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EDITORIAL COMMENT

Adverse Pregnancy Outcomes and Premature Myocardial Infarction

The Clock Is Ticking*

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Adverse pregnancy outcomes (APOs) including hypertensive disorders of pregnancy (HDPs), gestational diabetes, preterm delivery, and delivery of small for gestational age infants are now well-known risk factors for the development of future cardiovascular disease (CVD).[1,2] HDPs and CVD share common risk factors and prior study suggests that most (~79%) of the excess risk among individuals with a history of HDP is associated with chronic hypertension and elevated body mass index.[1,2] Beyond coronary disease, HDP increases an individual's risk of developing future heart failure and even valvular dysfunction through a postulated mechanism of accelerated vascular aging.[2] Prior work by Countouris et al[3] observed an increased risk of adverse left ventricular remodeling among patients with a history of HDP, especially among those who develop chronic hypertension, appreciable by echocardiography in as little as a decade after affected delivery.

The increased risk of CVD among individuals with a history of HDP as compared to those with normotensive pregnancies is most pronounced before the age of 65 years.[2] However, the contribution of APOs to the incidence and severity of premature myocardial infarction (MI) among younger women itself is not well understood. This is important as young women with MI are a particularly high-risk group, with a higher incidence of adverse 1-year outcomes as compared to younger men, despite a greater probability of presenting with MI with nonobstructive coronary arteries.[4] In this issue of *JACC: Advances*, Countouris et al[5] make a significant contribution to the current body of literature by examining the differences in premature MI among women with and without a history of prior APOs in their retrospective analysis of patients referred for coronary angiography for MI in a large hospital system comprised of over 40 hospitals. Authors found that among the 391 women with a history of premature MI referred for coronary angiography, a high proportion (39%) had a history of APOs. Furthermore, those with an APO history had a higher prevalence of diabetes (33% vs 15%, $P = 0.001$) and presented slightly earlier following affected delivery (19.6 years vs 21.5 years, $P = 0.012$) as compared to women without a history of APO. However, MI severity did not differ by history of APO, including incidence of ST-elevation MI, obstructive disease, multivessel disease, need for percutaneous coronary intervention, and associated shock. A notable strength of the study included validated diagnosis of APO history through chart abstraction. In addition, authors noted that coronary angiograms were directly reviewed for diagnosis verification, which is especially important as MI mechanisms can be more subtle in younger women, with spontaneous coronary artery dissection highlighted as an example.

Pregnancy affected by an APO is often considered a "failed stress test" that identifies individuals at higher risk for future CVD. However, evidence-based strategies to reduce this risk are still lacking, especially among younger patients. Current recommendations include routine screening for APOs during CVD risk assessment and incorporating APOs as a

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risk-enhancing factor for those deemed intermediate risk by conventional risk calculation in the assessment for primary prevention statin use.[6] However, as the risk for coronary disease is often underestimated among young individuals even in the presence of risk factors, many women at risk for premature MI due to APO history may still not meet eligibility for statin prescription using current risk stratification methods.[7]

Given the overlap in risk factors between HDP and CVD, the American College of Obstetrics and Gynecology recommends that those with APOs undergo cardiovascular screening within 3 months postpartum to capitalize on the window of opportunity presented for aggressive primary prevention of CVD.[6] However, postpartum patients experience of significant barriers to care including inconsistent access to health insurance and challenges to attending in person appointments in the context of new caregiving responsibilities. As an example, a retrospective analysis of patients with severe pre-eclampsia found that only 52% of patients attended the 6-week postpartum visit and among those who did, 21% were still hypertensive.[8] Black women and those with poor prenatal care (<5 visits) had the lowest rates of postpartum follow-up, highlighting significant disparities in access to postpartum care. There has been interest in transitional clinics to assist with aggressive primary CVD risk prevention, but among patients identified at elevated risk for CVD and referred to cardiology, only half actually scheduled a cardiology visit.[9]

As such, there is growing interest in virtual strategies for CVD risk factor screening and lifestyle modification. Digital strategies to date have demonstrated promise with respect to reduction in disparities for postpartum blood pressure ascertainment[10] and increasing levels of physical activity.[11] Such interventions promote known primary prevention strategies as established from the general population. Aggressive screening for hypertension and reduction in obesity are of particular importance following HDP given their impact on future CVD among those with hypertensive pregnancies.[1-3] Beyond this, however, it remains unknown whether prevention goals for patients should differ based on APO history (eg, whether different thresholds should be used to initiate pharmacotherapy for chronic hypertension among patients with a history of HDP). Furthermore, disease-specific interventions are lacking, and it remains unknown to what extent the endothelial injury and oxidative stress associated with APOs may be directly causal to future CVD risk. Better understanding the independent mechanisms by which APOs increase CVD risk may be particularly important for individuals who experience APOs in the absence of other traditional cardiovascular risk factors.

Countouris et al have added further evidence that APOs significantly contribute to the risk of premature MI among women, a group also known to have poorer MI outcomes. As such, following a pregnancy complicated by an APO, the clock is ticking to implement risk reduction strategies. In order to improve outcomes in this at-risk population, there are several key gaps in knowledge in need of urgent study: 1) better risk estimation models in younger women with APOs; 2) optimal strategies for health care delivery in the postpartum period to make care accessible and equitable, including best practices for digital health strategies; 3) determining if lower primary prevention thresholds for therapy are warranted for patients with a history of APOs; and 4) identification of novel disease-specific targets for risk reduction following APOs beyond current generalized CVD primary prevention factors.

With rising rates of both APOs and CVD in the United States, the time is now for investigations that better capitalize on the window of opportunity that APOs present to improve cardiovascular health.

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