Pregnancy Complications, Cardiovascular Risk Factors, and Future Heart Disease

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INTRODUCTION

Heart disease is the leading cause of mortality for women. In 2013, 1 (35%) in 3 deaths in women worldwide were from cardiovascular disease (CVD).1,2 The population adjusted risk of CVD mortality is greater for women than men at 20.9% versus 14.9%, respectively.3 Although the American Heart Association (AHA) states the risk for death from cardiovascular disease has decreased significantly for both women and men since 2000, the mortality for women was higher than that for men since the 1980s and the decline much slower.1,4 Based on recent data, the gender gap

KEYWORDS

- Heart disease mortality • Women • Pregnancy complications • Cardiovascular risk
- Pregnancy • Inflammatory phenotype • Cardiovascular disease
- Lifestyle modification

KEY POINTS

- Women with high parity and pregnancy complications of preeclampsia, gestational diabetes, and low birth weight are at increased risk for adult cardiovascular morbidity and mortality.
- Assessment of women at risk for cardiovascular disease should begin in the postpartum period.
- Breastfeeding may provide some protection against development of cardiovascular disease.
- Education of women and providers is essential to prevention of cardiovascular morbidity and mortality.
- Women with pregnancy complications are uniquely at risk and should have periodic screening, and institute lifestyle modifications to decrease risk for cardiovascular disease mortality.

INTRODUCTION

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remains, with the rate of death per 100,000 populations for women at 209 per 100,000 compared with 129.6 per 100,000 in 2017; a slight decline from 2010 for both genders.¹⁴

Unfortunately, only 45% of women and fewer than half of all primary care physicians identify heart disease as the leading cause for death in women or CVD as the top concern for adult women’s health despite efforts to raise nationwide awareness.⁵

Over the past decade, there has been growing evidence that women with a history of certain common pregnancy complications confer an increased risk for later development of CVD.⁶⁻¹¹ These include pregnancy conditions such as preeclampsia, gestational diabetes, and low birth weight due to preterm delivery or fetal growth restriction (Box 1).

Pregnancy has been referred to as a CVD “physiologic stress test”; women who develop these pregnancy complications are more likely to be identified with underlying, often undiagnosed, cardiovascular risk factors and are at higher risk CVD.¹² The physiologic changes of pregnancy indicate that 20% to 30% have at least 1 traditional or pregnancy-related risk factor that is a predictor for later development of CVD.¹³,¹⁴

Previous studies suggest a relationship with increased parity and CVD. In a study from 24 British towns of 4286 women and 4252 men aged 60 to 79 years with at least 2 children, each additional child increased the age-adjusted odds of coronary heart disease (CHD) by 30% (odds ratio, 1.30; 95% confidence interval [CI] 1.17–1.44) for women and by 12% for men (odds ratio [OR] 1.12; 95% confidence interval, 1.02–1.22). Adjustment for obesity and metabolic risk factors attenuated the associations between greater number of children and CHD in both sexes, although in women some association remained.¹⁵ In a more recent study composed of a diverse U.S. cohort, a history of 5+ live births was associated with CVD risk, specifically, myocardial infarction, independent of breastfeeding.

Having a prior pregnancy and no live birth is associated with greater CVD and heart failure risk.¹⁶ The theory behind this increase risk for CVD related to parity is through the cardiometabolic changes of the cumulative number of pregnancies, including weight gain, increased waist circumference, hyperlipidemia, and subclinical atherosclerosis. Women with higher parity had a higher body mass index (BMI), lower

**Box 1**

*Female-specific and pregnancy-related risk factors for cardiovascular disease*

*Pregnancy Complications*

Hypertensive disorders
- Gestational hypertension
- Preeclampsia
- Eclampsia

Gestational diabetes mellitus

Preterm delivery

- Less than 37 completed weeks gestation

Low birth weight for gestational age (fetal growth restriction)

- Less than 10th percentile birthweight for gestational age

*Female-Specific Risk Factors*

- Polycystic ovary syndrome
- Insulin resistance
- Functional hypothalamic amenorrhea
high-density lipoprotein cholesterol, higher triglycerides, and higher low-density lipoprotein cholesterol at baseline than women with fewer births. Other pregnancy-related changes are likely also a factor. These include increased left ventricular mass and systolic volume.

**HYPERTENSIVE DISORDERS**

Preeclampsia is one of the most common complications of pregnancy, occurring in 3% to 5% of all pregnancies. Preeclampsia is a leading cause of maternal and perinatal morbidity and maternal mortality. The condition is characterized by hypertension and proteinuria after 20 weeks' gestation. Factors that increase the risk for development of preeclampsia include obesity, diabetes and preexisting hypertension, advanced reproductive age, and primiparity. The physiologic and anatomic changes of preeclampsia suggest that it is a cardiovascular condition that involves vascular dysfunction, inflammation, and hypercoagulability.

Long-term complications of women with a history of preeclampsia/eclampsia include chronic hypertension, type 2 diabetes, metabolic syndrome, coronary artery disease, cerebral vascular disease, and end-stage renal disease. Evidence suggests that these acute cardiovascular changes of preeclampsia increase the risk for later development of CVD. A meta-analysis of 3.5 million women found that a history of preeclampsia is associated with a significant lifetime risk of stroke, ischemic heart disease, hypertension, and venous thromboembolism. Another study of 2.3 million women found that those with a history of preeclampsia had approximately a twofold risk for early cardiac, cerebral vascular, peripheral vascular disease, and cardiovascular mortality than those without preeclampsia. PREVFEM, a large retrospective study of women with preeclampsia before term conferred a 3.59 times higher risk of hypertension before age 40 years compared with an age-matched reference group with an uncomplicated pregnancy. Although the mechanism for the association between preeclampsia and later development of CVD has not been established, there is a strong association with significant vascular endothelial dysfunction and preeclampsia.

**GESTATIONAL DIABETES**

Gestational diabetes mellitus (GDM), glucose intolerance, occurs in 5% to 10% of pregnancies. Significant risk factors for GDM include obesity and family history of type 2 diabetes in first-degree relatives. GDM increases the risk for the development of type 2 diabetes and CVD. Ethnicity plays a role in onset of type 2 diabetes in women with GDM. For example, Latin American women with GDM have an earlier progression to type 2 DM compared with white and non-Hispanic black women. Kjos and colleagues reported a 47% cumulative incidence rate for Latin American women with GDM to develop non–insulin dependent diabetes by 5 years after the index pregnancy. In a recent study of women screened for DM 4 to 12 weeks postpartum from the index pregnancy with GDM, those with earlier gestational age onset of GDM, higher fasting blood glucose, and managed with medication were more likely to develop type 2 DM. A large database analysis of women with GDM showed a significantly higher risk of CVD, including angina pectoris, myocardial infarction, and hypertension, over a follow-up period of 7 years postpartum. Women with a history of GDM develop subclinical atherosclerosis, an increased risk of cardiac dysfunction, increased markers of endothelial dysfunction, and metabolic syndrome. A large population-based study in Ontario, Canada, looked at long-term health...
outcomes after GDM and demonstrated a higher risk for myocardial infarction, coronary bypass, coronary angioplasty, stroke, and carotid endarterectomy. It is important to evaluate risk for development of CVD in women with GDM. This must begin with screening 4 to 12 weeks postpartum for type 2 diabetes with a 75-g oral glucose tolerance test (OGTT) according to the American College of Obstetricians and Gynecologists (ACOG) or between 6 weeks and 6 months postpartum and an HgA1c every 2 years according to Diabetes Canada in women with GDM and follow-up based on established criteria. Follow-up of these women and the use of established biochemical and hemodynamic markers for cardiovascular morbidity might lead to a decreased risk and severity of cardiovascular events.

PRETERM AND LOW BIRTH WEIGHT

Preterm birth is defined as a birth less than 37 completed weeks’ gestation, and occurs in 6% to 12% of all deliveries worldwide. Low birth weight is defined as a newborn weight less than 2500 g at term or less than 5% for gestational age. There is an accumulated body of evidence that suggests idiopathic preterm labor and resultant preterm birth is the result of an upregulation of inflammatory pathway. It is well known that inflammation is an independent predictor of coronary artery disease. Several studies have demonstrated a significant association with preterm delivery and cerebral vascular stroke later in life. The hazard ratio for later development of CVD for those women with a preterm birth ranges from 1.3 to 2.6 compared with term births. The inflammatory phenotype leading to preterm birth may be the link for those women with preterm birth being at greater risk for CVD. Spontaneous preterm birth doubles the risk of CVD compared with those women with a term birth. A large-scale study tracking mothers’ subsequent admissions and deaths over 15 to 19 years indicates an intergenerational influence on birthweight that provides a correlation between the birthweights of parents and their offspring and the associated risk of mortality from CVD. The coincidence of fetal growth restriction and prematurity increased risk for CVD later in life.

There is some evidence that breastfeeding and the duration of breastfeeding has maternal metabolic benefits, including a lower incidence of the metabolic syndrome and provides some protection against CVD. Schwarz and colleagues examined the effect of lactation on CVD risk in 139,681 postmenopausal women in the Women’s Preventative Service Initiative (WPSI). There was a dose response relationship; women who had a lifetime history of breastfeeding of more than 12 months were less likely to have hypertension (OR 0.88, P < .001), diabetes (OR 0.80, P < .001), hyperlipidemia (OR .81, P < .001), or CVD (OR 0.91, P < .001) compared with women who never breastfed. This was significant despite the confounder of obesity. In another study of 2540 women with CHD who had breastfed for a lifetime total of 2 years or longer, 37% had a lower risk of CHD (95% CI 23%–49%; P < .001), adjusting for age, parity, and stillbirth history. This study was also adjusted for early adult adiposity, parental history, and lifestyle factors and even with those confounders the risk reduction was 23% lower for CVD compared with women who never breastfeed. An area for future research is to evaluate the breastfeeding impact on CVD for those with pregnancy complications, preeclampsia, preterm birth, and low birthweight on the later development of CVD.

POSTPARTUM SCREENING

As stated, CVD is the leading cause of premature death for women, and women’s cardiovascular health suffers because of male-dominated screening and diagnostic
tests and treatments. Women’s cardiovascular health has been identified as a key national priority in many countries, which should be addressed through improved awareness, screening, prevention, and intervention, and reducing care inequities for women in general and younger women in particular. Given the costs of treating CVD, novel and innovative ways to identify who should undergo cardiovascular risk (CVR) screening are critical to achieve these goals. For most women, pregnancy and the postpartum period provide a window of opportunity for screening and implementing intervention and therapeutic strategies to improve long-term health and prevent CVD. Postpartum CVR screening, counseling, and lifestyle intervention is now widely considered standard of care following the identified pregnancy complications.11

Various publications recommend initiating CVR screening within the first year postpartum, typically between 3 and 6 months. This would take the form of a complete history (including first-degree family history of CVD and CVRs), physical examination (ie, blood pressure, waist circumference, BMI) and biochemical testing (lipid profile, fasting glucose or 75-g OGTT for women with GDM, high-sensitivity C-reactive protein, and urine albumin:creatinine ratio) and counseling about lifestyle modification including physical activity and dietary changes, especially cholesterol and salt reduction. Even small changes in lifestyle can reduce CVR; regular moderate-intensity physical activity and even small amounts of weight loss can have a beneficial effect on lipids and cholesterol.

Postpartum screening and counseling also affords the opportunity for preconception counseling. Going into the next pregnancy without achieving prepregnancy BMI increases the risks for complications in pregnancy as well as increasing the risk of obesity in the longer term. It is also an opportunity to discuss the importance of earlier screening for GDM (if applicable), initiation of low-dose aspirin for reducing the risk of preeclampsia, and interventions for women with a high risk for recurrent preterm delivery for those with history of idiopathic preterm labor or preterm premature rupture of membranes.

The postpartum visit is the initial step to educate women and counsel them on the importance of optimizing current health and adhering to guidelines for ongoing care. For example, the AHA recommends that all adults ≥20 years of age have a cholesterol and other traditional risk factors checked every 4 to 6 years and for those with an elevated lipid profile receive dietary and if appropriate medication to improve the lipid profile. The AHA also recommends that blood pressure (BP) be screened during regular health care visits at least every 2 years for anyone ≥20 years of age and for those ≥40 years that screening of BP should be annually.48 As pregnancy after age 40 years has become more common and resultant risk of pregnancy complications for women older than 40 higher, adherence to this recommendation for annual BP follow-up for these women is even more significant. Finally, counseling should occur on the significance of achieving a healthier adult weight and the impact of excessive weight gain during pregnancy and adult weight retention after childbearing have on the later development of diabetes and thereby CVD risk. At postpartum follow-up, women should be encouraged to access educational resources and pointed to AHA Web sites such as the AHA Go Red for Women Web site49 or the pregnancy and heart disease–Go Red for Women Web site50 to supplement the education from the obstetrician, gynecologist, or other primary care providers. Lifestyle changes with regular exercise if not already part of the pregnant woman’s routine should be encouraged during pregnancy especially for those women who are overweight or obese. The exercise program should be continued postpartum to decrease weight retention and to achieve a healthier adult weight. ACOG supports aerobic exercise and strength conditioning during
pregnancy, and the American College of Cardiology/AHA 2013 lifestyle guidelines advocated for 10,000 steps daily for maintenance of heart health.14,51

SUMMARY

Multiparity and pregnancy complications confer an increased risk for cardiovascular morbidity and mortality in women. Obesity, excessive weight gain, and weight retention following pregnancy likely adds to the cumulative risk of pregnancy complications of preeclampsia, GDM, prematurity, and low birth for the development of CVD in women and higher risk of mortality compared with men. Pregnancy complications in the past have not been recognized in the AHA guidelines as a risk factor for CVD prevention.14 To improve the cardiovascular health of women, the obstetrician-gynecologists and women’s health care providers, primary care physicians, and cardiologists must ensure that a comprehensive history of pregnancy complications is included for all women at the annual well women’s visit. Coordinated care and follow-up for women with pregnancy complications where evidence suggests an increased risk for CVD should focus on education, lifestyle intervention, and early and enhanced cardiac screening with the goal of minimizing cardiovascular morbidity and mortality.

DISCLOSURE

The authors have nothing disclose.

REFERENCES


