First trimester differences in ultrasound parameters between pregnancies complicated by uteroplacental insufficiency and uncomplicated pregnancies: an observational study.

Published: 18-10-2021
Last updated: 19-10-2024

Primary objective:To investigate whether there are differences in DV flow measured during the 13-week GUO between pregnancies complicated by UPI and pregnancies not complicated by UPI.Secondary objectives:(1) To investigate whether there are...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Placental, amniotic and cavity disorders (excl haemorrhages)
Study type	Observational invasive

Summary

ID

NL-OMON51959

Source
ToetsingOnline

Brief title
FIT-study.

Condition

- Placental, amniotic and cavity disorders (excl haemorrhages)

Synonym
malfunctioning placenta., Uteroplacental insufficiency

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Biomarkers, Pregnancy, Ultrasound, Uteroplacental insufficiency.

Outcome measures

Primary outcome

Difference in DV flow measured during the 13-week GUO between pregnancies complicated by UPI and pregnancies not complicated by UPI.

Secondary outcome

(1) Difference in uteroplacental Doppler parameters measured during the 13-week GUO between pregnancies complicated by UPI and pregnancies not complicated by UPI.

(2) Explorative biomarker analyses in 13- and 32-week blood samples in pregnancies complicated by UPI and pregnancies not complicated by UPI.

Study description

Background summary

Important pregnancy complications, such as preeclampsia (PE) and fetal growth restriction (FGR) share uteroplacental insufficiency (UPI) as a common pathophysiology. PE and FGR represent a major concern in care for pregnant women and are a leading cause of perinatal morbidity and mortality.(1) For UPI and its subsequent pregnancy conditions, no causal treatment is available, besides adequate fetal monitoring and timely delivery.
Our research group retrospectively demonstrated that the pulsatility index (PI) in the ductus venosus* (DV) measured in the first trimester is elevated in fetuses who later became growth restricted due to UPI (data not published yet). At clinical presentation,UPI is also reflected in the resistance to blood flow in uteroplacental arteries (aa. uterinae and a. umbilicalis). It is unknown

whether these changes are already present in the first trimester. Prospectively evaluating DV flow in the first trimester between pregnancies complicated by UPI and pregnancies not complicated by UPI is needed to validate our observation, and is also needed to investigate whether there are already differences in uteroplacental ultrasound (US) Doppler parameters between these populations. Possibly, the risk for UPI and its high-impact pregnancy complications can be estimated in the first trimester based on US. This is especially interesting concerning pregnancies with a late onset (>=32 weeks of pregnancy) of FGR (as a consequence of UPI) since the accuracy of this diagnosis is poor.
Literature demonstrates that implementing well-known biomarkers (PlGF and soluble fms-like tyrosine kinase-1) in a first trimester screening algorithm for FGR (as a consequence of UPI) substantially improves detection rates.(2) However, it has not been investigated to what extent these biomarkers - next to newly developed, promising biomarkers following array studies - contribute to the accuracy of a first trimester screening strategy based on DV flow and possibly uteroplacental Doppler parameters.
We aim to investigate whether there are already differences during 13-week GUO** in DV flow and possibly uteroplacental Doppler parameters between pregnancies complicated by UPI and pregnancies not complicated by UPI***. Additionally, we want to study first trimester levels of known- and newly developed, promising UPI related biomarkers exploratively between these populations; eventually evaluating to what extent biomarkers possibly contribute to the accuracy of first trimester US based prediction of UPI that develops later in pregnancy. To comment on the most optimal moment for biomarker analyses, we will also collect blood samples during the extra US at 32 weeks* gestation.
Prospectively evaluating this in the first trimester of pregnancy might be a stepping stone towards a 1st trimester screening strategy for UPI based on Doppler parameters and possibly biomarkers. Such a newly to develop screening algorithm would allow clinicians to make a risk assessment, early in pregnancy with the possibility of intervening by means of antiplatelet agents or intensified fetal monitoring; this might prevent or milden the consequences of UPI. Clarifying the additional value of aforementioned first trimester screening strategy could become very valuable, since a 13-week SEO might become part of standard prenatal care.

*The ductus venosus is a shunt between the placental umbilical vein and fetal inferior vena cava.

**In contrast to the 13-week SEO (that is in Dutch: structureel echoscopisch onderzoek, SEO) - which is offered in research setting from September 2021 - there are specific indications for a 13-week GUO (that is in Dutch: geavanceerd ultrageluidsonderzoek, GUO: for indications see section D4). The 13-week GUO is in the context of prenatal diagnostics and falls under the scope of the prenatal care centers.

***UPI is defined as abnormal Doppler parameters in combination with deflection of the growth curve.(3) At the visit for the 13-week GUO, it is unknown if a pregnancy will be complicated by UPI or not. To evaluate whether UPI develops during pregnancy, Doppler parameters
and fetal growth will be evaluated 2 times during the pregnancy: during the 20-week SEO and during an extra ultrasound >=32 weeks* gestation (merely in the context of the study). To confirm UPI postnatally, the umbilical cord, placental disk and membranes will be collected after delivery and examined for severe maternal vascular malperfusion (MVM) lesions according to the Amsterdam consensus group criteria. (4)
Consent to access the participants* medical file will be asked in order to include data on the course of the pregnancy and delivery in the study. Participation in the study is completed as soon as the participant has given birth and the umbilical cord, placental disk and membranes are collected.

References:
(1) Youssef L, Miranda J, Paules C, Garcia-Otero L, Vellvé K, Kalapotharakos G, et al. Fetal cardiac remodeling and dysfunction is associated with both preeclampsia and fetal growth restriction. Am J Obstet Gynecol [Internet]. 2020;222(1):79.e1-79.e9.
(2) Crovetto F, Triunfo S, Crispi F, Rodriguez-Sureda V, Dominguez C, Figueras F, et al. Differential performance of first-trimester screening in predicting small-for-gestational-age neonate or fetal growth restriction. Ultrasound Obstet Gynecol. 2017;49(3):349-56.
(3) Gordijn SJ, Beune IM, Thilaganathan B, Papageorghiou A, Baschat AA, Baker PN, et al. Consensus definition of fetal growth restriction: a Delphi procedure. Ultrasound Obstet Gynecol. 2016.
(4) Khong TY, Mooney EE, Ariel I, Balmus NCM, Boyd TK, Brundler MA, et al. Sampling and definitions of placental lesions Amsterdam placental workshop group consensus statement. Arch Pathol Lab Med. 2016;140(7):698-713.

Study objective

Primary objective:
To investigate whether there are differences in DV flow measured during the 13-week GUO between pregnancies complicated by UPI and pregnancies not complicated by UPI.

Secondary objectives:
(1) To investigate whether there are differences in uteroplacental Doppler parameters measured during the 13-week GUO between pregnancies complicated by UPI and pregnancies not complicated by UPI;
(2) To exploratively study first and third trimester levels of known and newly developed UPI related biomarkers between pregnancies complicated by UPI and pregnancies not complicated by UPI; eventually evaluating to what extent biomarkers contribute to the accuracy of first trimester US based prediction of

UPI.

Study design

Observational prospective study.

Study burden and risks

The study population consists of singleton pregnant women with an indication for a 13-week GUO (for indications see section D4) in the UMCG. The 13-week GUO includes measurements on DV flow and uteroplacental Doppler parameters; in the context of the study we ask permission of the participant for including these data in the research database, analyzing the recorded data and an extra blood withdrawal (EDTA- and serumsample, 2 x 10 ml) for the explorative biomarkeranalyses.

UPI is defined as abnormal Doppler profiles in combination with deflection of the growth curve. At the visit for the 13-week GUO, it is unknown if a pregnancy will be complicated by UPI or not. To evaluate whether UPI develops during pregnancy, Doppler profiles and fetal growth will be evaluated 2 times during the pregnancy:
- During the 20-week SEO (that is in Dutch: structureel echoscopisch onderzoek, SEO).
- During an extra US at >=32 weeks* gestation. During the visit for this scan, again an EDTA- and serumsample (2x10 ml) will be taken for biomarkeranalyses.

The 20-week SEO is part of standard prenatal care in the Netherlands and includes measurements on Doppler parameters and fetal growth. A separate visit is not necessary; in the context of the study we ask permission of the participant for including these data in the research database and analyzing the recorded data.
The extra US at >=32 weeks* gestation is merely in the context of the study. A separate visit of circa 15 minutes is necessary but can easily be combined with a routine prenatal care visit. In general, pregnant women are very much in favour of an extra US investigation.
To confirm UPI postnatally, the umbilical cord, placental disk and membranes will be collected after delivery and examined for severe maternal vascular malperfusion (MVM) lesions according to the Amsterdam consensus group criteria. (1)

Consent to access the participants* medical file will be asked in order to include data on the course of the pregnancy and delivery in the study. Participation in the study is completed as soon as the participant has given birth and the umbilical cord, placental disk and membranes are collected.

References:

(1) Khong TY, Mooney EE, Ariel I, Balmus NCM, Boyd TK, Brundler MA, et al. Sampling and definitions of placental lesions Amsterdam placental workshop group consensus statement. Arch Pathol Lab Med. 2016;140(7):698-713.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Inclusion criteria

Singleton pregnant women referred to the UMCG for an indicated 13-week advanced anomaly scan (that is in Dutch: geavanceerd ultrageluidsonderzoek, GUO) will be included.
Indications for a 13-week GUO are:
- A first degree relative of the fetus, two second degree relatives of the fetus or other, further relatives with a comparable abnormality in the same bloodline are eligible for a 13-week GUO if the abnormality is expected to be visible at the 13-week GUO, that is: anencephaly, abdominal wall defect, spina bifida, megacystis, certain limb defects, holoprosencephaly, body stalk anomaly, diaphragmatic hernia, some congenital heart defects or use of

teratogenic medication of the mother which can cause visible abnormalities in the first trimester;
- Monochorionic twin pregnancy or larger multiple pregnancy;
- Women with a burdened obstetric history, that is: with previous abnormalities of the fetus/child, perinatal death or termination of pregnancy.

Exclusion criteria

Age <18 years;
Chromosomal abnormalities;
Fetal demise during pregnancy, not caused by uteroplacental insufficiency;
Termination of pregnancy;
Congenital anomalies;
Suspected/proven infections;
Pregnant women who are unable to reasonably assess their interests in participating in the study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-12-2021
Enrollment:	300
Type:	Actual

Ethics review

Approved WMO Date:	18-10-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-03-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-05-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-07-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
CCMO	NL79004.042.22