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Preeclampsia and Hypertension:

Courting a Long While: Time to Make It Official

Nisha I. Parikh, MD, MPH and Juan Gonzalez, MD, MS, PhD

Cardiovascular Division, Department of Medicine, University of California, San Francisco (Parikh); Pregnancy and Cardiac Treatment (PACT) Program, University of California, San Francisco (Parikh, Gonzalez); The Preterm Birth Initiative (PTBi), University of California, San Francisco (Parikh); Maternal Fetal Medicine Division, Department of Obstetrics and Gynecology and Reproductive Sciences, University of California, San Francisco (Gonzalez)

Preeclampsia is a multisystem disorder marked by the onset of hypertension after 20 weeks of gestation and new proteinuria or specific organ dysfunction. In the United States, preeclampsia complicates up to 3.8% of all pregnancies and is an important cause of maternal and fetal morbidity and mortality.¹ Like acute myocardial infarction, stroke, and malignant forms of hypertension, the acute trigger for the onset of preeclampsia is not fully understood. And much like the acute onset of cardiovascular diseases (CVDs), once preeclampsia is triggered, there is an ensuing cascade of vascular and endothelial dysfunction, inflammation, and coagulation dysfunction that can in turn lead to neurologic, cardiac, pulmonary, renal, and hepatic disease in pregnant women. Delivery is often one of the only means to stop this cascade of events.

Low-dose aspirin is recommended as a preventive medication for women at high risk for preeclampsia. Prompt identification of patients with preeclampsia is also vital because timely administration of antenatal corticosteroids reduces neonatal morbidity and mortality from iatrogenic (ie, medically directed) preterm delivery between 23 and 34 weeks of gestation in women for whom expectant management is not warranted. A recent randomized clinical trial of women at 34 weeks to 36 weeks and 5 days of gestation who were at high risk for late preterm delivery demonstrated that administration of antenatal corticosteroids significantly reduced the rate of neonatal respiratory complications.²

Preeclampsia and CVDs including hypertension are bound not only by common pathophysiology but also epidemiology. Indeed, high blood pressure prior to pregnancy is a risk factor for preeclampsia,³ and preeclampsia is in turn a risk factor for later hypertension and/or later elevated blood pressure in women.⁴ Thus, not surprisingly, obstetrics and gynecology and cardiovascular experts alike have called for the recognition of preeclampsia as an important predictor of CVDs in women.⁵

The US Preventive Services Task Force (USPSTF), in its newest recommendation (grade B recommendation),⁶ reaffirms its prior recommendation⁷ to screen for preeclampsia with

Corresponding Author: Nisha I. Parikh, MD, MPH, Cardiovascular Research Institute, University of California, San Francisco, 555 Mission Bay Blvd South, San Francisco, CA 94158, (nisha.parikh@ucsf.edu).

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blood pressure measurements throughout pregnancy. The accuracy of clinically based blood pressure measurements and their utility in predicting preeclampsia led the USPSTF to reissue its stance on using blood pressure measurements to screen for preeclampsia. However, blood pressure as a screening tool continues to be challenging because it is difficult to decipher whether chronic hypertension has worsened or preeclampsia is developing.

Also notable in the USPSTF update is the deemphasis on proteinuria measurements and, in particular, spot protein assessment for preeclampsia diagnosis.⁶ Accumulating data indicate that the amount of proteinuria does not predict maternal or fetal outcome. The American College of Obstetricians and Gynecologists convened the Task Force on Hypertension in Pregnancy,⁸ which issued a report eliminating the dependence of the diagnosis on proteinuria in recognition of the syndromic nature of preeclampsia. In the absence of proteinuria, preeclampsia is diagnosed as hypertension in association with other evidence of end organ damage.⁸

Using risk-prediction tools for preeclampsia screening was not endorsed by the most recent USPSTF guidelines,⁶ leaving an area for future important scientific and public health inquiry. Within cardiovascular medicine, cardiovascular risk-prediction algorithms are commonly used and spur continual improvement of CVD risk-prediction tools. The updating of CVD risk-prediction tools is driven by the growing availability of new and large data sets, inclusive of multiethnic populations that were not previously available for study. Given the importance of early detection of preeclampsia, the development of risk-prediction tools that can accurately predict preeclampsia onset, and predict maternal and fetal outcomes in preeclampsia, will be important to develop.

In addition, risk-prediction tools may be useful in identifying and triaging patients who require a higher level of care and identifying those who are candidates for other disease-modifying therapies. Also, preeclampsia can present for the first time in the postpartum period. Therefore, risk-prediction tools can help identify pregnant women who require closer monitoring during the postpartum period.

The development of risk-prediction tools for preeclampsia may be enhanced by the many lessons and methods that have been developed for risk prediction of CVDs.⁹ For instance, the incorporation of untargeted “-omics” biomarkers in addition to established risk factors may enhance secondary prevention in CVD¹⁰ and may also be a specific feature to test in future preeclampsia risk-prediction studies.

Maternal hemodynamics during the stages of pregnancy are dynamic and have a predictable trajectory in normal pregnancy. Measureable blood pressure changes begin at week 6 of pregnancy and drop to a low point between weeks 16 and 20. Blood pressure subsequently begins to rise again, approaching prepregnancy levels by term.¹¹ Intrapartum blood pressure trajectories in preeclamptic pregnancy are higher than in normal pregnancy, and there may be a utility to integrating multiple blood pressure measurements for greater accuracy of preeclampsia prediction and for prediction of fetal outcomes.¹² Determining the specific number and timing of blood pressure measurements that optimizes the sensitivity and

specificity of a preeclampsia prediction will be an important step forward. Assessing the extent to which home blood pressure cuffs (potentially enabled with mobile-enhanced technology) improve blood pressure monitoring will be important to test.

Our laboratory has been interested in the long-term effects of CVD-related pregnancy complications, including preeclampsia, on the cardiovascular health of the mother. While it is clear that preeclampsia is a risk factor for later high blood pressure, the most effective method to refer women with preeclampsia for more intensive postpartum blood pressure screening and treatment has not yet been developed. The USPSTF recommendation⁶ states that measurement of blood pressure in pregnancy is a reasonable screening test for preeclampsia. We believe that de novo development of high blood pressure in pregnancy should also be used to identify women at high risk for the development of early essential hypertension in women. Pregnancy is essentially a cardiovascular stress test, and the development of preeclampsia among other pregnancy complications is the earliest marker of patients at risk for future CVD.¹³ Streamlined methods within health care systems are needed to refer women with preeclampsia to clinicians capable of intensive cardiovascular risk-factor screening and management in the postnatal setting. Data suggest that women are motivated to seek health care during the early postpartum period,¹⁴ and we should leverage this window to institute lifestyle modifications in diet and physical activity that reduce blood pressure.

There is now an abundance of evidence demonstrating that salt reduction, increased fruit and vegetable intake, increased physical activity, weight loss, alcohol moderation, and smoking cessation can reduce blood pressure in men and women.¹⁵ Largely absent from prior studies of lifestyle modification were female participants of childbearing age. Indeed, our best known studies in this field excluded women who were lactating or thinking of becoming pregnant.¹⁶ The marriage of hypertension with preeclampsia would not be complete without considering the role of lifestyle modification for the prevention and treatment of preeclampsia and for the prevention of postpartum chronic hypertension among women with preeclampsia. Therefore, we would like to emphasize that focusing on life-style modification for women during the preconception, pregnancy, and postpartum periods would address an important scientific gap and may represent a low-cost, high-yield means to prevent and/or temper the adverse future sequelae of preeclampsia in both mothers and their offspring.

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