Congenital Heart Disease and Reproductive Risk: An Overview for Obstetricians, Cardiologists, and Primary Care Providers

Sabrina Phillips, M.D.[a]; *Michael Pirics,* M.D.[b]

[a]MAYO CLINIC, JACKSONVILLE, FLORIDA; [b]HOUSTON METHODIST HOSPITAL, HOUSTON, TEXAS

ABSTRACT: Patients with congenital heart disease have improved survival rates, and most patients are now expected to survive into adulthood. This improved survival has resulted in increasing numbers of women with congenital heart disease who are of childbearing age. This patient population requires specialized advice on contraception and pregnancy risk. Understanding the unique challenges this population presents is key to providing appropriate care.

INTRODUCTION

Long-term survival rates of infants born with congenital heart disease continue to improve, allowing the vast majority of patients with access to current surgical and medical technologies to reach adulthood. In most cases, however, this improved survival does not imply a cure of congenital heart disease but, rather, enhanced palliation. These maturing patients experience sequelae of their heart disease and repair that often requires medical, pharmacologic, and repeat surgical intervention. Women with congenital heart disease experience unique challenges across the spectrum of the reproductive health cycle, not only with pregnancy and delivery. Being aware and informed regarding these challenges is necessary for adult cardiologists to provide appropriate care for this distinctive patient population.

CONGENITAL HEART DISEASE EFFECTS ON DEVELOPMENT, MENSES, AND FERTILITY

Women with congenital heart disease experience psychosocial as well as medical concerns during adolescence and young adulthood that may impact their reproductive health. Dissatisfaction with physical appearance related to scars; difficulty with intrapersonal relationships; and concerns about fertility, inheritability of congenital heart disease, and possible negative effects on cardiac health related to pregnancy have all been demonstrated to negatively affect overall sexual health.[1] Importantly, the majority of patients rated the information provided by their physician regarding sexuality and congenital heart disease as suboptimal,[1] which underscores the importance of providing information on these issues to patients and their families starting at an early age. Recognizing the psychological impact of congenital heart disease and integrating life coaching and counseling into the care of these patients may improve overall quality of life.

Menarche in women with congenital heart disease has been shown to be delayed, with the longest delay noted in cyanotic women.[2] After menarche, women with cyanotic congenital heart disease are more likely to have dysfunctional uterine bleeding, which may represent a chronic anovulatory state, dysfunction of the hypothalamic-pituitary-ovarian axis, or abnormal uterine hemostasis.[2,3] Menorrhagia may also be a complication for women required to use long-term anticoagulants. Careful evaluation and treatment of these menstrual irregularities is indicated to prevent complications that include iron deficiency anemia and the long-term concerns associated with chronic anovulation.[2]

CONTRACEPTION

In-depth knowledge of contraceptive methods, including pharmacology, implementation, and interaction with cardiac physiology is necessary to provide appropriate counseling to the patient and cooperative care with gynecology colleagues. Women who have a cardiac condition that leads to a prohibitive risk of pregnancy should be counseled regarding permanent contraceptive methods or long-acting reversible contraception. Microinsert hysteroscopic sterilization is shown to be a safe and effective method for permanent contraception in women with severe cardiac disease, avoiding the risk associated with general anesthesia for surgical tubal ligation.[4] Estrogen-containing contraception is contraindicated in women with cyanotic congenital heart disease and should not be a first-line therapy for women with mechanical valves or single ventricle circulation. Both intrauterine devices (IUDs) that elute progestin as well as progestin implants provide long-term contraception with the advantage of inherent compliance. These methods may also help with menorrhagia associated with cyanotic congenital heart disease or with anticoagulation use. While theoretical concern for IUD-associated endocarditis has been raised, there is no compelling data to suggest that IUD use in women with

Prior cardiac event or arrhythmia
Reduced systemic ventricular systolic function (ejection fraction < 40%)
Left heart obstruction (aortic valve area < 1.5 cm^2, mitral valve area < 2 cm^2, peak left ventricular outflow gradient > 30 mm Hg by echocardiography)
Baseline New York Heart Association class > II or cyanosis (resting saturation < 92%)

Table 1.
Predictors of primary cardiac events during pregnancy (CARPREG study). Adapted from Siu S et al.[5]

congenital heart disease is associated with higher rates of endocarditis.

PRE-CONCEPTION COUNSELING

All women with congenital heart disease who desire pregnancy should be provided with expert pre-conception counseling regarding risks of cardiac complications during pregnancy, risk of cardiac disease in the offspring, risk of fetal morbidity and mortality, and long-term cardiac sequelae related to the hemodynamic stressors of pregnancy. Most women with congenital heart disease can complete a pregnancy, though women with the Eisenmenger complex, significant congestive heart failure, severe obstructive lesions, and connective tissue disorders with a risk of aortic dissection should be counseled against becoming pregnant. Appropriate risk assessment in individual patients requires a comprehensive understanding of the patient's anatomy and hemodynamics and how the marked physiologic changes of pregnancy and delivery will affect her.

Several risk stratification models are available to delineate maternal risk in women with congenital heart disease. The CARPREG[5] risk predictor model can be applied to women with congenital heart disease but was developed after prospectively studying women with both acquired and congenital heart disease. In this model, there are four predictors of primary cardiac events during pregnancy

(Table 1). One point is assigned for each risk factor present. The risk of a cardiac event during pregnancy is estimated at 5%, 27%, and 75% for a pregnancy with 0, 1, or > 1 point, respectively.[5] Although this approach to risk prediction is straightforward and can be very helpful during pre-conception counseling, it may provide a less accurate risk assessment for mothers with congenital heart disease as many conditions affecting these women, such as right heart dysfunction, are not addressed. Application of the CARPREG score in a cohort of women with congenital heart disease did indeed demonstrate that severe pulmonary valve

regurgitation and/or sub-pulmonary ventricular systolic dysfunction are important additional risk predictors that should be added to the model.[6] More recently, the ZAHARA study[7] evaluated pregnancy complications in women with congenital heart disease and demonstrated additional risk factors in predicting cardiac complications during pregnancy (Table 2). The expected rates of cardiac complications based on these factors are shown in Table 3.

The World Health Organization (WHO) has stratified risk of cardiac complication into four classes, with

Systemic atrioventricular (AV) valve regurgitation (moderate/severe)	0.75 points
Baseline New York Heart Association class ≥ II	0.75 points
Cardiac medication usage pre-pregnancy	1.50 points
Left heart obstruction (aortic valve area < 1.0 cm^2, peak left ventricular outflow gradient > 50 mm Hg)	2.50 points
History of arrhythmia	1.50 points
Pulmonary AV valve regurgitation (moderate/severe)	0.75 points
Mechanical valve prosthesis	4.25 points
Repaired or unrepaired cyanotic heart disease	1.00 points

Table 2.
Predictors of cardiac complication during pregnancy and associated points for risk calculation (ZAHARA study). Adapted from Drethen W et al.[7]

RISK SCORE	CARDIAC COMPLICATIONS IN TOTAL NUMBER OF PREGNANCIES (%)
0 – 0.50	2.9
0.51 – 1.50	7.5
1.51 – 2.50	17.5
2.51 – 3.50	43.1
> 3.51	70.0

Table 3.
Cardiac complications during completed pregnancies as calculated by the ZAHARA risk score. Adapted from Drethen W et al.[7]

recommendations on follow-up during pregnancy based on this risk strata (Table 4).[8] After assessing the risk of cardiac complication during pregnancy, the physician should review management strategies with the patient to address these potential complications. If the patient requires anticoagulation during pregnancy, options for anticoagulation regimens should be reviewed during the pre-conception visit.

Pregnancies complicated by maternal congenital heart disease result in higher rates of neonatal complications than those in the general population, as prematurity, fetal demise, and fetal growth restriction are all potentially related to the inability to increase cardiac output to meet the demands of pregnancy. This hypothesis is supported by a prospective study that demonstrated an increased rate of neonatal complications in

pregnancies where maternal cardiac output declined as gestation advanced or third-trimester umbilical artery Doppler flows were abnormal.[9] The CARPREG and ZAHARA studies also examined maternal factors that predicted adverse neonatal outcomes, and many of these factors—including maternal congestive heart failure, cyanosis, outflow tract obstruction, and tobacco use—would potentially limit cardiac output and oxygen content delivery to the placental circulation.[5,7] Maternal use of cardiac medications and anticoagulation also results in risk to the fetus, including teratogenicity, fetal growth restriction, and hemorrhage. All cardiac medications prescribed must be evaluated and a decision made as to which drugs to continue throughout pregnancy. A good understanding of the FDA schema for classifying the risk of drugs during pregnancy and breastfeeding is imperative. Many cardiac medications are classified as risk unknown (C), risk proven (D), or risk contraindicated (X) but may still be used if the benefit to the mother outweighs the potential risks. All statins, angiotensin converting enzyme (ACE) inhibitors, and angiotensin receptor blockers (ARBs) should be discontinued. Nitrates and hydralazine can be substituted for ACE inhibitors and ARBs in women with systolic heart failure.

The offspring of patients with congenital heart disease have an increased risk of having congenital heart disease. The risk is variable, as the genetic mechanisms resulting in cardiac defects are heterogeneous in most forms of congenital heart disease.[10] The overall risk in offspring was found to be 4.1% in the British collaborative study of patients with congenital heart disease.[11] Women with conotruncal defects should have testing for 22q11 microdeletion, as offspring of patients with this microdeletion will have a 50% chance of inheriting the microdeletion and a markedly increased risk of congenital heart defects. It is appropriate to obtain screening fetal echocardiography in most cases when parental congenital heart disease is present.

CLASS	MATERNAL RISK DURING PREGNANCY	CARDIOLOGY FOLLOW-UP DURING PREGNANCY
I	Maternal mortality risk the same as the general population; maternal morbidity the same to mildly increased	One or two visits
II	Maternal mortality risk mildly increased; maternal morbidity moderately increased	Each trimester
III	Maternal mortality and morbidity risk significantly higher than general population; specialized multidisciplinary care required	Monthly or bimonthly
IV	Maternal mortality and morbidity risk extremely high; pregnancy is contraindicated	Monthly or bimonthly if pregnancy is pursued

Table 4.
Modified World Health Organization Classification of Maternal Cardiovascular Risk. Adapted from the European Society of Cardiology Guidelines on the Management of Cardiovascular Diseases during Pregnancy.[8]

PREGNANCY AND DELIVERY MANAGEMENT

Mothers with congenital heart disease are best managed with a multidisciplinary team of caregivers, including maternal fetal medicine specialists, anesthesiologists, neonatologists, and cardiologists. Cardiology follow-up during pregnancy is determined by the patient's cardiovascular risk as outlined in the WHO stratification (Table 4). Delivery in a tertiary care center is recommended for mothers at high risk of cardiac decompensation. The preferred method of delivery in most women with congenital heart disease is vaginal delivery, with Cesarean delivery reserved for obstetrical indications, mothers with decompensated heart failure, and mothers who are anticoagulated with a vitamin K antagonist. Cesarean delivery may be the best option in mothers with pulmonary hypertension and severe obstructive valvular lesions. The cardiac output demands of labor can be tempered with good anesthesia/ analgesia, and most mothers benefit from epidural anesthesia. For women in whom excessive Valsalva is a concern, labor can be completed using a forceps-assisted delivery without maternal pushing. Postpartum attention to thromboembolic prophylaxis and fluid management is critical.

LESION-SPECIFIC MANAGEMENT AND OUTCOMES

Most women with atrial septal defect (ASD) and/or partial anomalous pulmonary venous return (PAPVR) can complete a pregnancy with low morbidity, excluding those who have a significant increase in pulmonary vascular resistance. Women with repaired ASD or PAPVR are classified as WHO group I, and those unrepaired are considered WHO group II. Closure of ASD during pregnancy should not be performed unless the mother has a significant change in cardiovascular status. While pregnancy is a hypercoagulable state, therapeutic anticoagulation is not routinely indicated during gestation to prevent paradoxical emboli. Recognized cardiac complications in this patient population include arrhythmia, preeclampsia, fetal mortality, and fetal growth restriction in mothers with unrepaired ASD, especially if the maternal age was > 30 years or the patient had a prior history of arrhythmia.[12] During labor and delivery, air filters should be used on all intravenous lines to prevent air emboli.

Women with unrepaired ventricular septal defects (VSD) generally fall into two categories: small restrictive defects with no significant hemodynamic consequences or large defects with significant elevation in pulmonary vascular resistance (the Eisenmenger syndrome). Women with repaired VSD are classified as WHO group I, whereas those with small, restrictive VSD are classified as WHO group II. Women with Eisenmenger syndrome are classified as WHO group IV, in which pregnancy is contraindicated. The ZAHARA investigators demonstrated

that compared to women with unrepaired VSD, those with repaired VSD were at higher risk of preterm labor and of having infants who were small for their gestational age; this may reflect some degree of cardiac compromise in those women who had VSDs large enough to require surgical intervention.[13] Women with unrepaired VSD demonstrated a higher incidence of preeclampsia compared to the general population.[13]

Women with coarctation of the aorta may have cardiac complications during pregnancy even after repair of the coarctation. Potential complications include pregnancy-induced hypertension, preeclampsia, ascending aorta dilatation, and aortic dissection or rupture. A review of cases from the Mayo Clinic demonstrated that 30% of women with coarctation had hypertension during pregnancy, with 73% of them having a hemodynamically significant native or residual coarctation.[14] Appropriate monitoring and treatment of blood pressure is indicated during pregnancy.

Tetralogy of Fallot has been successfully repaired since the late 1950s. As a result, it is now the most common lesion among previously cyanotic women who are considering pregnancy. Pregnancy after tetralogy of Fallot repair is usually well tolerated; however, concerning issues in this patient population include pulmonary valve regurgitation, right heart dysfunction, arrhythmia, and increased pulmonary vascular resistance in those women who initially had a systemic-to-pulmonary-artery shunt for palliation. Women with tetralogy of Fallot should undergo cardiology monitoring at least each trimester. Women with right ventricular systolic or diastolic dysfunction are at increased risk of volume overload during the first week postpartum, so earlier follow-up with a cardiologist is indicated in the postpartum period.

Women with more complex forms of congenital heart disease, including Ebstein anomaly, complete transposition of the great arteries (status post atrial or arterial switch operation), congenitally corrected transposition of the great arteries, and single ventricle circulation (status post Fontan palliation) have all been reported to have successful pregnancies but with increased risk to both mother and fetus. This patient population requires subspecialty management from pre-conception to postpartum.

CONCLUSION

Women with congenital heart disease that may complicate pregnancy are a growing population. Although most women can have a successful pregnancy, even those with complex anatomy, success is dependent on accurate pre-conception counseling and meticulous multidisciplinary management during pregnancy, delivery, and the postpartum period.

KEY POINTS

- Most women with congenital heart disease can have a successful pregnancy but may require multidisciplinary care.
- Vaginal delivery is the preferred method of delivery for most women with congenital heart disease.
- Women with even "simple" congenital heart disease benefit from pre-conception counseling regarding risks of pregnancy.

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