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Commentary

Arrhythmias in pregnancy: Commentary

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Cardiovascular disease is a significant contributor to maternal morbidity and mortality worldwide and is the leading cause of adverse pregnancy outcomes in the United States of America, accounting for approximately 25% of maternal deaths from 2008-2017. Maternal deaths in the United States have increased from 12.7 deaths per 100,000 live births in 2008 to 17.4 deaths per 100,000 live births in 2018. This data is sobering given the majority of maternal deaths are preventable and occur after delivery [1-5]. Pregnancy is analogous to a stress test, often unmasking underlying heart disease or exacerbating known heart disease. Cardiovascular complications of pregnancy may include arrhythmias, heart failure, myocardial infarctions, and acute aortic syndromes.

Arrhythmias are the most common complication in women with and without heart disease. The burden of sustained arrhythmias in pregnancy has increased significantly over the past decade [6-10]. In a nationwide study of more than 1200 hospitals, a 58% increase in arrhythmias were noted in pregnancies occurring between 2000 and 2012. This increase was driven by higher rates of atrial fibrillation and ventricular tachycardia, while rates of supraventricular tachycardia remained stable. Although the overall rate for ventricular arrhythmias remained low, ventricular arrhythmias markedly increase the risk of maternal and fetal morbidity and mortality, approximately 40-fold compared to a 13-fold increase with atrial fibrillation [6].

The drivers of a rising incidence of maternal arrhythmias include, increasing number of pregnancies in women with congenital heart disease and acquired heart disease, advanced maternal age, and obesity. New onset arrhythmias may occur at any time during pregnancy, but commonly occur toward the latter end. Women with a prior history of arrhythmias often experience an increased burden or exacerbation of a previously controlled arrythmia. With rising rates of obesity in the United States, the prevalence of arrhythmias in pregnancy may continue to increase. In a prospective cohort study assessing the effects of obesity on adverse pregnancy outcomes in pregnant women with heart disease, obesity significantly increased the risk of cardiac events. Of the 790 pregnancies in this study, 19% occurred in women with BMI >30 kg/m^2 (obesity), 25% in women with BMI 25 to 29.9 kg/m^2. Women with obesity were at higher risk of cardiac events when compared with women with normal weight (23% vs. 14%; p<0.006). Cardiac events were defined as cardiac death/arrest, arrhythmias, heart failure, myocardial infarction, stroke, aortic dissection, and thromboembolic events. Arrhythmias occurred in 11% (84/790 pregnancies), with the highest incidence in the obese group 14% (20/146) [11]. Age is also an important factor in pregnancy. With increasing age at the time of pregnancy, there is an increased risk of hypertensive disorders of pregnancy, heart failure, and arrythmias. In a study of atrial fibrillation and flutter in pregnancy women, Lee et al. showed that women less than age 30 were less likely to have atrial fibrillation in pregnancy, chronic hypertension, pregestational diabetes mellitus, obesity, and dyslipidemia. In women older than 30 years of age, there was a four-fold increase in atrial fibrillation and flutter in pregnancy in women older, and a five-fold increase in atrial fibrillation in women older than 40 years of age [9]. In women with known heart disease, it is important to note the type of structural heart disease when assessing the risk of arrythmias during pregnancy. Women with dilated cardiomyopathy, hypertrophic cardiomyopathy, or ischemic heart disease have a higher incidence of atrial fibrillation compared to peripartum cardiomyopathy [12-14].

The risk of arrhythmias persists in the peripartum period. Postpartum readmissions are highest within the first 30 days after pregnancy, peaking in the first seven days. The leading causes of readmissions include hypertensive disorders of pregnancy and cardiovascular disease. In a nationwide study of postpartum readmissions in women without heart disease, there was a 5.2% risk of

readmissions at 6 weeks in women with heart disease compared to a 1.4% risk in women without heart disease. Heart failure and arrhythmias were predominant among women with pre-existing heart disease. Arrhythmias also occurred in women without heart disease. These types of arrhythmias were not defined in this study [15]. Risk factors for readmission included advanced maternal age, multiple gestational pregnancy, lower socioeconomic status, and non-Hispanic black race. Women readmitted were more likely to have comorbid conditions including chronic kidney disease and pregestational diabetes mellitus. These findings have been echoed in studies examining rates and causes of postpartum readmissions [15-17].

Whether new onset AF in pregnancy predicts the development of future AF is unknown. Predicting recurrence of atrial fibrillation in women with new onset atrial fibrillation in pregnancy has not been studied. In the non-pregnant population, left atrial size and fibrosis are significant predictors of the development, progression of AF, and recurrence of AF. Clinical factors that increase the risk of atrial fibrillation also contribute to adverse left atrial remodeling. These factors include older age, obesity, hypertension, congestive heart failure, structural heart disease, excessive alcohol use, and obesity [18]. This highlights the importance of incorporating preventive care, nutrition and weight counseling in postpartum care.

Decisions guiding risk reduction of thromboembolism for women with nonvalvular atrial fibrillation during pregnancy vary amongst clinicians, with some advocating for low dose aspirin and others for therapeutic anticoagulation. The 2020 ESC atrial fibrillation guidelines recommend therapeutic anticoagulation with heparin or vitamin K antagonist according to the stage of pregnancy for patients with AF (Level of evidence Class IC). This is in contrast to the 2018 ESC guidelines on the management of cardiovascular disease in pregnancy recommending the guidance on decision of anticoagulation should use the same risk stratification as non-pregnant women [19,20]. It is important to note the CHADS2VASC score does not take into consideration the hypercoagulable state of pregnancy and has not been validated in pregnant women. If a woman does receive therapeutic anticoagulation, careful delivery planning is important, and risk of preterm delivery should be considered. Vaginal delivery is not recommended in women who are therapeutic on a vitamin K antagonist due to increased risk of fetal hemorrhage, including intracranial hemorrhage [20-23].

Ventricular arrhythmias represent a small proportion of arrhythmias in pregnancy with the majority of cases occurring in women with structural heart disease, ischemic heart disease or inherited arrhythmia syndromes. In a multicenter study assessing pregnancy outcomes in women with heart disease and ventricular arrythmias, New York Heart Association (NYHA) class was the most significant and independent predictor of ventricular arrhythmias. Women with a preconception NYHA class >1 had a two-fold higher risk of ventricular arrhythmias in pregnancy [24].

Maternal arrythmias increase the risk of adverse fetal outcomes [25]. This is partly due to adverse effects of drug therapy in pregnant women, including, but not limited to beta blockers, antiarrhythmics, and anticoagulation. In a meta-analysis of seven studies with a total of 301,638 pregnancies, more than 25% of pregnancies complicated by atrial fibrillation had adverse fetal outcomes, which included preterm birth, small for gestational age, respiratory distress syndrome, hemorrhage, death [8]. Infants of women with atrial fibrillation and flutter during pregnancy also have higher rates of neonatal intensive care unit admissions [9].

There are risk prediction tools have been developed to predict the risk of adverse cardiovascular events during pregnancy [26-29]. It is important to note the limitations in these risk prediction tools as research in pregnant women has largely been limited to observational studies and retrospective studies. Traditionally, pregnant women have not been included in randomized control trials. The Cardiac Disease in Pregnancy Study (CARPREG I, CARPREG II), and Zwangerschap bij Aangeboren HARtAfwijkingen (ZAHARA) scores were derived from pregnancy data in women with and without congenital heart disease [26-28]. The modified World Health Organization (WHO) classification incorporates congenital heart disease, cardiomyopathies, aortopathies, valvular disease and pulmonary hypertension [29]. The modified WHO Classification has been shown to perform best in predicting risk of adverse cardiovascular events in a number of studies [30-33]. No risk prediction tools have been developed to predict adverse cardiovascular events in women without heart disease; however, with the rising rates of maternal deaths from cardiovascular disease, traditional risk factors for cardiovascular disease should be taken into consideration during preconception counseling. In the non-pregnant population, obesity, hypertension, dyslipidemia, tobacco use, and diabetes mellitus increase the risk of arrhythmias, coronary artery disease, myocardial infarction and stroke. Care of pregnant women with heart disease requires a multidisciplinary approach. Preconception counseling, pregnancy and postpartum care is of utmost importance in this population, both serving as an opportunity to reduce maternal morbidity and mortality.

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