Early detection of cardiovascular risk factors after pregnancy complicated by hypertensive disorders or spontaneous preterm birth

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Observational invasive

Summary

ID

NL-OMON45089

Source
ToetsingOnline

Brief title
HyPreCare

Condition

- Heart failures
- Maternal complications of pregnancy
- Vascular hypertensive disorders

Synonym
cardiovascular disease after hypertensive disorders in pregnancy or after spontaneous preterm birth

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: ICaR-VU

Intervention

Keyword: cardiovascular disease, diastolic dysfunction, preeclampsia, preterm birth

Outcome measures

Primary outcome

Specific targets to identify women suitable for secondary prevention of cardiovascular disease at a relatively young age.

Preeclampsia study part:

-Vascular dysfunction primary outcome: difference in prevalence of the metabolic syndrome and/or circulating microparticles between cases and controls

-Diastolic dysfunction primary outcome: difference in diastolic heart function or heart failure between cases and controls.

Spontaneous preterm birth study part:

-Vascular dysfunction primary outcome: difference in prevalence of hypertension and/or circulating microparticles between cases and controls

-Diastolic dysfunction primary outcome: difference in the E*mean, one of the cardiac ultrasound parameters of diastolic heart function, between cases and controls.

Secondary outcome

Preeclampsia study part:

The secondary outcome measure will be a difference in cardiovascular parameters

and differences in metabolic venous blood measurements.

Spontaneous preterm birth study part:

The secondary outcome measure will be a difference in 10-year cardiovascular

risk, a difference in the prevalence of metabolic syndrome, and differences in

cardiovascular parameters and metabolic venous blood measurements

Study description

Background summary

Cardiovascular disease is the most important cause of death for women in the Western world. Since there is a lack of sensitive and specific tests for women, predicting cardiovascular disease remains challenging. Hypertensive disorders are a common complication of pregnancy. Epidemiological studies have described an association between hypertensive disorders in pregnancy and the development of cardiovascular disease later in life. Recently, we found that women with previous pregnancies complicated by hypertension have increased modifiable risk factors for cardiovascular disease, years after pregnancy compared to women with previous uncomplicated pregnancies. This implies that pregnancy can potentially be a tool as *stress test* unmasking underlying defects, thus identifying women at increased risk for cardiovascular events at young age. Since both women who have a pregnancy complicated by preeclampsia and women with cardiovascular disease show signs of (micro) vascular dysfunction, we hypothezise that both hypertension in pregnancy and cardiovascular disease in later life share pathophysiological features of vascular dysfunction and they might share, at least partly, the same pathomechanism. It is known that endothelial dysfunction is a predictor of cardiovascular disease and has a negative effect on microcirculation and compliance of the great arteries. Without intervention this will eventually lead to increased sytolic blood pressure, left ventricular hypertrophy, impaired coronary perfusion and heart failure and hereby it contributes to morbidity and mortality.

Accumulating evidence from epidemiologic studies now suggests that women with a history of preterm birth are at increased cardiovascular risk as well. Also for spontaneous preterm birth (SPTB) this seems to be the case. It is hypothesized that spontaneous preterm birth has a vascular component, analogous to

preeclampsia. This is supported by shared risk factors indicating abnormal placentation and placental insufficiency in both patients with SPTB and patients with preeclampsia. This implies that pregnancy complicated by spontaneous preterm birth, can potentially be used as a *stress test* as well, thus identifying women at increased risk for cardiovascular events at relatively young age, like hypertensive disorders of pregnancy.

This study focuses on the early detection of cardiovsacular risk factors after pregnancy complicated by hypertensive disorders or spontaneous preterm birth. By screening for risk factors in individuals on a local tissue and systemic level we provide an insight in risk profiles for cardiovascular disease after pregnancy complicated by hypertension or spontaneous preterm birth. This will contribute to a better understanding of the pathophysiological link between both disorders, with the ultimate aim to develop a highly sensitive and specific test to predict an individual*s cardiovascular risk later in life using pregnancy as a stress test and hereby creating opportunities for early intervention and secondary prevention at a relatively young age.

Study objective

We hypothezise that hypertension in pregnancy, spontaneous preterm birth and cardiovascular disease in later life share pathophysiological features of endothelial dysfunction. We will investigate this on two levels including local on tissue level and systemic level:

I: Identification of (micro) vascular dysfunction in women with a history of pregnancy complicated by early preeclampsia or spontaneous preterm birth, in which a proposed higher prevalence of hypertension and the metabolic syndrome will be seen. Besides, the total number of circulating microparticles and the cellular origin of the microparticles will be analyzed.

II: Identification of diastolic heart dysfunction in women with a history of pregnancy complicated by early preeclampsia or spontaneous preterm birth. Diastolic dysfunction is one of the earliest signs of cardiac failure especially in *asymptomatic* women.

Study design

For the identification of the endothelial dysfunction and diastolic dysfunction we designed an observational cohort study. Women will be invited 9-16 years after they gave labor in a University Medical Center in the Netherlands. The cases consist of 1. a group of women with a history of pregnancy complicated by preeclampsia (before 34 weeks gestation) and 2. a group of women with a history of spontaneous preterm birth (before 37 weeks of gestation). The controls will be matched on time of labor (+/- 3 monts), parity, ethnicity and maternal age and are women without any vascular complications of their pregnancy who gave

labor after 37 weeks of gestation in the same University Medical Center in the Netherlands. These women will be screened for the metabolic syndrome and other cardiovascular risk factors by answering a questionnaire, antroprometrics, venous blood samples which will be used in a subpopulation for investigating the number of circulating microparticles and cardiac ultrasonography.

Study burden and risks

Both parts of the study will result in basic knowledge of the pathophysiological process of cardiovascular disease in general and in particularly in women. More specifically this study will result in an increase of knowledge of the relationship between hypertensive disorders in pregnancy, spontaneous preterm birth and cardiovascular disease development in later life.
The methods of research we use (including questionnaires, anthropometrics, venous blood sampling, ultrasonography) are safe and hardly invasive. The venous blood sampling can result in a hematoma or vasovagal reaction.
Hereby most of the burden for the patient will be time related since patients have to invest half a day for the research.
We believe that the scientific gain that this study intends, outweighs the temporarily discomfort that may occur.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Women with a history of early preeclampsia (<34 weeks gestation) who gave labour in a University Medical Center in the Netherlands between 1998-2005 (preeclampsia cases)
Women with a history of spontaneous preterm birth (<37 weeks gestation) who gave labour in a University Medical Center in the Netherlands between 2001-2008 (SPTB cases)
Women with a history of uncomplicated pregnancy who gave labour after 37 weeks of gestation in a University Medical Center in the Netherlandsbetween 1998-2008 and within 3 months delivery of the case (controls)

Exclusion criteria

Multiple pregnancy, chronic hypertension, diabetes mellitus before pregnancy or gestational diabetes during the index pregnancy, cardiovascular disease before pregnancy, renal disease, coagulation disorders, history of pregnancy complicated by fetal anomalies.
For SPTB cases also: iatrogenic preterm birth, uterine anomaly, history of conisation of the cervix
For controls exclusion: no pregnancies complicated by vascular complications.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	07-09-2014
Enrollment:	687
Type:	Actual

Ethics review

Approved WMO Date:	24-04-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-08-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-05-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 26651
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL38972.029.12
OMON	NL-OMON26651