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Awareness of cardiovascular disease in women is increasing and is currently a main topic of the heart associations and foundations worldwide. Although several guidelines underscore sex differences in clinical presentation, treatment, and prognosis, almost no attention is given to a unique risk marker in women: the obstetric history. Large epidemiological studies have confirmed the association between a hypertensive disorder of pregnancy and the risk of future cardiovascular disease. Despite this, physician's awareness of a hypertensive disorder of pregnancy as a risk factor for cardiovascular disease is limited. There seems to be no structured follow-up of women after a hypertensive disorder of pregnancy, and guidelines on cardiovascular risk management after a hypertensive disorder of pregnancy are lacking. It is time to incorporate this easily identifiable risk marker into cardiovascular risk management in women.

The purpose of this review is to identify current barriers and opportunities for cardiovascular risk management after a hypertensive disorder of pregnancy and to suggest a practical approach for risk management.

Why Does Current Risk Prediction Fail in Young Women?

More women die of cardiovascular disease than of any other cause.[1] During the last decade, the focus of primary prevention has widened from individuals with the highest risk and largest short-term benefit (usually older people with previous cardiovascular events) to include individuals at an earlier stage of disease to prevent target-organ damage. Young women have a low absolute risk of cardiovascular disease, and premenopausal women are in general protected. Few women <65 years of age will be considered high risk with traditional risk prediction models for cardiovascular disease, such as the Framingham risk score, the Systematic Coronary Risk Evaluation (SCORE), and the QRISK score.[2-4] Still, women have a lifetime risk of cardiovascular disease of 30% to 40% at 50 years of age.[5,6] Using a 30-year prediction model, women with multiple risk factors (unfavorable lipids, hypertension, and smoking) had a 12% predicted risk of cardiovascular disease at 25 years of age, increasing to 42% at 45 years of age.[7] The obstetric history offers a unique risk marker to identify young women at risk for future cardiovascular disease.

What Is the Risk of Cardiovascular Disease After a Hypertensive Disorder of Pregnancy?

Preeclampsia occurs in 3% to 5% of all pregnancies,[8] a figure comparable to the prevalence of diabetes mellitus at reproductive age, a well-accepted risk marker for cardiovascular disease.[9] The prevalence of any hypertensive disorder of pregnancy is up to 5% to 10% of all pregnancies and rising with the epidemic of obesity.[8] Women with a history of preeclampsia have a doubled risk of stroke, cardiac ischemia, or venous thrombosis within 10 to 20 years after pregnancy.[10,11] Moreover, they have a 4-fold higher risk of chronic hypertension and a 3-fold higher risk of type 2 diabetes mellitus.[10,12] These comorbidities are observed at a relatively young age in mostly premenopausal women. Comparable risk estimates are found in women with a history of gestational hypertension only.[13–16] The risk of cardiovascular disease is further increased in combination with other risk factors of the obstetric history, such as preterm birth or fetal growth restriction. For example, preterm birth and preeclampsia are associated with an 8- to 10-fold higher cardiovascular mortality instead of a 2-fold higher cardiovascular mortality after term preeclampsia compared with term normotensive pregnancies.[17–19]

Which Cardiovascular Risk Factors Are Present Postpartum?

Risk factors that have been observed postpartum in women who had a hypertensive disorder of pregnancy show large overlap with traditional risk factors for cardiovascular disease. Consistent findings after a hypertensive disorder of pregnancy are the presence of an elevated blood pressure, body mass index, and insulin resistance.[20–26] An unfavorable lipid profile is frequently observed postpartum; low high-density lipoprotein cholesterol (≤1.29 mmol/L) is present in ≈40% and high triglycerides (≥1.7 mmol/L) in ≈20% of all women with a history of early onset preeclampsia.[27,28] Although lipid abnormalities are frequently present,[20,29,30] several studies did

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not find appreciable differences compared with women with previous normotensive pregnancies.[21,23,25,26,31] A wide range of other cardiovascular risk markers have been identified in case–control studies, such as raised circulating C-reactive protein tumor necrosis factor-α, vascular cell and intracellular adhesion molecule, adiponectin, attenuated flow-mediated dilatation, and increased intima-media thickness.[20,21,32,33] A significant consideration is that several measures in women with a history of a hypertensive disorder of pregnancy may still fall within a so-called normal range. Blood pressure abnormalities may not be detectable by routine blood pressure checks but only by use of 24-hour ambulatory blood pressure measurement; even then these blood pressure average levels will still seem to be normal although they are higher than in women who had had normal pregnancy.[26] The same holds true for other cardiovascular risk markers. The key message is that we need to define what is normal for blood pressure, lipids, and insulin resistance measures in young women at reproductive age.

What Is the Current Clinical Practice?

The obstetric clinic is often the first clinic where a woman's blood pressure is measured.[34] For many years, preeclampsia was considered a syndrome of pregnancy that completely resolves after pregnancy, and women are generally referred back to their general practitioner. Nowadays, the risk of cardiovascular disease may be communicated to the women at discharge shortly after delivery or at a 6-weeks postpartum evaluation at the obstetric outpatient clinic. After that, if cardiovascular risk counselling is given later in life, the history of a hypertensive disorder of pregnancy is often not taken into account. Most guidelines and textbooks on prevention of cardiovascular disease in women do not mention the obstetric history as a risk factor. In a hospital survey, only 5% of all internists asked about preeclampsia when taking the medical history of a woman.[35] The development of chronic hypertension after preeclampsia is frequently not adequately monitored; 21 years after preeclampsia approximately one third of the women was hypertensive, but this was only diagnosed in half of them.[36]

Recently, the latest guideline of the American Heart Association for the prevention of cardiovascular disease in women has included a hypertensive disorder of pregnancy as a major risk factor for cardiovascular disease.[1] They recommend postpartum referral by the obstetrician to a primary care physician or cardiologist, so that in the years after pregnancy risk factors can be carefully monitored and controlled without further specification. Until now, it has been clinic- or even clinician-dependent whether and how cardiovascular risk assessment is performed after a hypertensive disorder of pregnancy. A few clinics have started with postpartum cardiovascular risk counseling in a structured manner ≈3 to 6 months postpartum, usually in a multidisciplinary setting involving obstetricians, internal medicine specialists, and cardiologists.[37]

What Are Barriers to Include the Obstetric History in Cardiovascular Risk Counseling for Women?

Currently, it is unclear whether a hypertensive disorder of pregnancy is an independent risk factor for cardiovascular disease or whether this is all explained by traditional cardiovascular risk factors. Tools are lacking to give an individualized risk estimate of cardiovascular disease after a hypertensive disorder of pregnancy. A possible strategy to overcome the latter is not to use a classic risk prediction model but to calculate the risk as if the woman was 60 years of age[38] or to use a 30-year or lifetime risk prediction model.[6,7] However, this does not take the obstetric history into account. Most guidelines will use classic risk score models to identify high-risk women who need an intervention or treatment. We do not know whether criteria for treatment should be more strict for these women, as for those with diabetes mellitus. Despite these uncertainties (Table 1), the least we can do is to offer cardiovascular risk management based on existing guidelines about cardiovascular risk counseling in asymptomatic people in the postpartum period.

What Opportunities Does a Structured Postpartum Cardiovascular Screening Program Have to Offer?

A structured cardiovascular screening program, as proposed in Table 2, ensures adequate follow-up after a hypertensive disorder of pregnancy. It creates a moment to explain and discuss in detail the increased risk of cardiovascular disease. Such a screening will identify women with comorbidities, such as hypertension, obesity, type 2 diabetes mellitus, and hyperlipidemias. Moreover, it allows adequate referral of women with signs suggestive of underlying disease, such as persistent proteinuria or secondary hypertension. Most importantly, it gives the opportunity for primary prevention of cardiovascular disease by promoting a healthy lifestyle and offering tailored lifestyle interventions.

Motivational Factors for a Healthy Lifestyle

Several factors unique to this specific group of women are present to motivate them to adopt a healthy lifestyle (Table 3). Group interviews revealed that women are more aware of the importance of health after a complicated pregnancy and are motivated to adjust their lifestyle.[39] A healthy lifestyle is not only beneficial for their own future health but may also

Table 1. Unanswered Questions

- Further research should answer whether a hypertensive disorder of pregnancy is an independent risk factor for cardiovascular disease.
- There are no tools available to make an individualized risk estimate of cardiovascular disease that includes the obstetric history.
- We do not know the optimal timing and frequency to test for traditional cardiovascular risk markers after a hypertensive disorder of pregnancy.
- It is unclear whether to use traditional cutoff levels for blood pressure, glucose, and lipids to define abnormalities or whether normal ranges for young women with previous normal pregnancies should be developed.
- The role of screening for additional cardiovascular risk markers or target-organ damage to predict future cardiovascular disease should be clarified in this specific group of women.
- At present, there are no randomized, controlled trials in young people unequivocally demonstrating the benefit of antihypertensive or lipid-lowering medication on cardiovascular disease risk.
- Upcoming trials should prove the efficacy of lifestyle interventions in the reproductive age on the next pregnancy outcome and long-term cardiovascular health.

Table 2. Example of Cardiovascular Risk Management After a Hypertensive Disorder of Pregnancy

Time	Specialty	Measurements	Care
6 weeks postpartum	Obstetrician	1. Blood pressure	• Counseling about cardiovascular risk • Referral for screening 3-6 months postpartum
3-6 months postpartum	Multidisciplinary team preferred	1. Blood pressure, preferably including 24-h ABPM or automated home blood pressure 2. Screening for metabolic abnormalities; body mass index, fasting glucose, lipid profile 3. Dipstick for albuminuria and proteinuria	• Estimation of cardiovascular risk based on obstetric history (gestational hypertension, gestational diabetes mellitus, preeclampsia, preterm birth, fetal growth restriction) and concomitant risk factors (smoking, family history, hypertension, metabolic abnormalities) • Individualized lifestyle advices for all women; family centered; consider local lifestyle intervention programs • Individualized advice about next pregnancy; possible benefit of a healthy lifestyle on recurrence risk • Pharmacological treatment of high blood pressure and type 2 diabetes mellitus is indicated; treatment of lipid abnormalities can be considered
	Referral to specialist	1. In case of signs suggestive of secondary hypertension 2. In case of persistent albuminuria	• Screening for underlying secondary hypertension • Screening for underlying renal disease
Ongoing care	General practitioner	1. Yearly weight and blood pressure 2. Every other year glucose and cholesterol	• Lifestyle counseling • Weight management • Detection of the development of chronic hypertension, type 2 diabetes mellitus, or dyslipidemias

ABPM indicates ambulatory blood pressure monitoring.

improve the outcome of future pregnancies and the lifestyle of her partner and children. This is especially relevant as women with a hypertensive disorder of pregnancy give often birth to small for gestational age infants, who themselves have a higher risk of later cardiovascular disease.[40,41] Women gain on average 2 kg of weight after each pregnancy, and this is even more after a hypertensive disorder of pregnancy.[42,43] Interpregnancy weight gain is associated with a doubled risk of gestational hypertension, gestational diabetes mellitus, or preeclampsia during the next pregnancy.[44] Therefore, the postpartum period should be an important target for weight management and lifestyle counseling.

What Is the Benefit of a Healthy Lifestyle?

Lifestyle interventions during reproductive age have potentially a large effect on future cardiovascular health. The benefit of a healthy lifestyle is evident from large epidemiological studies such as the INTERHEART study.[45] The adverse effect of hypertension, smoking, and diabetes mellitus on cardiovascular disease was larger in women and young people than in men and elderly people.[45–47] In a cohort of young women, a favorable cardiovascular risk profile (low blood pressure, low cholesterol, nonsmoking, and nondiabetic) was associated with 80% lower cardiovascular mortality than in women with >2 of these risk factors.[48] The lifetime risk of cardiovascular disease at 50 years of age in women with optimal risk factors was only 8%, in contrast to a 50% risk in women with >2 risk factors based on long-term follow-up of the Framingham cohort.[5]

Table 3. Motivational Factors for a Healthy Lifestyle After a Hypertensive Disorder of Pregnancy

- The hypertensive disorder of pregnancy is a wake-up call.
- A healthy lifestyle reduces the risk of future cardiovascular disease.
- The next pregnancy is likely to benefit from a healthy lifestyle because it may reduce the recurrence of a hypertensive disorder of pregnancy.
- All family members are likely to benefit from a healthy lifestyle, which is particularly important for an infant born premature or small for gestational age.

What Is the Effectiveness of Postpartum Lifestyle Interventions?

Several lifestyle intervention trials specifically designed for women with a history of a hypertensive disorder of pregnancy are currently listed in clinical trial registries. Some preliminary reports indicate that women after preeclampsia are willing to participate in such an intervention program and will have improved weight, lipid profile, and vascular function after 3 months.[49,50] However, in general the effectiveness of lifestyle interventions is often disappointing. Even in structured programs with frequent contact moments for support, the effect on, for example, weight loss is usually modest and difficult to pursue in the long term. Lifestyle interventions in the postpartum period failed to show a positive effect in approximately one third of the trials reported in a meta-analysis.[51] On the other hand, other lifestyle interventions have proven to be effective, especially for clinical outcome variables, such as blood pressure, glucose, or lipid control.[52,53] Such outcomes can be used as motivational tools to convince and motivate women to adhere to their new lifestyle. The potential effect of lifestyle change on the next pregnancy is evident from a study in obese women who had bariatric surgery as intervention, showing impressive reductions in the recurrence of hypertensive disorders in pregnancy.[54] Upcoming research should prove the (cost) effectiveness of postpartum lifestyle interventions in women with a history of a hypertensive disorder of pregnancy on the outcome of a subsequent pregnancy and long-term cardiovascular health.[51]

What Are Indications for Pharmacological Treatment?

Blood Pressure–Lowering Treatment

One in 4 women will develop chronic hypertension after a hypertensive disorder of pregnancy.[10] Still, there is no consensus about the management of hypertension in the immediate postpartum period and as a consequence when to discontinue or pursue the adopted management.[55,56] Long-term blood pressure–lowering aims to reduce the risk of cardiovascular disease, but this effect has not been unequivocally proven in young people. In the general population, systolic blood pressure lowering of 10 mm Hg reduces the risk of stroke by 40% and of coronary heart disease by 20% in both primary and secondary prevention.[57] The European Society of Hypertension and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recommend the treatment of a blood pressure ≥140/90 mm Hg in adolescents.[58,59] In line with this, after a hypertensive disorder of pregnancy, blood pressure–lowering treatment is recommended above this threshold. The possible benefit of treatment of high-normal blood pressures should first be evaluated in clinical research.[60]

Lipid-Lowering Treatment

According to the Third Adult Treatment Panel, pharmacological treatment is indicated in all women when low-density lipoprotein is >4.9 mmol/L, in women with ≥2 cardiovascular risk factors when low-density lipoprotein is >4.1 mmol/L, lowering this threshold in women with a 10-year cardiovascular disease risk >10% to low-density lipoprotein >3.4 mmol/L.[61] Accordingly, <5% of all women with a history of early onset preeclampsia will fulfill the criteria for lipid-lowering medication.[28] Meanwhile, the American Heart Association recommends treatment of low-density lipoprotein >4.1 mmol/L already when only 1 major cardiovascular risk factor is present, including a hypertensive disorder of pregnancy.[1] In the general population, there remains debate about the efficacy of lipid-lowering treatment for primary prevention of cardiovascular disease.[62,63] Hence, more research is necessary to decide on which cutoff level to use for treatment in this specific group of women. For now, lipid-lowering treatment can be considered after a hypertensive disorder of pregnancy if 1 of the above criteria is fulfilled.

Glucose Control

Approximately 1 in 7 women will develop type 2 diabetes mellitus in the years after a hypertensive disorder of pregnancy.[64] Pharmacological treatment of overt type 2 diabetes mellitus is indicated. However, there is no consensus with respect to how prediabetes mellitus (impaired fasting glucose or glucose intolerance) is to be managed. A recent meta-analysis indicates that lifestyle interventions seem more effective than pharmacological interventions in preventing diabetes mellitus.[65]

What About Aspirin for Stroke Prevention?

The Women's Health Study provided evidence for the efficacy of aspirin in the primary prevention of stroke in women, although the largest benefit was for women >65 years of age.[66] Possible benefits of aspirin use should be carefully balanced against the increased risk of gastrointestinal bleeding. Future research should explore the possible benefit of aspirin for primary prevention in this specific group of women.

In summary, we recommend a postpartum cardiovascular risk assessment for all women with a hypertensive disorder of pregnancy to give these women the best possible long-term outcomes. We do realize that more research is needed to give definitive answers about the timing of screening, the markers to be tested, and the cost-effectiveness of such a program. Moreover, the development and implementation of effective lifestyle intervention programs in the postpartum period are crucial. For now, cardiovascular risk management after a hypertensive disorder of pregnancy should be on the basis of guidelines for cardiovascular risk assessment in asymptomatic people. Key points of this review are presented in Table 4. We hope that this review encourages obstetric units to develop a clearly defined local protocol concerning postpartum cardiovascular screening in conjunction with local general practices.

Table 4. Summary Points

- There seems to be no structured follow-up of women after a hypertensive disorder of pregnancy, and guidelines on cardiovascular risk management after a hypertensive disorder of pregnancy are lacking.
- Currently used 10-y risk prediction models for cardiovascular disease are likely to underestimate the risk of cardiovascular disease in this group of young women.
- Any physician performing cardiovascular risk counseling in women should be aware of the importance of obstetric risk factors for later cardiovascular health.
- A postpartum cardiovascular risk screening should be based on guidelines for cardiovascular risk assessment in asymptomatic people.
- Lifestyle interventions in the reproductive age may reduce prolonged exposure to cardiovascular risk factors, may positively influence the next pregnancy, and contribute to a healthy lifestyle for the partner and children.

Disclosures

None.

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