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THE PREGNANT PATIENT WITH CONGENITAL HEART DISEASE

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Introduction

Due to the advances in cardiovascular care of children born with congenital heart disease (CHD), the population of adults with congenital heart disease (ACHD) has increased substantially over the past 60 years. Similarly, the number of women with CHD who reach child-bearing age has also increased. With this reality comes the responsibility to educate these women on factors that would decrease the likelihood of an adverse outcome during pregnancy. It is well known that pregnancy may result in circulatory changes that could adversely affect the health status of a healthy patient. In a patient with CHD, with or without repair, the normal change in circulatory burden could increase adverse effects. Certain lesions are considered to be high risk (e.g., patients with Marfan syndrome and pulmonary hypertension), based on anecdotal evidence and small case study reports. Most advice given to patients with intermediate risk lesions (i.e., Fontan operation, transposition of great arteries, cyanotic heart disease without pulmonary hypertension) are based on theoretical determination of risk, and there are few studies done to validate these recommendations. This review serves to summarize the literature findings and make current recommendations on managing pregnancy in patients with CHD.

Background

Congenital heart disease remains the most common birth defect, affecting 8 out of 1,000 live births.[1] With advances in medical, surgical, and intensive care, 85% of this population reach adulthood.[1] In women with CHD, their medical care is often complicated by the desire to bear children. Their health status is frequently complicated by multiple cardiac operations (frequently beginning in infancy) that have direct effects on the heart, brain (due to the effect of multiple cardiopulmonary bypass runs), and mental status (due to the effects of chronic childhood illness). Traditionally, almost all women with CHD were advised to avoid pregnancy.[2] However, recent literature has shown that pregnancy can be successful with acceptable maternal and neonatal outcomes.[3, 4] Although this population almost necessitates retrospective study, landmark studies by Siu et al. and Drenthen et al. over the past decade have offered important insight into this challenging patient group, where the reality of double morbidity and mortality occur with every pregnancy.[5, 6]

During pregnancy, maternal changes in fluid dynamics results in an increase in cardiac output that provides for nutrition of a growing fetus. The increase in plasma volume (approximately 50–60% above baseline), with concomitant erythrocyte volume increase, and an increase in the baseline heart rate also act to increase cardiac workload.[2] These changes stabilize in the second trimester and resolve in two to six weeks post-partum. Thus, the circulatory and respiratory systems of women with CHD will be challenged during pregnancy and can result in major obstetrical, cardiac, and neonatal adverse outcomes. In 2001, Siu proposed the CARPREG Risk Score that predicts the most important factors of adverse outcomes in pregnancy (Table 1).

These data illustrate conditions that increase the risk of cardiac problems in pregnancy.[5] Drenthen and colleagues also state that moderate to severe AV valve regurgitation, mechanical valve prosthesis, and maternal history of cyanotic CHD have also been associated with cardiac complications during pregnancy.[6] Expert opinion recommends that pregnancy be avoided in the following conditions:

Table 1. CARPREG Risk Score
• History of prior cardiac event or arrhythmias
• NYHA class >2 or cyanosis
• Left heart obstruction (MV area <2 cm^2, AV area <1.5 cm^2, or LVOT gradient >30 mmHg)
• LVEF <40%

Table 1. CARPREG Risk Score. Adverse outcomes in pregnancy can be predicted by the number of factors present in women with CHD. The risk of cardiac complications is based on total points (1 point per risk factor): 0 points = 5%, 1 point = 27%, >2 point = 75%

Marfan syndrome with dilated aortic root (>4 cm), moderate to severe left ventricular outflow tract obstruction (≥30 mmHg), left ventricular ejection fraction (LVEF) <30%, and pulmonary hypertension (Table 2).

Table 2: Contraindications for Pregnancy
• Marfan syndrome with dilated aortic root (>4 cm)
• Pulmonary hypertension (pulmonary vascular resistance >6 Wood Units)
• Moderate to severe left ventricular outflow tract obstruction (≥30 mmHg)
• LVEF <30%

Table 2. Contraindications for pregnancy in women with CHD.

Classes of Congenital Heart Lesions

The classification of congenital heart lesions into low, moderate, or high-risk pregnancy categories has been traditionally based on prior observational studies relating the lesion to the probability of maternal or neonatal morbidity and/or mortality.[7] This classification has been confirmed by recent published prospective studies.[5, 6] The following discusses the different classes of congenital heart

lesions with respect to their risk of mortality and/or morbidity, recommendations for antepartum management, and delivery recommendations.

Low-Risk Pregnancy Lesions

Isolated left-to-right shunt lesions fall into this category and include atrial septal defects (ASDs) and ventricular septal defects (VSDs). Small ASDs generally do not cause a murmur and can often go unrecognized until adulthood. Small VSDs are by definition pressure-restrictive and produce holosystolic murmurs that may still be present if unrepaired. Small ASDs and VSDs usually lead to an insignificant amount of left-to-right shunting and thus are generally of no clinical consequence in the pregnant patient. Larger ASDs or VSDs usually lead to larger left-to-right shunts and increased pulmonary blood flow (often up to two or three times normal), and these defects may often lead to problems such as dyspnea on exertion or pulmonary hypertension that lead to higher pregnancy risk. The challenge thus lies in the management of moderate-sized ASDs or VSDs with normal pulmonary vascular resistance. Though these patients remain at low cardiac risk during pregnancy, and symptoms arise from right-sided volume overload due to the physiologically increased plasma volume of pregnancy. Symptomatic relief can be treated with a diuretic (e.g., hydrochlorothiazide or furosemide). Symptomatic palpitations related to increased right heart size and volume can be treated with beta-blockers such as metoprolol, atenolol, or propranolol.

Studies have shown an increase in birth of SGA (small for gestational age) infants to mothers with repaired VSD. [4, 6] Preeclampsia has been noted to occur more frequently in women with uncorrected ASDs and VSDs, but there is little difference in other maternal complications of patients with repaired and unrepaired small-moderate ASDs. However, neonatal morbidity and mortality is slightly increased, which some theorize is from the limited maternal cardiac output that may result in placental insufficiency. In addition, there is also the small risk of a paradoxical embolism across an atrial septal communication.[8] In all patients with atrial septal defects, we recommend the use of air filters to all intravenous (IV) lines to decrease this risk, especially at times of elevated right-atrial pressure (e.g., during labor). There are those who recommend correction of ASDs prior to pregnancy regardless of evidence of hemodynamic compromise, but this has yet to be the standard of care.[9] These defects should be managed according to the ACC/AHA guidelines for congenital heart disease in adults.[10]

Pregnancy in patients with a history of surgically repaired aortic coarctation is also considered to be low risk if there is no detectable aneurysm or defect at the site of repair and no significant gradient (<20 mmHg). The presence of aneurysm or significant coarctation leads to a high-risk pregnancy status, and these patients should be managed at a center with experience in maternal heart disease. Cesarean section is recommended in these patients.[2, 11]

Moderate-Risk Pregnancy Lesions

Moderate-risk lesions include moderate mitral stenosis (mean gradient 5–10 mmHg, valve area 1.0–1.5 cm^2), moderate aortic stenosis (mean gradient 20–40 mmHg, valve area indexed for body surface area 0.7–1.0 cm^2/m^2), lesions with a systemic right ventricle such as congenitally corrected transposition of the great arteries (cc-TGA) and TGA after the Mustard/Senning procedure, patients after Fontan palliation (total caval pulmonary connection), and cyanotic lesions without pulmonary hypertension (such as unrepaired Tetralogy of Fallot and its variants).

Tetralogy of Fallot (ToF) is the most common cause of cyanotic heart disease and is well-described in the literature.[12, 13] This lesion has been successfully treated surgically since the groundbreaking surgical repair by Drs. Blalock, Taussig, and Thomas at Johns Hopkins Hospital in 1944. Thus, this lesion has generated thousands of adult patients who have repaired ToF but who often continue to have long-term sequelae from their surgical repair. The main long-term complication is pulmonary regurgitation, which is generally well-tolerated during pregnancy. The main maternal complications include right ventricular dysfunction and atrial and ventricular arrhythmias. Left ventricular dysfunction has also been reported.[14] In uncorrected ToF, the right ventricular outflow tract obstruction and VSD lead to cyanosis from the right-to-left shunt, and these can occur with increasing levels of severity that affect outcome. Specific complications during pregnancy can usually be related to the degree of residual pulmonary stenosis and cyanosis.[12] Fetal complications can occur from the chronic cyanosis, including intrauterine growth restriction (IUGR), prematurity, and neurologic impairment.

Transposition of the Great Arteries/ Systemic Right Ventricle

While ToF is the most common cause of cyanotic heart disease, transposition of the great arteries (TGA) is a common cardiac cause of neonatal cyanosis[15] and consists of two types: transposition with arterial discordance (called Dextro-TGA or D-TGA), and transposition with ventricular discordance (Levo-TGA, or L-TGA); L-TGA appears most times with arterial discordance, frequently called congenitally corrected TGA (ccTGA).[16, 17] In both cases, the anatomy leads to a systemic right ventricle that develops cardiomyopathy and systemic ventricular dysfunction often by 20 years of age. In the late 1960s, correction of this congenital defect consisted of redirecting blood flow in the atria via the Mustard or Senning procedure, also known as the "atrial switch procedure."[18, 19] Beginning in the mid-1980s, the atrial switch procedure was replaced by the arterial switch operation of Jatene, an operation that results in a systemic left ventricle and should provide a better long-term outcome. However, hundreds of Mustard/Senning patients exist worldwide and are now of childbearing age. In patients with a systemic right ventricle, complications in pregnancy predictably include worsening systemic ventricular failure, preeclampsia and premature labor, and arrhythmias, both bradycardia and tachycardia.[18, 20-22] Siu et al. conferred an increased risk of maternal and neonatal complications.[5] Pregnancies in patients with ccTGA were found to have an increased rate of fetal loss, with maternal morbidity similar to patients with TGA after a Mustard/Senning procedure due to the presence of a systemic right ventricle.[16]

Bicuspid aortic valve that leads to aortic stenosis (AS) can affect pregnancy when it results in mild-moderate AS, but this is generally well-tolerated.[23, 24] However, LV dysfunction, pulmonary edema, and arrhythmias occur in a very small percentage of pregnant patients.[23, 24] This may be due to the compensatory mechanical changes in left ventricle motion that occur to maintain cardiac output in the presence of a fixed obstruction.[25]

Prosthetic heart valves create a challenge during pregnancy. Anticoagulation for mechanical heart valves should be adjusted since coumadin must be stopped during the first trimester due to the well-documented risk of embryopathy. Current guidelines support three approaches: (1) low-molecular-weight heparin subcutaneously twice daily throughout pregnancy, (2) unfractionated heparin subcutaneously twice daily through pregnancy, or (3) unfractionated or low-molecular-weight heparin subcutaneously twice daily until gestational week 13, then warfarin from weeks 13-35, and then a change back to unfractionated or low-molecular-weight heparin subcutaneously until delivery. Since the teratogenic effect of warfarin occurs in the first trimester, data may support its use in the second and third trimesters. Individual management strategies should be discussed jointly with the cardiologist, obstetrician, and patient. Antibiotic prophylaxis is not recommended based on the 2007 American Heart Association guidelines, but

some obstetricians still routinely administer antibiotics at the time of rupture of membranes.

The Fontan operation has improved the potential for long-term survival in patients with single ventricle physiology.[26] In this procedure, a total cavopulmonary connection is created by anastomosing the vena cavae to a branch pulmonary artery, thus completely bypassing the right side of the heart. It has previously been recommended that Fontan patients not become pregnant as the modified circulation has a fixed ability to accommodate increased cardiac output, and hemodynamic changes in pregnancy could increase pulmonary pressures, leading to decreased flow from the venous circulation. In a study involving 6 women with 10 pregnancies,[27] complications included a 50% spontaneous abortion rate, New York Heart Association functional class deterioration , increased detection of significant arrhythmias, premature rupture of membranes, premature delivery, and intrauterine growth restriction. Thus, Drenthen et al. advise against pregnancy due to the significant neonatal morbidity.[27] However, other studies in Fontan patients illustrate lower rates of maternal and neonatal complications and thus specific pregnancy recommendations remain controversial.[26] Pre-pregnancy counseling to discuss the maternal, cardiac, and neonatal risks for these patients is essential.

High-Risk Pregnancy Lesions

As mentioned earlier, the four main lesions with the highest cardiac risk are Marfan syndrome with dilated aortic root (>4 cm), pulmonary hypertension, severe left ventricular outflow tract obstruction (>40 mmHg), and LVEF <30%. These patients should be routinely advised to avoid pregnancy. In patients with Marfan syndrome, the dilated aortic root could lead to aortic dissection or aneurysm, particularly during the second stage of labor.[28] In pregnant Marfan patients, beta-blocker therapy should be instituted, and a cesarean section is recommended at approximately 36-37 weeks gestation or when the aortic root is >45 cm.[11] Eisenmenger syndrome and severe pulmonary hypertension have an unacceptably high maternal and fetal mortality rate that both approach 50%. Pregnancy is strongly discouraged and termination should be recommended. Pregnancy termination in the last two trimesters poses a high risk to the mother, but the risk of termination should be balanced against the risk of continuation of pregnancy. Even after successful delivery, the risk of maternal death may be increased.[29, 30, 10]

Pregnancy and Delivery Recommendations

As with most patients, a planned pregnancy is preferred in patients with congenital heart disease. Unplanned pregnancies could theoretically be decreased or avoided if women of childbearing age with CHD had prenatal counseling according to their congenital heart lesion. Ideally, care during the antenatal period would involve consultation with a congenital cardiologist and a maternal-fetal medicine specialist in a tertiary care center. Counseling on potential complications to the mother and the fetus should be provided, and any procedures to optimize cardiac function should be discussed at the time of initial consultation. Fetal echocardiography for early detection of fetal cardiac disease is also recommended, ideally at 18–22 weeks gestation.

In most pregnant cardiac patients, vaginal delivery can usually be recommended with labor positioning in the left lateral position. Forceps or vacuum assistance can be used during delivery to shorten the second stage of labor. It is important to decrease the fluid shifts that can occur during the intra- and post-partum period as they may produce significant complications such as pulmonary edema or ventricular volume overload. Specific medications to avoid during pregnancy include angiotensin-converting enzyme inhibitors, angiotensin-II receptor blockers, amiodarone, warfarin (during the first trimester), and spironolactone. If medically indicated, induction of labor is generally well-tolerated in women with cardiac disease.[31] However, left-sided heart lesions are an indication for cesarean section, especially moderate-to-severe aortic stenosis (i.e., aortic valve gradient >30 mmHg), moderately dilated aortic root (>4.5 cm), thoracic aortic aneurysm, or significant aortic coarctation (>20 mmHg).[32] These patients should also have cardiac rhythm monitoring and pulse oximetry during labor and the postpartum period. In patients with moderate-to-complex CHD, close post-partum observation is recommended for 2–3 days, and this period should be increased to 7–14 days in patients with pulmonary hypertension.

Summary

Pregnancy in patients with congenital heart disease provides a challenging clinical management scenario. Patients should be counseled on their obstetrical, cardiac, and fetal risks, and pregnancy should be avoided in patients with high-risk lesions. In patients with pulmonary hypertension and/or Eisenmenger syndrome, termination should be recommended. Cardiac risk can be stratified according to the CARPREG Risk Score. Co-management between an adult congenital heart disease cardiologist and maternal-fetal medicine specialist is recommended in order to optimize the outcome for the mother and baby.

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