Perspective Piece

Obstetrics and Gynecologic History – A Missed Opportunity for Cardiovascular Risk Assessment

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Abbreviations:
APO = adverse pregnancy outcomes
ART = assisted reproductive technology
ASCVD = atherosclerotic cardiovascular disease
CV = cardiovascular
HDP = hypertensive disorders of pregnancy
HRT = hormone replacement therapy
PCOS = polycystic ovarian syndrome
POI = premature ovarian insufficiency

Atherosclerotic cardiovascular disease (ASCVD) remains a significant cause of morbidity and mortality in women, with the event rates particularly rising in young women. Women are disproportionately affected by traditional cardiovascular (CV) risk factors such as diabetes and hypertension compared with men. In addition to standard risk factors, there are many risk factors that are either female predominant, such as autoimmune conditions and psychological stressors, or female specific, such as hormonal changes, throughout the course of a lifetime and pregnancy-related issues. Among the most important risk factors specific to women are conditions occurring during pregnancy and history related to fertility and gynecologic conditions. The value of such history has become more apparent in recent literature, however the translation of this knowledge to clinical practice has been poor. The importance of recognizing specific obstetric and gynecologic conditions and the specific conditions to screen for are the focus of this discussion.

Obstetrics History

Pregnancy is often referred to as a "stress test" in relation to the significant changes in cardiac output and associated heart rate/stroke volume that occur. There are also changes in metabolic regulation which, when dysfunctional, can lead to adverse neonatal and maternal outcomes. These conditions associated with long-term CV risk are collectively referred to as adverse pregnancy outcomes (APO) and are listed in the Figure (1). APOs, including hypertensive disorders of pregnancy (HDP) and gestational diabetes, have been associated with elevated risk of CV events including myocardial infarction, heart failure, and stroke. Neonatal outcomes such as spontaneous preterm birth and intrauterine growth restriction are not only

associated with adverse infant outcomes, but also adverse long-term maternal CV outcomes. It is unknown whether the association between APO and ASCVD risk is due to underlying predisposition to ASCVD or whether pregnancy triggers onset of vascular dysfunction (Figure). However, what has become more readily evident is that APO not only leads to peri-partum neonatal and maternal adverse outcomes but is associated with significant long-term ASCVD risk. In this case, it is of the utmost importance to recognize such history so that proper screening and potential risk modification can be implemented. In the US, over 80% of women experience at least one pregnancy. Documenting such history provides insight into risk and the results of this "free" stress test can be obtained without cost by simply asking women about their obstetric history. Maternal recollection of events during their pregnancy has been shown to be an accurate reflection of their obstetric history. Recent multi-disciplinary society guidelines have acknowledged the importance of recognizing APOs in evaluating, identifying and potentially modifying, ASCVD risk (2). ACOG guidelines recommend routine screening of BMI, lipids, and blood pressure in all women with history of APO (3). Newly released AHA/ACC guidelines on blood cholesterol now include APOs as potential "risk enhancers" in consideration of ASCVD risk. Even among women without APOs, parity in of itself has been associated with ASCVD risk in that parous women compared with nulliparous women exhibit greater ASCVD risk, which increases proportionally to each live birth. Obtaining a cardio-obstetric history is critically important to accurately assessing ASCVD risk, when women otherwise might appear to be low-risk for ASCVD.

Infertility and Assisted Reproductive Technology

Discussion of reproductive history should also include assessment of history of recurrent miscarriage, infertility conditions, and use of assisted reproductive technology (ART). There is some evidence suggesting recurrent miscarriage (3 consecutive miscarriages) is associated with ASCVD, and optimization of modifiable ASCVD risk factors in women with this history is recommended. Polycystic ovary syndrome (PCOS) is a common cause of infertility affecting 5-10% of women. PCOS is associated with increased risk of hypertension, dyslipidemia, gestational diabetes, and type 2 diabetes, thus allowing opportunities for risk screening and modification. Therefore, in women with PCOS, the ESC and ACOG guidelines have recommended periodic screening for diabetes and ASCVD risk factors, respectively. ART, which includes intrauterine insemination and in vitro fertilization, has been associated with elevated risk of gestational hypertension, pre-eclampsia, and APOs. The mechanism is unclear but may be mediated through excessive fluid shifts in the setting of ovarian activation (referred to as ovarian hyperstimulation syndrome) and/or hormone-related effects on endothelial function. Although a meta-analysis on this subject concluded no significant association between ART and CVD risk, this analysis was composed of only six studies and could not make a definitive assessment of long-term venous thromboembolic risk, and also suggested an increased risk of stroke. Furthermore, failure to conceive following ovulation induction as part of ART has been associated with increased ASCVD risk. As such, care should be taken to inquire about ART history while further studies investigate this potential association.

Hormonal Therapy

Several gynecologic conditions that affect fertility and menopause have been associated with increased risk of ASCVD. It is known that the risk of ASCVD increases following menopause. Similarly, surgical menopause and premature ovarian insufficiency (POI) are associated with increased risks of CVD. POI occurs in approximately 1% of the female population, and current AHA/ACC, ESC, and Dutch guidelines all recommend optimizing modifiable ASCVD risk factors in this high-risk group. As hormone replacement therapy (HRT) in post-menopausal women is linked to increased risks of stroke and venous thromboembolism, for women with surgical menopause and POI, HRT should only continue until the average age of menopause. Combined oral contraceptive pills that contain estrogen are associated with increased risk of venous thromboembolism, and are contraindicated in women with ischemic heart disease, cyanotic heart disease, heart failure, or arrhythmia, and in those with pulmonary hypertension taking endothelin receptor antagonists. Contraceptive methods for women with cardiac disease is a delicate issue that deserves special consideration but is outside the scope of this review article.

Future Directions

As the value of screening for female-specific risk factors related to obstetric and gynecologic history is more widely recognized to better assess ASCVD risk, the next question is which providers should be screening for such conditions. In the immediate postpartum period it is imperative that women with HDP have close follow up to assess adequate blood pressure control. Developing a system to transition such women to regular follow up with a primary care physician or cardiologist is key to avoid gaps in care. A recommended list of obstetric and

gynecologic conditions to screen for is presented in the Table. Automated referral systems post delivery and facilitating visits at hospital discharge can alleviate attrition in postpartum follow up. For the long term, as many of these young women of childbearing age often do not have other chronic medical conditions, they may not routinely seek primary care. However, a key opportunity for screening is within obstetric and gynecological (OB-GYN) office visits. A significant number of women rely on OB-GYN providers as their primary care provider. Such visits provide a valuable opportunity to screen women for ASCVD risk factors and also utilize OB-GYN history for either implementation of screening or risk reduction and/or referral to a primary care physician or cardiologist (2). Such an initiative was put forth through a partnership between SCAI-WIN and ACC in 2012, demonstrating proof of concept for improving risk assessment and referral. Education also needs to be highlighted within primary care specialties where primary prevention can be implemented in young women. Innovative approaches to bridging gaps in care such as this are needed to capture women who are at risk.

Table. Recommended adverse pregnancy outcomes and gynecologic conditions for cardiovascular disease risk screening

Pregnancy history
Hypertensive disorders of pregnancy
Gestational hypertension
Pre-eclampsia
Eclampsia
Chronic hypertension
Gestational diabetes
Preterm birth (<37 weeks)
Intrauterine growth restriction/low birth weight/small for gestational age
Parity
Miscarriages
Assisted reproductive technology
Infertility
Gynecologic history
Polycystic ovarian syndrome
Premature ovarian insufficiency
Use of oral contraceptives
Menopausal status
Use of hormone replacement therapy

FIGURE

Figure. Potential mechanisms for the association between adverse pregnancy outcomes and future cardiovascular disease risk. CHD = coronary heart disease; CVA = cerebrovascular accident; CVD = cardiovascular disease.

Reprinted from Wu P, Mamas MA, Gulati M. Pregnancy as a predictor of maternal cardiovascular disease: The era of cardioobstetrics. *J Womens Health (Larchmt)*. 2019;28:1037-50.

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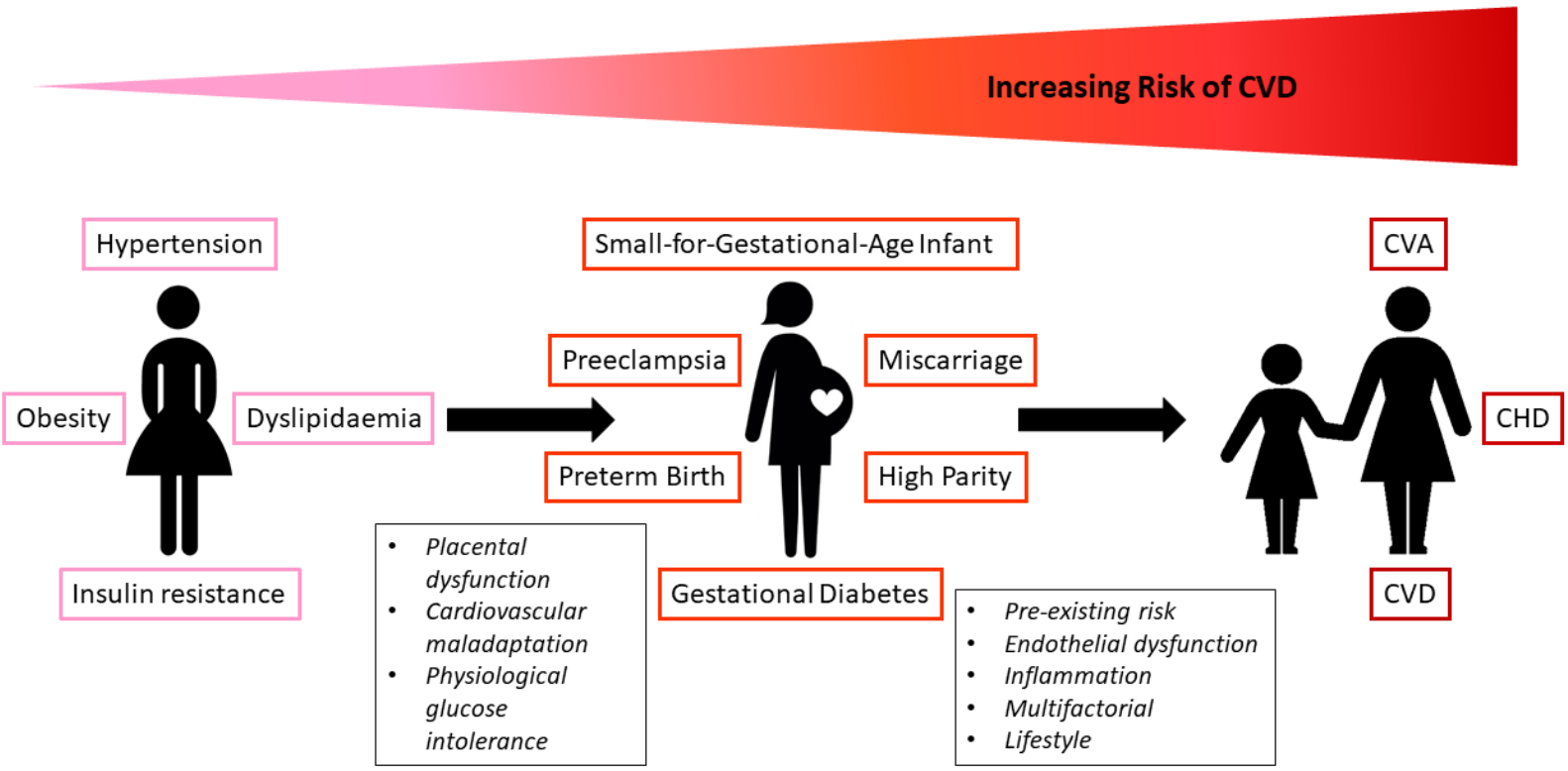
Increasing Risk of CVD
Hypertension
Obesity
Dyslipidaemia
Insulin resistance
Small-for-Gestational-Age Infant
Preeclampsia
Preterm Birth
Miscarriage
High Parity
Gestational Diabetes
CVA
CHD
CVD
• Placental dysfunction
• Cardiovascular maladaptation
• Physiological glucose intolerance
• Pre-existing risk
• Endothelial dysfunction
• Inflammation
• Multifactorial
• Lifestyle