Harnessing the Power of Pregnancy and Pregnancy-Related Events to Predict Cardiovascular Disease in Women

Our current cardiovascular risk prediction tools may underestimate short-term risk in women, even among high-risk young women, simply because of age and therefore may be insufficient to help us tackle the startling epidemic of cardiovascular disease (CVD) in young women. The use of sex-specific risk factors may help improve cardiovascular risk assessment. Pregnancy, experienced by 85% of women, has been likened to a cardiac stress test and provides important clues about a woman’s underlying predisposition for both near- and far-term CVD events.

In this issue of Circulation, 3 articles take a deeper dive into understanding the association of pregnancy-related complications with future CVD and arrhythmias with pregnancy. Tanz et al characterize the risk of cardiovascular events (myocardial infarction and stroke) in women who experienced a preterm delivery. Using data from ~70,000 participants in the Nurses’ Health Study II, the investigators demonstrate that preterm delivery (<37 weeks gestation) was associated with future CVD (HR of 1.42). Further dividing preterm delivery into moderate preterm (<37 weeks and ≥32 weeks) and very preterm (<32 weeks) demonstrated the highest risk in those with very preterm delivery. The longitudinal nature of the study allowed the authors to adjust for multiple preexisting CVD risk factors and to determine how much of the risk was attributable to the subsequent development of traditional risk factors (eg, hypertension, diabetes mellitus). Surprisingly, adjusting for preexisting risk factors only modestly attenuated the association, and <15% of the associated risk could be attributed to the development of traditional risk factors.

Whereas pregnancy complications such as preeclampsia, gestational hypertension, and gestational diabetes mellitus are more widely known to be related to later cardiometabolic disease in women, the association between preterm delivery and CVD in women is less well appreciated by both clinicians and researchers. The association between preterm delivery and both fatal and nonfatal CVD has been previously demonstrated, with the risk of CVD with preterm delivery being even more pronounced among women delivering a small-for-gestational-age baby. Tanz and coworkers extend this body of literature by providing more detailed accounting of prepregnancy and subsequent CVD risk factors. This study by Tanz et al both confirms the association between preterm delivery and CVD in a well-characterized US-based cohort and suggests that the association is mediated through alternative pathways other than the traditional CVD risk factors.

This article adds to the growing body of evidence that pregnancy is nature’s stress test, which unmask an increased cardiovascular risk among women who experience specific pregnancy complications, including preterm delivery. The advantage to knowing a woman’s pregnancy complication history is that we glean this information early in a woman’s life, allowing ample time for both primordial and primary prevention. Thus, we recommend taking a pregnancy history inclusive of the following complications as part of a complete cardiovascular history in women: preterm delivery complications, preeclampsia, gestational hypertension, and gestational diabetes mellitus.
delivery history, preeclampsia/gestational hypertension, gestational diabetes mellitus, and infant size. Pregnancy loss, including miscarriage and stillbirths, has also been linked to later CVD in women, and mechanisms underlying this association are uncertain.8

Two additional research letters in this issue of Circulation leverage large insurance cost and claims databases to characterize the burden of arrhythmias in pregnancy and to relate this to maternal and fetal outcomes. Chang et al9 evaluated the burden of paroxysmal supraventricular tachycardia (SVT) in pregnancy using a national Taiwanese insurance database of 2.3 million women. Approximately 0.3% of the women in the study developed SVT. The women who developed SVT during pregnancy were more likely to have adverse maternal and fetal outcomes, including severe maternal morbidity, cesarean section, low birth weight, preterm labor, fetal stress, and obvious fetal abnormalities. In a secondary analysis, Chang et al demonstrated that women with a history of ablation were less likely to have recurrent SVT during pregnancy compared with those with a history of paroxysmal SVT without ablation; however, surprisingly, the adverse event rates were not different between women with and without history of ablation therapy. This finding raises the possibility that a woman’s underlying predisposition to SVT may be responsible for the adverse maternal and fetal outcomes rather than the presence of SVT per se. Given the nonrandomized nature of ablation in this claims database, both selection bias and residual confounding are still possible; thus, the findings of Chang et al support the need for a randomized controlled trial to evaluate the efficacy of ablation for SVT in reducing adverse maternal and fetal events.

In a separate report, Vaidya et al used data from the US Nationwide Inpatient Sample to identify temporal trends in arrhythmias in 57 million pregnancies from 2000 to 2012.10 During this period, the authors reported an increase in pregnancy-related hospitalizations with arrhythmias. The rise was due largely to an increased burden of atrial fibrillation and ventricular tachycardia, whereas hospitalizations for SVT remained stable over time. Higher maternal age may be contributing, as evidenced by the substantial increase in arrhythmias in women 41 to 50 years of age. Racial disparities were also reported, with an increased frequency of any arrhythmia in pregnancy among black women compared with other racial groups. Understanding the relative contribution of specific arrhythmias and the mechanism for this difference may help in targeting this health disparity. The increased frequency of maternal in-hospital death and maternal and fetal complications among women with arrhythmias in pregnancy suggests that these are not entirely benign events.

Whether pregnancy suppresses or exacerbates arrhythmias is unknown. First occurrence of SVT has not been shown to be higher during pregnancy.11 Longitudinal studies are needed that relate arrhythmia in pregnancy with future cardiovascular events in women. These studies will help us understand whether having an arrhythmia in pregnancy serves as a noninvasive elec-

**Figure.** Pregnancy-related complications and cardiovascular disease (CVD) events: the association between pre-pregnancy risk factors and post-pregnancy outcomes.
trophophysiology study or electrophysiology stress test and would allow us to predict whether a woman will have an arrhythmia or CVD later in her life. In addition to risk prediction, future translational and bench studies have the potential to help us uncover biological mechanisms that predispose to arrhythmia development among women in pregnancy and may add insight into mechanisms leading to arrhythmias in the general population. This would be of importance in lethal electric syndromes such as long-QT and Brugada syndromes for which counseling about pregnancy and peripartum risk may be important. One study showed that the risk of a cardiac event is higher in the postpartum interval in women with hereditary long-QT syndrome.12

There remain many unanswered questions about the mechanism of the associations discussed (Figure). Addressing these scientific gaps will require a multipronged approach, including outcomes research complemented by bench research and translational studies to understand the burden of the problem and pathophysiological mechanisms underlying these associations. In addition, new models aimed at improving the accuracy of risk prediction in women are needed, and the efficacy of these tools must be tested. There is much work to be done to harness the power of pregnancy and pregnancy-related events to understand, predict and prevent CVD in women.

DISCLOSURES
None.

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FOOTNOTES

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REFERENCES


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