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Cardiovascular remodeling in small-for-gestational-age fetuses

Submission date
16/06/2017

Recruitment status
No longer recruiting

Registration date
02/08/2017

Overall study status
Completed

Last Edited
08/08/2017

Condition category
Pregnancy and Childbirth

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Small for gestational age (SGA) is commonly defined by an ultrasound based estimated weight below the 10th percentile. These fetuses were long considered to be small babies with good post birth outcomes. Clinical studies over the last decade have demonstrated that on average SGA have poorer perinatal results, less than ideal neurodevelopment and higher postnatal cardiovascular risks compared with adequate for gestational age (AGA) newborns (newborns born with normal weight). This data suggests that SGA fetuses are in reality forms of late-onset fetal growth restriction (FGR) where placental insufficiency is not reflected in the Doppler. Consequently, there is a need to develop additional markers of poor perinatal outcome allowing identify late-onset FGR among SGA fetuses. Newer findings suggest that FGR induces cardiac changes that could explain the increased predisposition to cardiovascular disease in adult life even in the FGR subgroups with normal fetal Doppler. The aim of this study is to develop a way to predict mean blood pressure of babies at one year of life using parameters of cardiac function and to correlate birth outcome and other diagnostic antenatal parameters.

Who can participate?
Mothers who are at 32 weeks gestational age who are suspected to have a small baby.

What does the study involve?
Participating mothers are followed each for two to three weeks until delivery using ultrasounds, echocardiography, electrocardiography and cardiotocography. During birth, participants receive the normal care. Blood from the umbilical cord is collected and the birth outcomes are recorded. Babies are followed to measure blood pressure and to monitor their heart (using echocardiography and electrocartiography) at 12 months of age.

What are the possible benefits and risks of participating?
Participants may benefit from increased surveillance during pregnancy and their babies first year of life. There are no risks with participating.
Where is the study run from?
Technical University of Munich Department of Obstetrics and Perinatal Medicine, Klinikum rechts der Isar (Germany)

When is the study starting and how long is it expected to run for?
April 2014 to December 2019

Who is funding the study?
Else Kröner-Fresenius Stiftung, EKFS (Germany)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CU_001_300

Study information

Scientific Title
Fetal programming: Evaluation of cardiovascular remodeling in late-onset small-for-gestational-age fetuses and prediction of adverse birth and intermediate-term cardiovascular outcome

Acronym

CURIOSA

Study objectives
Study aims:
1. To develop and evaluate a prognostic model for mean RR at one year of age using parameters of cardiac function (average acceleration capacity, TAPSE, right sphericity index, Strain-rate, aortic distensibility, isovolumetric relaxation time)
2. Evaluate the correlation between the above mentioned diagnostic antenatal parameters and other secondary short- and intermediate-term adverse outcomes; adverse birth outcome [pH <7. 15, operative delivery for fetal distress (fetal scalp blood analysis pH < 7.20 or abnormal fetal heart rate tracing)], abnormal child growth pattern and abnormal metabolic profile. Abnormal cardiovascular outcome at birth and at 12 months of age (aortic intima media thickness > 75th centile and/or RR > 95th centile)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of the Faculty of Medicine of the Technical University of Munich (Ethikkommission der Fakultät für Medizin der Technischen Universität München), 24/07/2014

Study design
Prospective longitudinal observational study

Primary study design
Observational

Secondary study design
Longitudinal study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Fetal programming, cardiovascular remodeling, late-onset intrauterine growth restriction

Interventions
This study is a prospective longitudinal observational study that includes participants consecutively. All cases are seen at the high risk SGA outpatient ward. The source population is recruited from the population under treatment with term fetuses (Gestational age ≥32 weeks at inclusion and born after 37 weeks gestation) suspected of growth restriction defined as an estimated fetal weight or fetal abdominal circumference, measured below the 10th population or customized percentile or a change of abdominal circumference <5mm in 2 weeks (=reduced growth velocity according to Green Top Guidelines).

Diagnostic tools
During pregnancy: Pregnancies complicated with suspected growth restriction are followed each two to three weeks until delivery in a routinue fashion including fetal biometry, advanced ultrasound investigation (including fetal functional echocardiography: Aortic intima media thickness, aortic distensibility, right/Left sphericity index, right/Left cardiac output, tricuspid annular plane systolic excursion (TAPSE), right E/A ratio, tight E´,left myocardial performance index, including IRT measurement, strain/strain rate), feto-maternal Doppler, measurement of amniotic fluid and placenta, and registration of fetal heart rate with fetal ECG (AN 24 MONICA device) and simultaneously with conventional computerised CTG for 40 minutes.

Obstetric ultrasound examinations are performed using Voluson E8 or Samsung HS 70A whereas functional echocardiographic parameter are measured using Samsung HS 70 A. All functional echocardiographic parameters are calculated off-line within four weeks after evaluation according to a standardised protocol based on a trace method with the assistance of commercially available software (TOMTEC ImageArena software). AGA group will be scanned to get 15 controls for each gestational week from 32 to 41 weeks of gestation.

During birth: Participants receive the standard evaluation during labour as do other pregnancies complicated by FGR. Fetal cord blood is taken after cord clamping for metabolic analysis. Placenta is sent to examination by a stated placental pathologist. Birth outcomes are recorded.

Participating infants are followed up for a postnatal cardiovascular evaluation using a blood pressure measurement and echocardiography as well as electrocardiography at 12 months of age.

For evaluation of normal pattern of newer fetal echocardiography parameter and metabolic profile, a group of gestational-age matched (AGA) controls will be examined.

Intervention Type
Mixed

Primary outcome measure
Prediction of mean blood pressure (BP) (in mmHg) at one year of age is measured using the average acceleration capacity (bpm), tricuspid annular plane systolic excursion (mm), right sphericity index, Strain-rate, aortic distensibility, isovolumetric relaxation time (ms)) during pregnancy.

Secondary outcome measures
1. Adverse birth outcomes are measured using
1.1. Mortality defined as intra-uterine death or death before hospital discharge
1.2. Acidosis defined as arterial cord blood pH<7.15
1.3. Apgar at 5 minutes <7
1.4. Admission to NICU
1.5. Operative delivery for fetal distress (fetal scalp blood analysis pH < 7.20 or abnormal fetal heart rate tracing
2. Abnormal child growth pattern are measured using patient records (as defined below the 10th percentile of normal population) during first year of life
3. Abnormal metabolic profile (umbilical cord blood) at birth in comparision to the control group
4. Abnormal cardiovascular outcomes are measured using aortic intima media thickness >75th centile and/or BP > 95th centile at birth and at 12 months of age
5. Prediction of mean blood pressure (BP) at one year of age (mm Hg) using the following

measurements: metabolic profile, fetal functional echocardiographic parameters others than the ones used for primary outcome
6. Correlation of mean blood pressure (BP) at one year of age (mm Hg) and autonomic nervous system [average acceleration and deceleration capacity (bpm)] and antenatal/ fetal functional echocardiographic parameters
7. Correlation of antepartal cardiac function parameters and those at 1 year of life

Overall study start date
01/04/2014

Completion date
31/12/2019

Eligibility

Key inclusion criteria
1. Pregnant women aged 18 and older
2. Fetuses with a gestational age ≥ 32 weeks
3. Suspected of growth restriction defined as an estimated fetal weight or fetal abdominal circumference measured below the 10th population or customized percentile or a change of abdominal circumference <5mm in 2 weeks measured by ultrasound

Participant type(s)
Mixed

Age group
All

Sex
Both

Target number of participants
150 SGA, 150 controls. Inclusion criteria: Fetuses with a gestational age ≥ 32 weeks, suspected of growth restriction defined as an estimated fetal weight or fetal abdominal circumference, measured below the 10th population or customized percentile or a change of abdominal circumference <5mm in 2 weeks measured by ultrasound. Inclusion starts from a gestational age ≥ 32 weeks, however if delivery occurs before term, (<37 weeks gestation), the patient will be excluded.

Key exclusion criteria
1. Born <37 weeks gestational age
2. Known chromosomal and/or structural anomaly
3. Multiple gestation
4. Mothers with cardiac heart disease
5. Mothers' severe systemic disease
6. Antihypertensive medication
7. Antenatal intra-uterine infection

Date of first enrolment
01/09/2016

Date of final enrolment
30/09/2019

Locations

Countries of recruitment
Germany

Study participating centre
Frauenklinik und Poliklinik, Klinikum rechts der Isar of the Technical University of Munich
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Sponsor information

Organisation
Else Kröner-Fresenius Foundation (Else Kröner-Fresenius-Stiftung)

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Sponsor type
Other

ROR
https://ror.org/03zcxha54

Funder(s)

Funder type
Charity

Funder Name
Else Kröner-Fresenius-Stiftung

Alternative Name(s)
Else Kroener-Fresenius-Stiftung, Else Kröner Fresenius-Stiftung, Else Kroner-Fresenius Foundation, EKFS

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Germany

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal

Intention to publish date
31/03/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from PD Dr. Silvia Lobmaier, Section of Obstetrics and Perinatal Medicine of the Department of Gynecology of Klinikum rechts der Isar, Technical University of Munich, Germany

IPD sharing plan summary
Available on request