold. Bland-Altman graphs were constructed to evaluate the systematic and random errors of EFW and FLV for BW and the nutritional indices.

Results and Conclusion

Data has not yet been analyzed.

P28 | Labour, maternal and neonatal outcomes in IUGR fetuses induced at term

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Objectives
The primary objective is to investigate whether onset and management of labour, and neonatal and maternal outcomes have peculiar characteristics in term infants who are induced for intrauterine growth restriction (IUGR, defined as fetal growth <5th centile). The secondary objective is to investigate if induction after or before 39 weeks in IUGR fetuses improves the same triggers.

Method
For the primary objective, we selected as control group all the pregnancy with normal estimated fetal growth, induced for prolonged PROM (premature rupture of membranes, >24 h) after 37 weeks. Exclusion criteria included gestational age less than 37 weeks, breech presentation, stillbirth, maternal diseases and fetal anomaly. We collected retrospectively data obtained from Children's Hospital V. Buzzi, from January 2017 and May 2018: 43 inductions for IUGR and 109 inductions for PROM were carried out in the period evaluated. All women were induced with the same method (vaginal dinoprostone up to 24 hours). For the secondary objective, we analyse the data regarding only the 43 IUGR fetuses, dividing them for gestational age: 20 IUGR fetuses induced before 39 weeks and 23 after 39 weeks

Results
No statistically differences were found between IUGR and PROM in term of duration of induction, neonatal (pH, Apgar at 1-5 minutes, NICU admissions) and maternal (mode of delivery, blood loss, morbidity) outcomes. Between the two IUGR groups there was a better trend in neonatal outcomes in inductions ≥ 39 weeks (pH 7.29±0.07 vs 7.25±0.08, and one NICU admission vs 3).

Conclusions
Induction for IUGR seems not to have worse outcomes compared to induction in a group of physiological term pregnancy. In the IUGR group, induced fetuses after 39 weeks seem to have better outcomes, but further studies with larger samples are needed to confirm these hypotheses

P29 | Prediction of pregnancy outcome in extreme early-onset fetal growth restriction: An exploratory prognostic factor study

Lynne Warrander | Emma Ingram | Alex Heazell, Ed Johnstone | The University of Manchester, Manchester, UK

Objectives
To characterise a cohort of pregnancies affected by extreme early-onset fetal growth restriction (eFGR) and identify prognostic factors predicting outcome (live born still living, versus death (stillbirth/ death before discharge)). eFGR was defined as estimated fetal weight/abdominal circumference <3rd centile, or between the 3rd-10th centile with Doppler abnormalities; diagnosis prior to 28 weeks', delivery planned/prior to 32 weeks' gestation.

Method
We performed a retrospective cohort study of 151 eFGR-affected pregnancies from a single UK tertiary maternity unit between 2009-2017. Variables included in analysis: perinatal outcome, maternal characteristics, fetal/placental biometry and Doppler parameters.
Data recorded at time of eFGR diagnosis were used in univariate analysis to investigate associations between maternal/ultrasound prognostic factors and outcome. The relationship between growth trajectory and pregnancy outcome was assessed by mixed level regression.

Results
60% of pregnancies resulted in live birth alive at discharge and 40% in death (60% stillbirth, 40% death before discharge). Maternal characteristics, including booking blood pressure, did not differ significantly by outcome. Gestational age at delivery was 29.7 weeks (SD 1.9) weeks in those surviving, compared to 27.9 weeks (SD 2.3) weeks in those that died (P<0.001); birthweight was 836g (IQR 388g), and 480g (IQR 263g) respectively (P<0.001).

Univariate analysis showed gestational age, estimated fetal weight, amniotic fluid index, umbilical artery end-diastolic flow and placental biometry at diagnosis as potential prognostic factors to predict outcome in eFGR. Pregnancies ending in death had lower estimated fetal weight throughout pregnancy but similar growth trajectory (Figure 1).

Conclusions
Routine ultrasound parameters can be used as prognostic factors in eFGR, both at time of diagnosis, and longitudinally as growth progresses. The factors identified here will be subject confirmatory analysis, prior to using backwards multiple logistic regression to develop a multivariate model to predict outcome in eFGR.
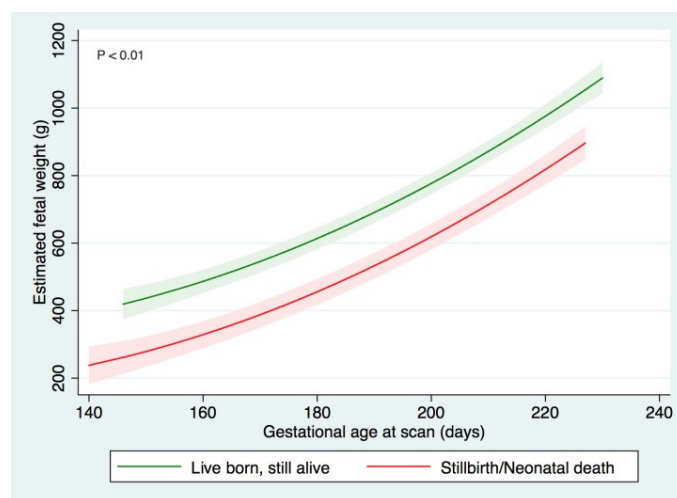

Figure 1: Comparison of growth trajectory by outcome in eFGR

P30 | Treasure hunting: Establishing a Midwife-Led fetal growth assessment (MFGA) clinic to identify the high risk fetus in the low risk pregnancy

B Kelly | H Watson | H Rice | P Gargan | P Whitley | Belfast Health and Social Care Trust, Northern Ireland

Background
We focused our attention on the monitoring of fetal growth and detection and management of suspected FGR/Small for gestational age (SGA) in the low-risk population of women. Surveillance of fetal growth in the 3rd trimester of pregnancy using regular fundal height measurement (FHM), ultrasound (USS) biometry or a combination of both methods continues to be the mainstay for the assessment of fetal wellbeing.

Method
In the past, arranging a 3rd trimester USS to assess growth was a challenge, as the hospital antenatal clinics were often busy and already at full capacity, but also women who were referred often remained within a Consultant-led pathway. The MFGA Clinic was set up in February 2017 to provide a direct referral route for midwives to arrange an USS for low risk women

attending a Midwife-led care (MLC) pathway, where there was a suspicion of FGR/SGA following a FHM. Women referred into the MFGA clinic by midwives, are scheduled to have an USS appointment within the recommended 72 hour period and will have one of the 21 available appointment over 3 afternoons a week.

Results
Over a 13 month period, the clinic received 360 referrals for USS, of which 357 were given appointments for an USS. Fifty three women were identified as requiring serial USS for suspected FGR/SGA following referral to the MFGA clinic, with 30% of babies born (n=16) having a birthweight <10th centile. Of 16 babies born with a birthweight <10th centile, 68% had a birthweight <5th centile (n=11), which includes 1 case of FGR/ SGA identified as requiring urgent review at 36 weeks (birthweight centile at delivery of 0.5) (See Fig 1).

Conclusions
The new midwifery led growth assessment clinic has rapidly established itself as an important part of the service for identifying women at risk. The overall performance of growth screening, in terms of the proportion of FGR/SGA babies who are detected antenatally, depends on adequate resources for third trimester USS, which were often difficult to access for women on an MLC pathway.
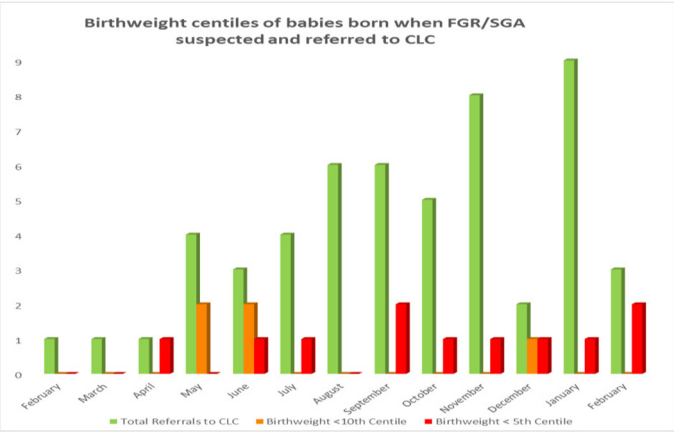
Figure 1

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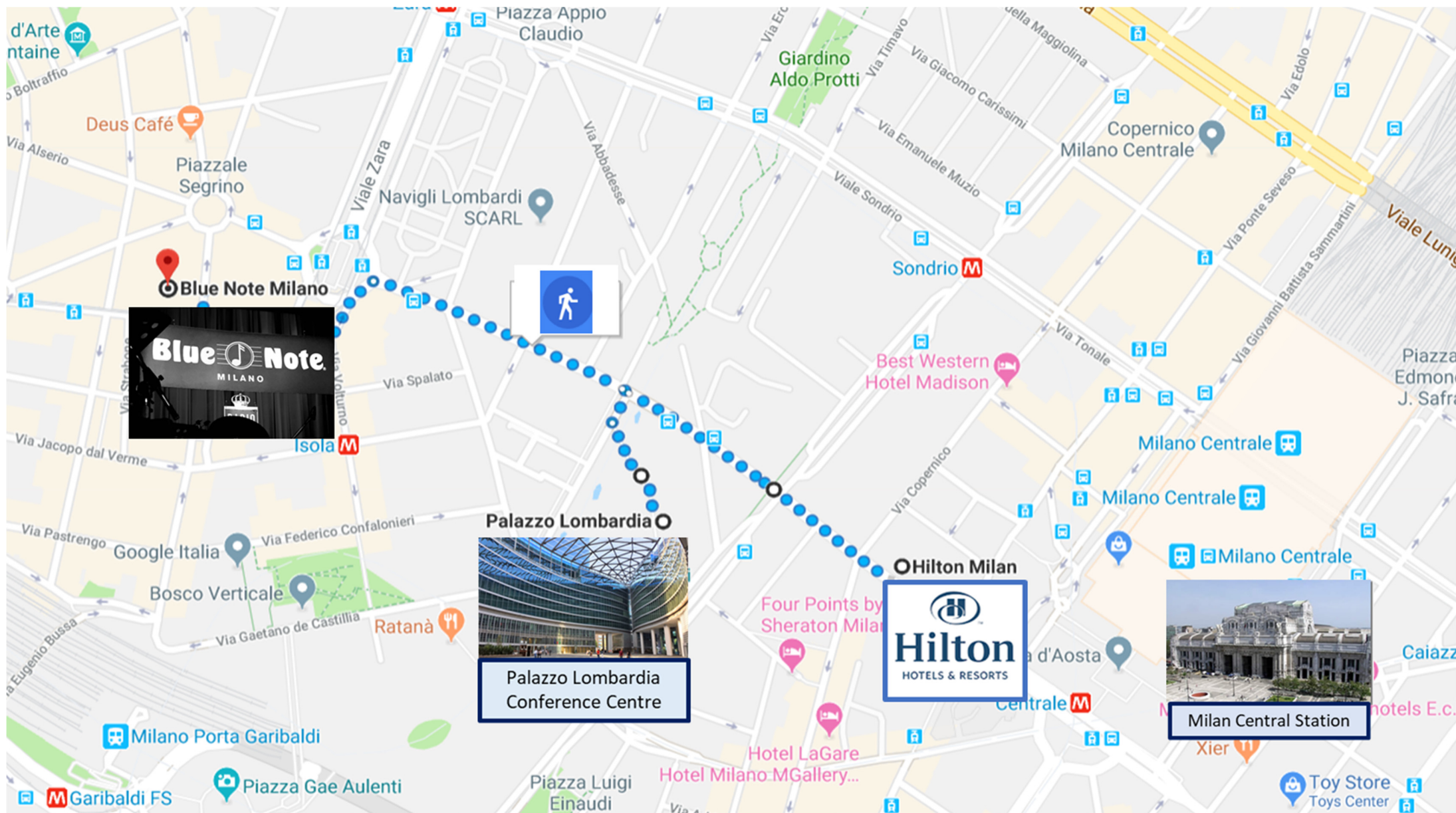
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89

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