Primary Breast and Colon Cancer: Is Hypertension/Preeclampsia during Pregnancy an Independent Marker for Individual Risk Stratification?

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Hypothesis.In women with preeclampsia endovascular remodeling and invasion of the spiral arteries is less prominent which will result in overwhelming placental oxidative stress and pregnancy failure. Abnormal function of trophoblast and stroma cells...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Observational non invasive

Summary

ID

NL-OMON32468

Source
ToetsingOnline

Brief title
Primary Breast and Colon Cancer and Preeclampsia during Pregnancy

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Breast neoplasms malignant and unspecified (incl nipple)
- Maternal complications of pregnancy

Synonym
Preeclampsia and Cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Breast cancer, Colon Cancer, Preeclampsia, Pregnancy

Outcome measures

Primary outcome

The stroma-percentage in colon and breast cancer with

- pregnancy outcomes: preeclampsia, intrautiene growth r

Secondary outcome

none

Study description

Background summary

Introduction:
Colon and breast cancer are leading causes of cancer-related death in the Netherlands (10%, 2007 CBS stat line). Survival is directly related to detection and the type of cancer involved. However, tumor staging insufficiently discriminates between cancer patients with poor and better prognosis. Recently Mesker et al, described an independent parameter for survival using the stroma-percentage within the primary tumor of colon cancer patients. Patients with high stroma-percentage had a worse survival independent for either tumor stage, tumor status and lymph node status compared to patients with a high carcinoma-percentage. The stroma-percentage is available upon routine HE histological sections. (1,2) For breast cancer this parameter was validated on a set of 600 patients confirming the results of the former performed studies. (de Kruijf et al, submitted to JCO)

Pregnancy is also characterized by tumor invasion: adequate placenta invasion in the uterus is essential in pregnancy outcome.
In normal pregnancy spiral arteries undergo striking remodeling. They change from typical muscular arteries to flaccid tubes with no muscularis or elastic lamina with a diameter at least four times greater than that of non-pregnant

vessels. Shortly after the invasion of trophoblasts into the superficial endometrium, the maternal erythrocytes can be observed within the precursors of the placental intervillous space. Abnormal placentation is evident in preeclampsia. Preeclampsia is a pregnancy specific syndrome that is diagnosed by the new appearance of increased blood pressure and proteinuria. It is a leading cause of maternal mortality in developed countries and increases perinatal mortality up to five-fold. Since its etiology is largely unknown, panoply of pathophysiological abnormalities is described.
Intrauterine growth restriction results also in abnormal placental growth and angiogenesis with a prevalence of 5%.

Ten percent of the pregnant women will have problems with hypertension during pregnanacy, of which 3-7% will develop preeclampsia. Inclusion of women with intrauterine growth restriction will result in at least 5% of the total population of pregnant women to be involved with abnormal placental growth / angiogenesis.
Risk factors for abnormal placental growth / angiogenesis / preeclampsia are advanced maternal age during pregnancy, null parity, multiple gestation, diabetes, SLE and chronic hypertension. Smoking is a protective factor for preeclampsia, not for intrauterine growth restriction.

Hypothesis.
In women with preeclampsia endovascular remodeling and invasion of the spiral arteries is less prominent which will result in overwhelming placental oxidative stress and pregnancy failure. Abnormal function of trophoblast and stroma cells and their interaction play an important role in abnormal placentation.
We hypothesize that preeclampsia during pregnancy is an independent, early clinical genetic marker of invasion for abnormal placental growth, pregnancy outcome including preeclampsia, intruterine growth restriction, abruptio placentae as well as cancer with high stroma formation (and thus worse prognosis).
The expected percentage of women in the population to be investigated would be 5% (12 patients with breast cancer and 17 patients with colon cancer) However, when a genetic predisposition is the cause of abnormal invasion this percentage is expected to be much higher in the series to be investigated.

Study objective

Hypothesis.
In women with preeclampsia endovascular remodeling and invasion of the spiral arteries is less prominent which will result in overwhelming placental oxidative stress and pregnancy failure. Abnormal function of trophoblast and stroma cells and their interaction play an important role in abnormal placentation.
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clinical genetic marker of invasion for abnormal placental growth, pregnancy outcome including preeclampsia, intruterine growth restriction, abruptio placentae as well as cancer with high stroma formation (and thus worse prognosis).
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Study design

Methods.
For women with colon and breast cancer we will determine the stroma-percentage and gain insight in their pregnancy outcomes. Variables including tumor stage, tumor status and smoking will be analyzed in a regression analysis.
Abnormal trophoblast invasion is defined in preeclampsia as well as recurrent abortion, intra-uterine growth restriction and abrutio placentae.

Invitation participation.
Patients included in the databases for breast and colon cancer will receive an invitation to participate in this trial. An inquiry form will be sent to each patient.

Study burden and risks

- Pssible emotional disturbance of these women
- from other research programms interviewing in depth women who have had severe preeclampsie, this was not a major problem

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 breast en colon cancer

Exclusion criteria

< 18 years of age
known death

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-07-2010
Enrollment:	300

Type:	Actual

Ethics review

Approved WMO Date:	12-04-2010
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL30048.058.09