Speckle tracking echocardiography in growth restricted fetuses.

Published: 04-02-2022
Last updated: 05-04-2024

Primary objective: To investigate baseline* left ventricle longitudinal strain rate values in a population of growth restricted fetuses and to compare these with a population of appropriate for gestational age fetuses.Secondary objective: To...

Ethical review	Approved WMO
Status	Pending
Health condition type	Foetal complications
Study type	Observational non invasive

Summary

ID

NL-OMON51474

Source
ToetsingOnline

Brief title
STRAIN.

Condition

- Foetal complications

Synonym
Fetal growth restriction, function of the heart

Research involving
Fetus in utero

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Antenatal steroids, Cardiac function., Fetal growth restriction

Outcome measures

Primary outcome

Left ventricle longitudinal strain rate at baseline and after administration of antenatal steroids in growth restricted fetuses compared with appropriate for gestational age fetuses.

Secondary outcome

Other speckle tracking- and conventional hemodynamical Dopplerparameters at baseline and after administration of antenatal steroids in growth restricted fetuses compared with appropriate for gestational age fetuses. These parameters include:

- Measurements on global-, transverse- and basaleapical longitudinal contractility;

- Systolic-, diastolic- and global function parameters: mitral- and tricuspid annular plane systolic excursion, peak early- and late transvalvular filling velocities and left and right myocardial performance index.

- Morphometric parameters (left and right sphericity index);

- Pulsatility index (PI) in the uterine arteries, umbilical artery, middle cerebral artery and ductus venosus.

Study description

Background summary

A promising tool in the evaluation of fetal wellbeing in fetal growth restriction (FGR) is two-dimensional speckle tracking echocardiography (2D STE). In 2D STE, movement of the entire myocardium is analyzed. The method does not use Doppler information, making it less angle dependent, thus attractive to use in the moving fetus.(1) Speckle tracking echocardiography is already embedded in the field of adult cardiology (2) and has the potential for broad application in fetal medicine. However, currently it is poorly integrated since initially the software was only available on dedicated cardiovascular ultrasound machines that were not generally available to the broader medical community. With changes in imaging technology and the availability of machine-independent software, it is now possible to obtain DICOM clips from virtually any ultrasound machine used for fetal imaging and to analyze deformation of the fetal heart with machine-independent software.(3)
One of the most commonly used parameters in 2D STE to assess cardiac function is strain rate, defined as the velocity of the fractional change of the myocardial wall. A recent review by van Oostrum et al. (1) shows that studies on fetal myocardial deformation values (e.g. strain rate) in growth restricted fetuses, give conflicting results. Patey et al. (4) demonstrate that growth restricted fetuses have significantly higher left ventricle longitudinal strain rate compared to pregnancies with normal outcome, suggesting that increased longitudinal myocardial deformation is required under hypoxemic conditions to maintain the same cardiac output as that of normal term fetuses. On the contrary, Crispi et al. (5) and Krause et al. (6) showed no difference in deformation values between growth restricted- and appropriate for gestational age fetuses.
FGR increases the risk of (iatrogenic) preterm birth, hence growth restricted fetuses are prone to receive antenatal steroids to promote fetal lung maturation. Steroids are powerful regulators of vascular tone; if a compensatory cardiac mechanism exists in a growth restricted fetus - as suggested by Patey et al. (4) - administration of steroids might nullify this mechanism. This, in turn, can lead to cardiac decompensation.
In conclusion, no unambiguous evidence exists concerning 2D STE values of cardiac function in growth restricted fetuses compared with appropriate for gestational age fetuses. Through this, it cannot be estimated if the effect of antenatal steroids on cardiac function of growth restricted fetuses is detrimental or beneficial.
The primary objective of this study is to investigate left ventricle longitudinal strain rate in a population of growth restricted fetuses and in a population of appropriate for gestational age fetuses at baseline (e.g., before administration of antenatal steroids). We hypothesize - in line with Patey et al.* (4) - that left ventricle longitudinal strain rate is increased at baseline in growth restricted fetuses compared with appropriate for gestational age fetuses.
The secondary objective of this study is to investigate the possible effect of antenatal steroids on left ventricle longitudinal strain rate between growth restricted fetuses and appropriate for gestational age fetuses (receiving antenatal steroids because of an imminent preterm birth). This effect has - to

our knowledge - not yet been assessed using 2D STE. We hypothesize that antenatal steroids cause a compensatory mechanism - that possibly exists in a growth restricted fetus (identified by an increased strain rate) - to fade.
Given the fact that 2D STE parameters are not yet fully integrated in clinical practice, we will also record conventional hemodynamical (Doppler)parameters before and after administration of antenatal steroids.
The results of this study provide more insight into the baseline left ventricle strain rate and possible changes in left ventricle strain rate after administration of corticosteroids in the two study populations. The study is of essential clinical importance, since the results possibly incite follow-up comparative research in which is investigated which treatment strategy yields an optimal balance between fetal lung development and cardiac performance.

*Our hypothesis is in line with Patey et al.(4) given the application of a stricter FGR definition (estimated fetal weight below the 10th percentile AND Doppler evidence for placental dysfunction) compared with Crispi et al.(5) and Krause et al.(6) (both only estimated fetal weight below the 10th percentile, irrespective of Doppler findings). Also, the study of Patey et al.(4) was conducted more recently (2019) compared to the study of Crispi et al.(5) and Krause et al.(6) (2014 and 2017 respectively).

References:
1. van Oostrum NHM, Derks K, van der Woude DAA, Clur SA, Oei SG, van Laar JOEH. Two-dimensional Speckle tracking echocardiography in Fetal Growth Restriction: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2020;254:87-94.
2. Pastore MC, De Carli G, Mandoli GE, D*Ascenzi F, Focardi M, Contorni F, et al. The prognostic role of speckle tracking echocardiography in clinical practice: evidence and reference values from the literature. Heart Fail Rev. 2021;26(6):1371-81.
3. Devore GR, Polanco B, Satou G, Sklansky M. Two-Dimensional speckle tracking of the fetal heart. J Ultrasound Med. 2016;35(8):1765-81.
4. Patey O, Carvalho JS, Thilaganathan B. Perinatal changes in fetal cardiac geometry and function in diabetic pregnancy at term. Ultrasound Obstet Gynecol. 2019;54(5):634-42.
5. Crispi F, Bijnens B, Sepulveda-Swatson E, Cruz-Lemini M, Rojas-Benavente J, Gonzalez-Tendero A, et al. Postsystolic shortening by myocardial deformation imaging as a sign of cardiac adaptation to pressure overload in fetal growth restriction. Circ Cardiovasc Imaging. 2014;7(5):781-7.
6. Krause K, Möllers M, Hammer K, Falkenberg MK, Möllmann U, Görlich D, et al. Quantification of mechanical dyssynchrony in growth restricted fetuses and normal controls using speckle tracking echocardiography (STE). J Perinat Med. 2017;45(7):821-7.

Study objective

Primary objective:
To investigate baseline* left ventricle longitudinal strain rate values in a

population of growth restricted fetuses and to compare these with a population of appropriate for gestational age fetuses.

Secondary objective:
To investigate the possible effect of antenatal steroids on left ventricle longitudinal strain rate between growth restricted- and appropriate for gestational age weight fetuses (receiving antenatal steroids because of an imminent preterm birth).

*Before administration of antenatal steroids.

Study design

Prospective observational study.

Study burden and risks

The study population consists of singleton pregnant patients undergoing antenatal steroids for medical indication: these patients will receive antenatal steroids regardless of whether they participate in the study or not. Not the research group, but the patients* attending physician decides whether and when treatment with antenatal steroids is initiated. The administration of antenatal steroids is part of standard care and is completely separate from this (observational) study. The Dutch national guidelines are followed in this regard; see guidelines from the Dutch Association for Obstetrics and Gynecology (NL: Nederlandse vereniging voor Obstetrie en Gynaecologie, NVOG) on premature birth (NL: NVOG richtlijn Dreigende vroeggeboorte) and fetal growth restriction (NL: NVOG richtlijn Foetale Groei Restrictie (FGR)).
In the context of the study, ultrasound examination including measurements on cardiac function and other hemodynamical parameters will be performed 3 times in total:
- Before or within the first 8 hours after the first dose of antenatal steroids;
- 24 hours after the second dose* of antenatal steroids;
- 2-4 days after the second dose of antenatal steroids.

Each ultrasound examination takes up circa 20 minutes, but can be combined with an ultrasound examination that is performed on clinical indication. Due to this and the fact that patients receiving antenatal steroids are hospitalized, participation in the study takes logistically seen little extra effort.

Participation in this study will not benefit the pregnant women nor the fetuses personally. The present study investigates the effects of antenatal steroids on cardiac function in growth restricted fetuses; knowledge about these effects may change the view on current policy to administer antenatal steroids to growth restricted fetuses.

The data of the ultrasound scans will be saved in Astraia (ultrasound database). In case an ultrasound scan yields unexpected findings, which are of importance for the pregnant participant and/or the fetus, the researcher will discuss this with the attending physician. If needed, the attending physician will discuss follow-up policy with the pregnant participant and her partner.

Ultrasound examination is not associated with risks for the pregnant patient and the fetus and is therefore the imaging technique of choice for the pregnant patient.

Consent to access the participants* medical file will be asked, only for retrieval of demographic- and baseline characteristics of the participant, as well as pregnancy- and neonatal outcomes. Participation in the study is completed after the maternity period.

*The second dose of antenatal steroids is administered 24 hours after the first dose of antenatal steroids.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Inclusion criteria

- An imminent iatrogenic preterm birth (between 24 and 34 weeks* gestation) of a growth restricted fetus, receiving antenatal steroids in the context of standard care to promote fetal lung maturation. Fetal growth restriction is defined as an abdominal circumference or estimated fetal weight <10th percentile with Doppler evidence of placental dysfunction;

- An imminent preterm birth (between 24 and 34 weeks* gestation) of an appropriate for gestational age fetus, receiving antenatal steroids in the context of standard care to promote fetal lung maturation. Appropriate for gestational age is defined as an abdominal circumference or estimated fetal weight >=10th percentile and no abnormal Doppler findings.

Exclusion criteria

- Age <18 years;
- Fetal aneuploidy;
- Cardiac congenital anomalies in the fetus;
- Suspected or proven congenital infections;
- Administration of the first dose antenatal steroids >8 hours ago before the first (baseline) ultrasound;
- Pregnant patients who are unable to reasonably assess their interests in participating in the study.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2022
Enrollment:	72
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Betamethasone
Generic name:	Betamethasone
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	04-02-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2021-006453-65-NL
CCMO	NL79617.000.21