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Cardiovascular screening and prevention strategies in women with history of preeclampsia: one size does not fit all

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Preeclampsia (PE), a pregnancy specific disorder resulting in increased blood pressure, affects 2% to 8% of all pregnancies and has been associated with the occurrence of the major cardiovascular diseases (CVD) later in life[1-4]. Women with history of PE, compared to women with normotensive pregnancies, have an increased risk of hypertension, dyslipidemia, renal dysfunction, diabetes and CVD[1-4] . Also, the growing evidence has suggested increased cardiometabolic risk in the offspring exposed to hypertensive disorders of pregnancy (HDP)[5-7]. A recent population-based cohort study, including data from 1.3 million women, examined the association between HDP and increased CVD risk as early as 1 year after the index pregnancy[8]. The study showed that HDP (eclampsia, PE, gestational hypertension) could be used as an opportunistic screening tool to identify women at higher risk of future cardiovascular events.

In their study published in the European Journal of Preventive Cardiology, Lagerweij et al.[9] studied a life-long impact of preventive cardiovascular screening strategies initiated after women experienced PE during pregnancy. In this microsimulation study, screening benefits were assessed in terms of costs and quality-adjusted-life-years (QALYs) and incremental cost-effectiveness ratios (ICERs) compared with no screening. In brief, in a hypothetical cohort of 2,000 women entering the simulation model at the average age of a first pregnancy in the Netherlands (i.e. 30 years old), authors reported that early (i.e. starting in women's 30s and 40s) and repeated (in 5-year interval) CVD risk screening and risk-based lifestyle interventions after PE may potentially reduce CVD risk and improve health outcomes. Yet, preventive CVD risk screening and risk-based lifestyle interventions in women with history of PE and with Framingham Risk Score (FRS) of 2% or 5% (used as absolute risk threshold for intervention) were not cost-effective.

Currently advised annual checkups for women with history of PE[10] will most likely fail to identify women in increased long-term CVD risk, mainly due to young age of women in the first years after the pregnancy. To date, very little information is available on trajectories of cardiovascular risk factors and development of CVD in women with HDP, as well as there is lack of studies investigating biomarkers that could be used in this subgroup of women to develop better screening, risk stratification and preventive strategies to reduce cardiovascular risk. Women-specific factors (e.g. age at menarche, number of pregnancies, gestational diabetes, PE and polycystic ovarian syndrome) have been associated with risk of developing CVD[11-13], yet the CVD risk scores including women-specific factors as risk predictors are not thorough-examined and available. Therefore, CVD risk stratification (i.e. using FRS[14] or HeartScore[15]) in young women soon after pregnancy most likely will not properly identify women in increased CVD risk during the first decade (or two) after pregnancy. Indeed, in a study done by Lagerweij et al.[9] the recommended generic CVD risk threshold (FRS>10%) was too high, yielding hardly any women in the high cardiovascular risk category, therefore, authors decided to apply lower risk thresholds of FRS>2% and >5%. A screening strategy starting at 30 years of age and with a 5% FRS threshold resulted in the largest decrease in CVD events, i.e. 3.2% of all life-long CVD events can be prevented by screening every 5 years. The number of women needed to screen to prevent one CVD event was largest when preventive screening starts at age 30 with a risk threshold of 2%[9]. These results may suggest that the use of women-specific cardiovascular risk assessment tool at baseline could better identify HDP women at increased cardiovascular risk and therefore, the number of women to be screened could be lower. There is a need to develop women-specific CVD risk prediction models, which will be able to better classify cardiovascular risk in early postpartum period and during reproductive age. Proper risk stratification may be a crucial first step to be able to create feasible and cost-effective preventive strategies in women with history of HDP.

The latest International Society for the Study of Hypertension in Pregnancy (ISSHP) guidelines recommended annual follow-up of all women after HDP focusing on assessment of CVD risk factors, education regarding the long-term CVD risks associated with HDP, and counseling regarding lifestyle modification (exercise, diet, body weight)[10]. Up to date, there is a paucity of intervention studies evaluating the effectiveness of potential strategies to decrease the risk of future cardiovascular events in women with history of hypertensive disorders of pregnancy. A randomized controlled trial (RCT) of 151 women assessed an online education program (vs. general information offered to control group) to increase awareness of risk factors and personalized phone-based lifestyle coaching in women who had a PE affected pregnancy in the 5 years preceding enrolment[16]. Although, women in intervention group felt better informed concerning their risk profile, there were no significant differences in participation in physical activity, adherence to the recommended diet and secondary outcomes of self-reported body weight and blood pressure among intervention and control groups[16]. The "RedCarRisk" study is investigating the improvement in arterial stiffness after engagement with a 6 months conditional workout program after PE affected pregnancy and is due to report outcomes in 2020 [17]. The "BP2"trial includes women 12 months after a pregnancy affected by a hypertensive disorder and compares the optimized usual care, brief education (30 min consultation with physician and then nutritionist), and extended lifestyle intervention. Primary outcomes include change in blood pressure, weight and waist circumference while secondary outcomes include self-reported changes (via validated questionnaire), vascular function, serological measures, maternal satisfaction with the program and cost-effectiveness[13]. The findings from these two trials are expected in the next two or three years and will provide important insights on effectiveness of interventional studies soon after the HDP. Meanwhile, the results of the simulation study done by Lagerweij et al. support the hypothesis that early CVD risk screening and risk-based lifestyle interventions may modestly improve cardiovascular health in women with history of PE[9].

HDP control during pregnancy and in postpartum period has been well maintained; yet cardiovascular risk control in these women on a long run remains challenging. To ensure the effectiveness of cardiovascular preventive strategies in HDP women, we need to improve the screening methods after pregnancy, for instance by creating a HDP and women specific cardiovascular risk stratification model. For this purpose, extensive international collaborations applying artificial intelligence and machine-learning algorithms in large medical data sources may be used to identify clinically meaningful patterns following HDP not only in women but also in offspring (considering their increased cardiometabolic risk). Further, to create women-specific cardiovascular risk tools we need to disentangle the underlying biological mechanisms and explore potential biomarkers (i.e. hormones, epigenetic markers) of elevated cardiovascular risk after HDP. Finally, future studies need to examine the effect of different lifestyle patterns in reducing the risk of CVD in PE women, and whether medications such as statins and antihypertensives could be combined with lifestyle interventions, and if yes, when and to which extent.

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