

CADETTE (Cardiac displacement from third trimester to early childhood)

Fetal heart muscle function in growth retardation.

Significance for the condition of the fetus and for the cardiac function of the newborn and older child

Background

Obstetric ultrasound is an important tool for assessing the fetus during a pregnancy, regarding gestational age, growth and possible malformations. Traditionally, in the routine ultrasound examination, a general assessment is made that the cardiac anatomy is normal. Certain information about the condition of the fetus and placental function is obtained by analyzing flows, for example, in the umbilical cord. An unfavorable intrauterine environment, disturbances in blood flow or substrate supply etc. can result in growth retardation. During a pregnancy with such a complication, repeated considerations are made of the risk of preterm birth versus continued or progressive growth retardation.

New methods for evaluation and treatment of ultrasound data provide improved opportunities to analyze the cardiac muscle function of the fetus.

Our hypothesis is that growth retardation also affects the heart muscle and its function, and that with sensitive methodology, the effect on heart function can be evaluated as an indicator of the general condition of the fetus. Our hypothesis is also that such cardiac function determination can contribute to decision-making when choosing the time of delivery. We also plan to study whether an effect on cardiac function can be demonstrated in newborns and older children who have been stunted intrauterine.

We also want to set cardiac function parameters in growth-retarded and normal fetuses in relation to other data about the fetus/child.

Material and method

This study is a prospective case-control study in which fetuses from normal pregnancies will be compared with fetuses that have intrauterine growth retardation. Parents will be asked in connection with control examinations at the Women's Clinic, where they have been referred due to suspicion of fetal growth retardation. A group of fetuses judged to be growth retarded by specialist ultrasound examination is compared with a control group. The control group is asked among the patients who come for a routine ultrasound in pregnancy weeks 18-20.

Examinations will be carried out in the third trimester and after delivery. During the ultrasound examinations, standardized, moving ultrasound sequences of the heart are saved. Analysis is done offline with Siemens measurement technology (velocity vector imaging, VVI, Siemens medical solutions). With this technique, the chamber wall velocity (velocity), displacement and thickening (strain and strain rate) can be quantified

During the evaluation, the walls of the heart are marked and the software can then produce movement speed and movement in different directions. The fetuses that are part of the control group are examined on 2 occasions, about 4 weeks apart. This takes place during weeks 28-36. For the fetuses that are assessed as growth retarded, image collection is done during the regular ultrasound checks when the pregnancy is followed.

The data we collect about the mother are diseases of the mother and possible treatment. Mother's age, smoking, BMI, possible abnormalities in pregnancy, number of pregnancies and which pregnancy in order. Method of delivery and possible abnormalities during pregnancy such as hypertension, preeclampsia, steroid treatment before birth.

Other data that we plan to collect from the fetus is the flow profile in the umbilical artery, ductus venosus and arteria cerebri media in the fetus. Abdominal circumference, estimated weight. After delivery, check in the journal entries, the child's height, weight, head circumference, gestational age at birth, the acid base of the umbilical vein and the umbilical tree, Apgar score, number of days in hospital for care after delivery, possible complications.

After delivery, we plan to examine the child with ultrasound of the heart at days 1-3, and months 4-6 and at 7 years of age.

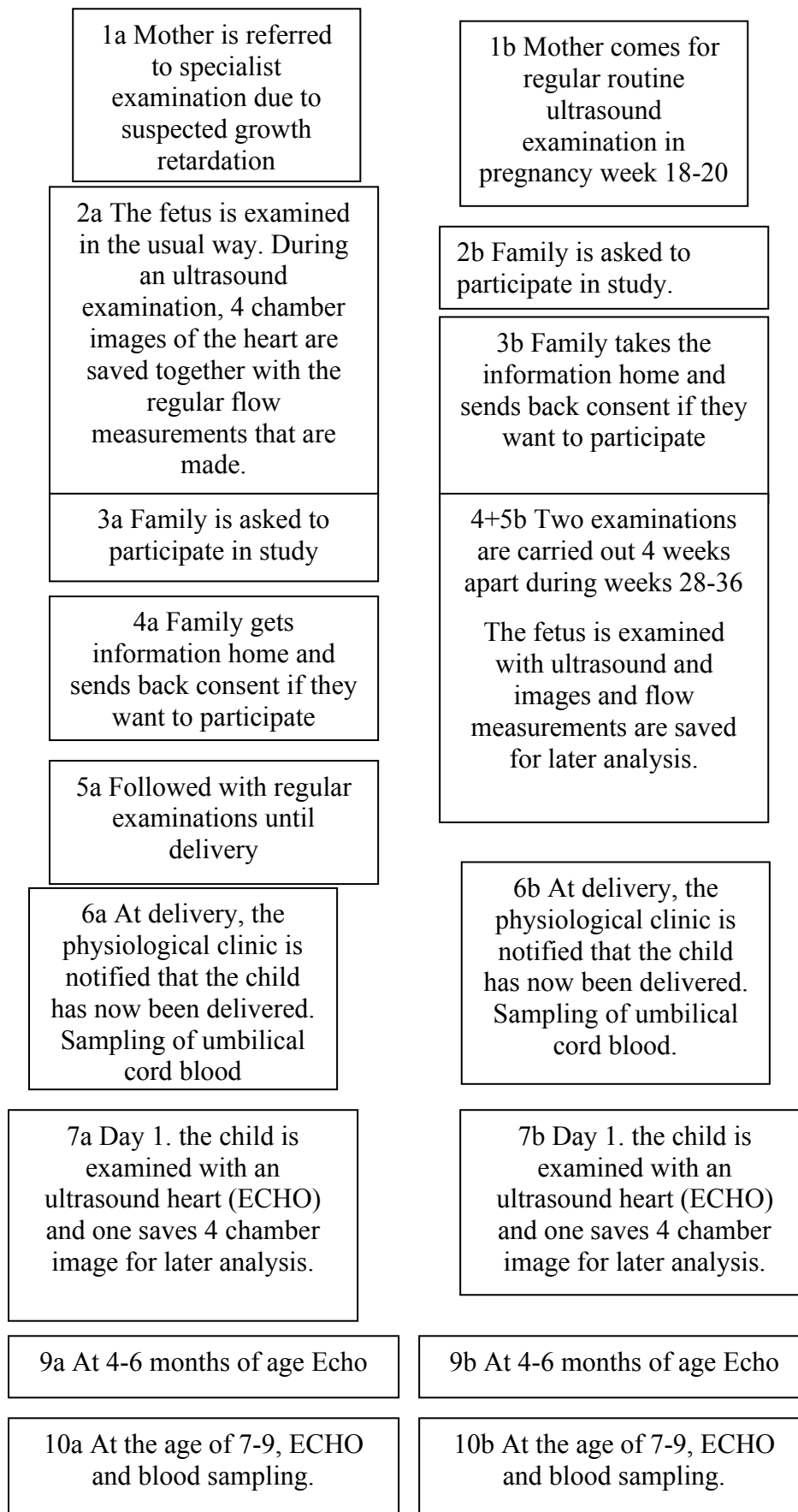
Sampling of umbilical cord blood and blood samples at age 7 where growth factors and cardiac markers are analyzed.

We plan to examine between 20-30 fetuses with growth retardation and 40-60 fetuses in the control group.

Inclusion of research subjects: Growth retardation during routine ultrasound control of pregnancy, verified during specialist control. Pregnancy length is determined based on the Crown Rump Length taken during the first trimester. Growth retardation is defined by a deviation more than 22% from the normal curve at a given gestational length or a growth rate that deviates more than 10% compared to the previous measurement in relation to expected weight.

Inclusion of control subjects: Control subjects are recruited among mothers who come for routine ultrasound check-up at week 18. These are randomly selected and asked

Exclusion criteria in both research subjects and control cases are demonstrated major malformations, twin pregnancy, signs of intrauterine infection during pregnancy, significant or treatment-requiring illness in the mother.



Expected results

We hope to increase knowledge about what relationship exists between growth retardation and heart function in fetuses? What does the development look like over time closest to birth. What is the significance of a possibly early disturbed heart muscle function and in the newborn child.

Data regarding myocardial function assessed with our methodology in growth inhibition are sparsely investigated in the literature. An own pilot study and literature data indicate that with increasing gestational length (and size of the fetus) displacement (movement of the chamber wall) and speed in the chamber wall increase by around 40-50% between the period before week 27 to the period between week 28-30.

In a recently published study where stunted fetuses were followed until delivery and compared to a healthy control group, a significant difference between the stunted fetuses and the healthy controls was shown in some measures.

In child populations from 0-18 years, it has been seen that certain myocardial measurements have changed over time as the children grow.

Growth-retarded children have been shown in studies to have an impact on their heart function while growing up. They also develop cardiovascular disease more easily in adulthood than non-retarded children.

Based on the studies done on stunted fetuses, our hypothesis is that displacement and velocity are reduced by 10% in stunted fetuses compared to normal fetuses.

Powerberäkning Bilaga 1

1. Usefulness of myocardial tissue Doppler vs conventional echocardiography in the evaluation of cardiac dysfunction in early-onset intrauterine growth restriction

Montse Comas, MD; Fàtima Crispi, MD; Rogelio Cruz-Martinez, MD; Josep Maria Martinez, MD; Francesc Figueras, MD; Eduard Gratacós, MD

2. Developments in echocardiographic techniques for the evaluation of ventricular function in children.
Dragulescu A, Mertens LL.

3 Systolic myocardial velocity alterations in the growth-restricted fetus with cerebroplacental redistribution.

Larsen LU, Sloth E, Petersen OB, Pedersen TF, Sorensen K, Uldbjerg N.

Beräkningssida

<http://infovoice.se/fou/bok/statmet/variater/10000042.shtml>

Powercalculation

Artikel 1

Left peak anular velocity during early systole (Left PVS cm/s),

Left peak anular velocity during atrial contraction (Left PVA cm/s)

Right peak anular velocity during atrial contraction (Right PVA cm/s)

Right peak anular velocity during early diastole (Right PVE cm/s)

	Mean Control	Mean Studygroup	SD	2 sided P value 0,05	Power	Sample size	
Left PVS	6,9 (1,2)	5,6 (0,6)	2,0	0,05	0,80	38	
Left PVA	8,5 (1,4)	6,2 (0,7)	2,2	0,05	0,80	15	
Right PVA	10,8 (1,5)	9,1 (1,2)	2,8	0,05	0,80	43	
Right PVE	8,5 (1,3)	6,2 (0,7)	2,5	0,05	0,80	19	

In article 2, which is an overview article on the method, a normal variation of the above-mentioned measurements is specified, a normal variation of approx.

Article 3

In article 3, they have followed Peak systolic tissue velocity (cm/s) in the left and right ventricles

	Mean Control	Mean study group	SD	2 sided P value 0,05	Power	Sample size	If changed to + 20 % in SD
Left ventricle	3,30 (3,05-3,55)	2,41 (1,96-2,86)	0,7	0,05	0,80	10	(SD=1,2) 29
Right ventricle	4,16 (3,88-4,44)	3,98 (3,43-4,53)	1,0	0,05	0,80	485	(SD=1,6) 1241

Study protocol translated from Swedish to English
CADETTE study
Olov Änghagen 2014-03-18

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Jan Engvall Professor Fysiologiska kliniken Universitetssjukhuset, Linköping
Tomas Gottvall Medicine Doktor Överläkare Kvinnokliniken Universitetssjukhuset, Linköping
Eva Nylander Professor Fysiologiska kliniken Universitetssjukhuset, Linköping
Nina Nelson Professor Barnkliniken Universitetssjukhuset Linköping
Olov Änghagen Barnläkare Överläkare Barn och ungdomskliniken Motala/Linköping

Christina Johansson, verksamhetschef för Barn och ungdomskliniken Motala/Linköping
Kjell Jansson, verksamhetschef för Fysiologiska kliniken, US, Linköping
Ann Josefsson, verksamhetschef för Kvinnokliniken, US, Linköping

Contact

Olov Änghagen,
Barnläkare, doktorand
Barn- och ungdomsmedicinska kliniken
Linköping/Motala
Universitetssjukhuset
581 85 Linköping
Tel 010-103 00 00
epost olov.anghagen@regionostergotland.se

Tomas Gottvall
Medicine Doktor Överläkare
Kvinnokliniken
Universitetssjukhuset
581 85 Linköping
Tel 010-103 00 00
E-post tomas.gottvall@lio.se

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NCT02583763

Nina Nelson
Professor, överläkare
Barn- och ungdomsmedicinska kliniken
Linköping/Motala
Universitetssjukhuset
581 85 Linköping
Tel 010-103 00 00
epost nina.nelson@lio.se