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Maternal Mortality in the United States and the HOPE Registry

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Abstract

Purpose of review Maternal mortality in the United States is highest among all developed nations and continues to rise. The leading cause of morbidity and mortality during pregnancy and the postpartum period is cardiovascular disease. While there are large European and Canadian studies exploring the care and outcomes of moms with heart disease in pregnancy, there are no large prospective studies to guide the care of this growing group of patients in the US. We review the current approach to the management of patients with heart disease in pregnancy and the gaps in knowledge thereof.
Recent findings Currently, antenatal management and delivery planning are highly variable

for patients with heart disease in pregnancy and maternal risk models' application to the US patient population is limited by their derivation from an international cohort of patients and their focus on patients with congenital heart disease. As the need for interdisciplinary care between cardiologists and obstetricians becomes evident, and as broad research efforts within this space are very much needed, we propose a research collaborative called the Heart Outcomes in Pregnancy: Expectations (HOPE) for Mom and Baby Registry. The HOPE Registry aims to address key clinical questions surrounding the preconception period, antenatal care, delivery planning and outcomes, and long-term postpartum care and outcomes of these unique patients.

Summary We have made progress in recent years by recognizing the clinical need to address and standardize the management of patients with heart disease in pregnancy. We now must initiate and propel US-based cardio-obstetrics research to address key gaps in knowledge and variability in the care of patients with heart disease in pregnancy.

Introduction

The rising maternal mortality rate in the United States (US) has justifiably garnered both national and international attention in recent years. Maternal mortality is a key indicator of a nation's health and quality of care. In the United States, the rate rose 26% from 2000 to 2014 [1] and continues to rise. The US maternal mortality rates are the worst among industrialized nations, ranking only above Mexico for the 31 countries that report on maternal mortality [2]. This stands in stark contrast to the United Nations Millennial goal to have reduced maternal mortality by 75% by the year 2015.

Several factors contribute to this worrisome US trend. First, we have had major limitations in our ability to recognize and report pregnancy-associated mortality. Not until 2003 did the US mandate a question regarding maternal deaths be added to all death certificates [3, 4]. However, addition of this field was not standardized, further delaying implementation and resulting in incomplete or erroneous data collection. These barriers to reporting may be related to underfunding of maternal healthcare over the past two decades, as we have seen defunding in state and federal health care programs [5–7]. Another potential cause is the highly variable adoption of and funding for Medicaid, the primary insurance for many pregnant women (https://www.kff.org/womens-health-policy/fact-sheet/medicaids-role-for-women/). This is particularly distressing because early and consistent prenatal care favorably impacts the life of the mom and baby [7].

According to the CDC, prenatal care is strongly associated with favorable maternal and fetal outcomes, with a very large proportion of the almost 700 patients who died having no (8.5%) prenatal care and almost a quarter presenting in the 2nd trimester or later [8]. In Texas, where maternal mortality rates are among the worst in the nation, there was a change in access to women's health services with the following years reporting a near doubling in the maternal mortality rate [1, 9, 10]. Further, there are significant racial disparities in maternal mortality. In California, African American women represent only 6% of all deliveries, but 22% of all pregnancy-related deaths [11]. Across the country, African American women have a 3.4-fold higher risk of dying in the intra- and postpartum periods as compared with their Caucasian counterparts [12]. This is even more pronounced in the older maternal population, with black women over the age of 40 having the highest rate of dying at 192 per 100,000 [12]. The most recent morbidity and mortality report published by the CDC found that more black women are dying in the postpartum period as compared with other racial groups, which could be attributable to loss of affordable health insurance or access to care after the 6-week postpartum visit. These concerning trends highlight the need to better understand the social determinants of health and barriers to appropriate care.

The American College of Obstetrics and Gynecology attempted to address these issues by implementing new guidelines for postpartum care [13]. Traditionally, bundled coverage for postpartum care included only a one-time visit at 6 weeks. However, the majority of maternal deaths occur in the 42–365 days after delivery, leaving a gaping window of opportunity to impact the health of these high-risk women. As of May 2019, it is recommended that women with any pregnancy-associated complication including hypertension, diabetes, or underlying cardiovascular risk factors now be seen within the first week postpartum [14•].

In the US, California stands out as an outlier in the maternal mortality statistics, having experienced a marked decline since 2006 and the only state continuing to improve. Since 2006, California has reduced their maternal mortality by 57% and for African Americans, by 50%. The foundation for this improvement has been the state's concerted effort to reduce the maternal death rate by initiating a statewide, pregnancy-associated maternal mortality review committee and contracting with the California Maternal Quality Care Collaborative (CMQCC) to investigate the primary causes of maternal death (hhttps://www.cmqcc.org.). This collaborative developed evidenced-based tool kits to address the most common causes of mortality and they continue to build on these data. From the California collaborative data, as well as that from the United Kingdom (UK), we have learned that outcomes improve when obstetrical care is standardized.

Careful review of the California and the pregnancy mortality surveillance system (PMSS) data has provided important insights into the causes of maternal mortality. Although cardiovascular disease accounts for only 4% of all pregnancies in the United States, it is present in 26% of all deaths, surpassing traditional causes including hypertensive disorders, hemorrhage, and embolic events [5, 8]. Most of these deaths are occurring during the intra-and postpartum timeframe with acquired cardiovascular disease being the most deadly; greater than 90% of maternal deaths due to cardiovascular disease can be attributable to the growing number of acquired heart disease [15]. What is even more striking is that studies evaluating the preventability of maternal deaths have deemed that up to 68% of these deaths were potentially preventable [5, 13].

The challenge in caring for this high-risk group of women is the lack of observational data guiding management. Identification of risk factors through history, physical exam, and previously established risk models (such as the CARPREG or ZAHARA risk models) is a first step toward identifying who will require further surveillance or who should avoid pregnancy altogether. However, these models were developed largely from European and Canadian patient cohorts and may not be generalizable to American women, where the rates of traditional cardiovascular risk factors and acquired cardiovascular disease are more common than those of our European counterparts. As well, the climbing rates of obesity and advanced maternal age at first pregnancy further increase the risk for cardiovascular disease. There remain significant gaps in knowledge regarding how pregnancy impacts cardiovascular conditions, and vice versa, further highlighting the need for observational US-based data.

Preconception consultation offers an opportunity to mitigate pregnancy-associated risks and can allow for intervention in an effort to optimize future maternal and fetal outcomes. As mentioned, risk of cardiac complications can be estimated with several different risk stratification models including ZAHARA or CARPREG I and II scores [16, 17]. The modified WHO guidelines also provide broad classes of risk based on congenital heart defects, NYHA functional class, and presence of pulmonary arterial hypertension, and are likely more applicable to an American population (https://www.who.int/news-room/fact-sheets/detail/maternal-mortality.). However, as most pregnancies in the United States are unplanned, many of these women present already well into their first trimester after the physiologic adaptions to pregnancy have already begun.

Most often, the initial prenatal visit offers the first opportunity to address the risks associated with heart disease in pregnancy. High-risk pregnant women with cardiovascular disease will often benefit from consultation with a high-risk obstetrics provider and should be cared for throughout gestation in a coordinated, multidisciplinary manner at a tertiary care center [18•]. Optimizing care through a combined cardiology and obstetrics approach does improve both maternal and fetal outcomes (unpublished data). The challenge is that although we have evidence of increasing gestational ages, increased birth weights and decreased cesarean sections (unpublished data) when care are integrated, there is no evidence-based protocols from which we can draw guidance. Perhaps we should be careful about unpublished data and just say we expect care to be better due to the multidisciplinary approach, and not mention the unpublished data part.

An association of growth restriction (estimated fetal weight < 10th percentile) has been seen in women with congenital heart disease [19, 20] as well as women with decreased cardiac output with structurally normal hearts [21]. Therefore, many of these women are screened serially with obstetric ultrasound at 28, 32, and 36 weeks to assess fetal growth. Additionally, there are some studies that suggest that stillbirth risk increases in this population [22], and antenatal surveillance is offered at many centers, especially for women with cyanotic heart disease. However, timing and efficacy of antenatal surveillance has not been assessed in women with heart disease.

There is also a lack of consensus on timing of delivery, resulting in marked variability in treatment patterns. Women affected by pregnancy-associated cardiovascular conditions such as hypertension are delivered between 37 0/7 weeks and 39 6/7 weeks, depending on medications status and blood pressure. Pre-eclampsia and related disorders are delivered early depending on gestational age of diagnosis and obstetric criteria (ACOG). Worsening cardiac status, defined by worsening New York Heart Association class and/or echocardiographic measures, may prompt need for earlier delivery, but again, there is a lack of data as to whether early delivery improves maternal outcomes.

ACOG currently recommends vaginal delivery in women with heart disease; however, the increasing cardiac output during the second stage of labor may not be well-tolerated in some conditions [14•]. Cardiac output continues to increase during both labor and delivery, and cesarean section is typically reserved for women with severe obstructive lesions (i.e., severe aortic stenosis), aortopathies with an enlarged aortic root, and severe pulmonary hypertension [23]. Operative vaginal delivery can allow for vaginal delivery, avoiding the morbidity associated with cesarean sections, without Valsalva in medium risk cardiovascular conditions [24]. However, these are also not without risk as women sustain vaginal lacerations that can lead to pelvic floor laxity and fecal and urinary incontinence in later life [25].

Cardiac arrhythmias are also a common complication during pregnancy in women with underlying structural heart disease. This has been demonstrated by several studies and recently reaffirmed by CARPREG II, which demonstrated a 16% incidence of cardiac complications in pregnancy, primarily due to arrhythmias (9.3% of pregnancies) and heart failure (6.2% of pregnancies) [16, 17]. Cardiac arrhythmias are more likely to present in the second trimester, whereas heart failure is more prevalent in the third trimester or postpartum. Fortunately, maternal cardiac death from arrhythmias or cardiac arrest is rare (0.6%). The current recommendations for treatment of arrhythmias resemble that in the non-pregnant population; however, the effects of pharmacological agents specifically antiarrhythmic drugs (AADs) and their effects on the fetus have to be taken into consideration [26]. Unfortunately, there is a paucity of clinical data and randomized trials on the safety of AADs in pregnancy. Majority of AAD are FDA category C implying that there is inadequate and well-controlled studies in humans, but adverse effects have been shown in animal studies.

Outcomes data are desperately needed in order to develop optimal fetal surveillance guidelines, recommendation on timing and mode of delivery, and risk estimation of the long-term effects of pregnancy on heart disease in order to solve these pressing issues and reduce both morbidity and mortality in pregnant women with heart disease.

There do remain notable gaps in knowledge regarding the best approach to management of this growing group of patients. These gaps include identifying whether existing risk models are applicable and valid among our US demographic. Further, though ROPAC and other investigator groups have elucidated important descriptive data and approaches to maternal risk assessment, standardized antepartum management (frequency and type of fetal monitoring) and delivery planning remain areas of great interest and uncertainty. Lastly, patient-centered outcomes that focus on disease-specific assessment of functional capacity and psychosocial limitations require further study.

In an effort to address these gaps in knowledge, we have developed a framework for the first multisite, multidisciplinary, prospective registry exploring outcomes of mothers afflicted with cardiovascular disease in the United States. This research collaborative is called the Heart Outcomes in Pregnancy: Expectations (HOPE) for Mom and Baby Registry. As we work to secure funding for this 5 to10-year endeavor, we have forged strong relationships with over 40 other academic centers. These centers' principal investigators, driven by the same enthusiasm as our own to explore these clinical questions, include a cardiologist and maternal fetal medicine specialist partnering at each contributing site. In phase 1 of HOPE, we plan to enroll 1000 women with cardiovascular disease in pregnancy, including congenital heart conditions, coronary heart disease, spontaneous

coronary artery dissection, and heart failure. We plan to follow these patients at 6 weeks and 6 months post partum, and annually thereafter for 5 years. We have identified several key aims, including to:

1. Describe the presenting features of pregnant women with heart disease. Therein, we plan to describe the health status (symptoms, function, and quality of life) outcomes for pregnant women with structural heart disease, heart failure, and coronary disease.
2. Describe the antenatal monitoring patterns, growth, and perinatal outcomes of babies whose moms have heart disease.
3. Describe the management of pregnant women with heart disease and its association with maternal and fetal outcomes.
4. Document contraception counseling, and patient perception thereof.
5. Describe anesthesia and mode and timing of delivery planning.

In the absence of evidence in how to best manage pregnant women with heart disease, there is wide variability in practice. By systematically and prospectively capturing the pre-term monitoring and delivery approaches used for these patients, we will be able to associate these treatment strategies with maternal and fetal outcomes, overall and as a function of patients' presenting severity of cardiac disease. These data will form the foundation for future guidelines be defining the best strategies of antenatal and postpartum management of women with heart disease.

As we organize the foundational aspects of this registry (clinical report forms, an online portal, institutional review board documentation, and protocol), we continue to leverage this strong network as we to contribute to the science and the data guiding the care of patients with heart disease in pregnancy in America.

Compliance with Ethical Standards

Conflict of Interest
The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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