

VU Research Portal

Assessment of Cardiovascular Disease after Hypertensive Pregnancy Disorders

Visser, V.S.

2015

document version

Publisher's PDF, also known as Version of record

[Link to publication in VU Research Portal](#)

citation for published version (APA)

Visser, V. S. (2015). *Assessment of Cardiovascular Disease after Hypertensive Pregnancy Disorders*. [PhD-Thesis - Research and graduation internal, Vrije Universiteit Amsterdam].

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

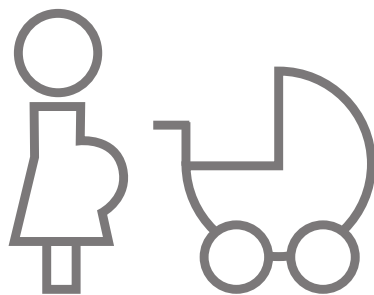
- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

E-mail address:

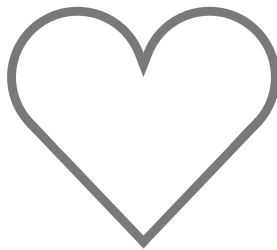
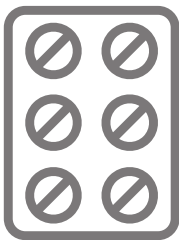
vuresearchportal.ub@vu.nl



ADDENDUM

English Summary

A



ASSESSMENT OF CARDIOVASCULAR DISEASE AFTER HYPERTENSIVE PREGNANCY DISORDERS

Hypertensive pregnancy disorders are common complications during pregnancy. It is well investigated that women with a history of hypertensive pregnancy disorders have a higher risk of development of cardiovascular disease later in life. Therefore a complicated pregnancy by hypertension is a kind of 'stress test' for disease later in life. This hypothesis opens a window of opportunity for preventive measurements in women with a history of hypertensive pregnancy disorders in order to finally prevent cardiovascular disease.

In this thesis we focus on the assessment of cardiovascular disease after hypertensive pregnancy disorders.

This thesis is divided in two parts. In part one we focus on markers after hypertensive pregnancy disorders including homocysteine. Further we describe the association of hypertensive pregnancy disorders and oncologic tumors with focus on impaired stroma invasion. In part two, we describe prediction of cardiovascular disease after hypertensive pregnancy disorders, assessment of awareness of gynecologist and advise in guidelines on this subject. Finally we assessed the lifestyle changes women experienced after they were informed on a higher risk of cardiovascular disease. We conclude this thesis with a general discussion.

Chapter 1 provides an introduction and the outline of this thesis.

Part 1

Chapter 2 presents a systematic review and meta-analyses on non-classic cardiovascular biomarkers after hypertensive pregnancy disorders. These non-classic biomarkers give insight in the link between hypertensive pregnancy disorders and later cardiovascular disease. 21 Studies on 16 non-classical cardiovascular biomarkers were described in this review; 12 studies on 4 biomarkers were included in meta-analyses on ICAM, VCAM, homocysteine and fibrinogen. Only meta-analysis on homocysteine showed a significant higher level of homocysteine in women with a history of hypertensive pregnancy disorders compared to women with normotensive pregnancy. We concluded that homocysteine might play a role in the shared pathogenesis of hypertensive pregnancy disorders and cardiovascular disease later in life. As a consequence homocysteine could be a potential biomarker for assessment of cardiovascular disease after hypertensive pregnancy disorders, however since there was a significant range of homocysteine levels the clinical consequences of these results are limited. Therefore this biomarker was analyzed in more detail in the next chapter.

Chapter 3 describes a study on homocysteinemia after hypertensive pregnancy disorders at term pregnancy. Women with a history of hypertensive pregnancy disorders and women with a history of normotensive pregnancy were included in a follow up study 2.5 years after pregnancy. 2.5 years after pregnancy women were tested for homocysteine levels. We found higher levels of homocysteine levels in women with a history of hypertensive pregnancy disorders compared to women with a normotensive pregnancy. The higher homocysteine levels after pregnancy complicated by hypertension contribute to the conclusion of the previous mentioned systematic review

on non-classic biomarkers that included a meta-analysis that showed significant higher homocysteine levels after hypertensive pregnancy disorders. Furthermore, it could give more insight in etiology of cardiovascular disease after hypertensive pregnancy disorders since homocysteine is a sensitive biomarker for endothelial dysfunction and this endothelial dysfunction is mentioned to be the link between hypertensive pregnancy disorders and cardiovascular disease later in life.

In **Chapter 4** we describe the hypothesis on shared pathogenesis of impaired placentation in preeclampsia and impaired stroma invasion in breast and colon cancer with low tumor stroma rate. This hypothesis is based on the fact that both placentation and tumor stroma invasion share deviating angiogenesis. Therefore we investigated if women with breast or colon cancer with low tumor stroma rate are more likely to have a history of pregnancy complicated by preeclampsia. We found that more women with low tumor stroma rate reported previous preeclampsia, although no significance was reached. Thus, a shared pathogenesis in preeclampsia and breast or colon cancer with a low tumor stroma rate is a possible mechanism in abnormal angiogenesis.

Part 2

Chapter 5 describes a prognostic model of indicators for prediction of chronic hypertension after a pregnancy complicated by hypertensive pregnancy disorders. This prognostic model was created to gain insight for women after hypertensive pregnancy disorders which risk factors are known to develop chronic hypertension and extrapolated cardiovascular disease later in life. We included different indicators known before pregnancy including maternal age, ethnicity, education, parity, family history on hypertension, cardiac event or stroke, hypertensive pregnancy disorders and smoking, indicators from early pregnancy including BMI and blood pressure early in pregnancy, indicators during pregnancy including if preeclampsia or pregnancy induced hypertension was developed, if there was progression to severe disease and highest blood pressure and indicators post partum including small for gestational age neonate and blood pressure six weeks post partum for a complete prognostic model on chronic hypertension. We found that a prognostic model including the indicators; higher maternal age, lower education, negative family history on hypertensive pregnancy disorders, higher BMI at booking, higher diastolic blood pressure at pregnancy intake and a higher systolic blood pressure during pregnancy has a predictive value for chronic hypertension after hypertensive pregnancy disorders. Since this information can be assessed by complete history at subsequent pregnancy at booking and by simple non-invasive testing, we advise to use this information in women with a history of hypertensive pregnancy disorders after validation in order to make assessment of the cardiovascular disease risk in individual women possible.

Chapter 6 states that a high blood pressure six weeks post partum is an important sign for development of chronic hypertension after a pregnancy complicated by hypertensive disease. We found that 40% of women who experienced hypertensive pregnancy disorder still have hypertension six weeks post partum. In women with hypertension six weeks post partum we found a three times higher risk of chronic hypertension compared to women who were normotensive at six weeks post partum (OR 3.3, 95% CI 1.8-6.3). Since a blood pressure measurement is a simple test and these data indicate its advantage in early identification of women with a higher risk on chronic hypertension, we advise to perform a blood pressure measurement in all women with a history of hypertensive pregnancy disorders at six weeks post partum.

Chapter 7 assessed the information and the follow up advice given by gynecologist on the increased cardiovascular risk in women with a history of preeclampsia. In a web-based questionnaire, gynecologists were asked to answer questions on their informative roll on (prevention of) cardiovascular disease in women with a history of both early and late preeclampsia. In women with a history of early preeclampsia, more than half of the gynecologists advised yearly blood pressure measurements and the majority of gynecologists advised on healthy life style adjustments. In late preeclampsia blood pressure measurement was advised in about 40% of the women yearly and about half of the gynecologists advised on healthy life style adjustments. Further, we found an increased advice on healthy life style adjustments in both early and late preeclampsia over time; 2011 compare to 2014. We concluded that the majority of women with a history of preeclampsia are informed on the increased risk of cardiovascular disease and the possible preventive measurements, but that there is still room for improvement. This improvement could possibly be accomplished by development of national and local guidelines with specific recommendations on follow up in women with a history of preeclampsia.

Chapter 8 evaluates the preventive measurements of cardiovascular disease taken by women with a known higher risk on cardiovascular disease after hypertensive pregnancy disorders. For this cohort study we questioned women who participated in a study that evaluated the cardiovascular risk at 2.5 years after pregnancy complicated by hypertension (HyRAS study). For the HyRAS study, a cardiovascular risk assessment was achieved by physical examination and laboratory testing at 2.5 years post partum. If one of the tests performed showed that the women were at higher risk of cardiovascular disease, the women and their general practitioner were informed on this increased risk so that possible intensive monitoring or preventive measurements could take place. One year after the HyRAS study, we questioned the women who demonstrated an increased risk, on interventions changing their cardiovascular risk factors including lifestyle alterations and use of medication. In our study we found that a minority of the women with a history of hypertensive pregnancy disorders and a proved increased risk on cardiovascular disease later in life made alterations to a healthier lifestyle or used medication. These results show a limited awareness in women and their general practitioners on cardiovascular disease risk after hypertensive pregnancy disorders, which could diminish the chance of early detection and possible prevention of cardiovascular events later in life of these women.

Chapter 9 analyses the recommendations in local protocols on hypertension in pregnancy in the Netherlands. For this comparative analysis, local Dutch protocols are gathered and scored on 83 indicators based on key recommendations from the national guideline by the Dutch Society of Obstetrics and Gynecology (NVOG) to evaluate completeness and similarity of local protocols. Results show that the median score of the local protocols was 32.5, which means that 32.5 of the 83 indicators were admitted in the protocol. Some indicators were addressed poorly especially recommendations in the subject of policy during pregnancy. Since total scores of protocols were low, we state that our data indicates that local protocols are inadequate. By improvement of local protocols, quality of care for women with hypertensive pregnancy disorders could improve.

In the **addendum** concerning the analysis of local Dutch protocols, we describe the specific recommendations on follow up of women after a hypertensive pregnancy disorder. In only one of

the local protocols it was stated that women should receive information on their higher cardiovascular risk after hypertensive pregnancy disorders and advise on preventive measurements for cardiovascular disease later in life are stated in none of the local protocols. National guidelines in the Netherlands and abroad did adjust over the past years and include recommendations on follow up of these women at higher cardiovascular disease risk. If local protocols will include these recommendations as well, this could be favorable in awareness and preventive measurements in women at higher risk and therefore decrease cardiovascular events.

Chapter 10 provides a general discussion of the results described in this thesis, and implications for future research. Since cardiovascular disease is still a major cause of mortality and morbidity in women, and hypertensive pregnancy disorders can be seen as a first sign of a higher cardiovascular risk, hypertensive pregnancy disorders followed by preventive measurements for cardiovascular disease can improve women's health. At this point, important insights in prediction of cardiovascular disease after hypertensive pregnancy disorders are gained and more awareness on the increased cardiovascular risk after hypertensive pregnancy disorders is seen, but further research should be performed for the optimal management of women after hypertensive pregnancy disorders to decrease cardiovascular events.