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Amy J. Ortman, MD[1]

Abstract

Advances in the surgical palliation and correction of congenital heart lesions have improved survival and increased the number of patients living into adulthood. Although pregnancy outcomes will be favorable for most patients with congenital heart disease, the cardiovascular challenges associated with pregnancy and delivery are best managed with a multidisciplinary approach during the puerperium. This review addresses the prevalence, physiology, risk assessment, peripartum complications, and anesthetic management of the pregnant patient with underlying congenital heart disease.

Keywords

congenital heart disease, cardiovascular risk, cardiovascular risk factors, monitoring, noncardiac surgery

Epidemiology

The most common birth defects in humans are cardiac lesions. The lesions involved in congenital heart disease (CHD) range from severe lesions that result in significant morbidity and mortality in infancy, to small septal defects that may close spontaneously or may be discovered in asymptomatic adults. As such, the incidence of CHD varies greatly depending on how it is defined. The incidence of moderate to severe CHD is approximately 6 per 1000 live births. When minor defects are included, the incidence increases to 75 per 1000 live births.[1]

Improved surgical and medical care has led to a growing population of adults living with CHD, even those with complex disease. An estimated 85% of patients born with complex lesions have survived into adulthood since the development of neonatal surgical repair in the 1970s.[2,3] Current surgical mortality rates are less than 5%, and it is estimated that within the next decade, as many as 1 in 150 young adults will have some form of CHD.[3]

Clinicians are faced with new challenges as patients with CHD survive longer and reach childbearing age. Although the prevalence of heart disease in pregnancy has remained relatively stable at 1.0% to 1.5%, the proportion of women affected by congenital lesions has increased.[4,5] Congenital lesions now account for approximately 80%[6,7] of chronic heart disease in pregnancy, with shunt lesions predominating (20% to 65%).[7]

Cardiovascular Changes in Normal Pregnancy

To accommodate the increased metabolic demands of the mother and fetus, multiple cardiovascular changes occur during pregnancy: cardiac output, heart rate, and circulating volume increase, whereas vascular resistance decreases. These changes are of minimal or no consequence in the healthy parturient, but may be poorly tolerated in a patient with CHD.

Antepartum

In response to the metabolic demands of the growing fetus, uterine blood flow increases substantially from 50 mL/min to 700 to 900 mL/min at term.[8] The increase in uterine perfusion is mediated, in part, by an increase in circulating blood volume; red blood cell mass increases by 20 to 30%, whereas plasma volume increases by 45%,[9,10] accounting for the physiologic anemia of pregnancy.

Systemic vascular resistance (SVR) decreases in pregnancy, beginning early in the first trimester. Vascular resistance reaches a nadir at 35% below prepregnancy levels in the second trimester, then gradually increases until term where it remains 20% below baseline.[11] Cardiac output begins to increase as early as the fifth week of pregnancy and continues to rise through the second trimester when it plateaus at approximately 50% above prepregnancy levels.[12] Increased blood flow through the pulmonary circulation is counterbalanced by a drop in pulmonary vascular resistance (PVR). As a result, pulmonary artery pressures

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remain unchanged.[11,13] Myocardial contractility and left ventricular mass also increase during pregnancy.[14]

Intrapartum

During labor, cardiac output increases again—by up to 50% in the second stage. A portion of this increase is caused by the sympathetic stimulation that occurs in response to pain, which leads to an increase in blood pressure, heart rate, and myocardial oxygen demand.[15] Additionally, with each contraction 300 to 500 mL of blood enters the maternal circulation.[13]

Postpartum

In the immediate postpartum period, circulating volume and cardiac output are increased even further as vena caval compression is relieved, and uterine blood flow diminishes.[13] In the ensuing days to weeks, the extravascular fluid accumulated during pregnancy is mobilized and eliminated, and hemodynamics slowly return to the prepregnancy state.

Risk Assessment and Stratification

General Considerations

Although the prevalence of CHD in pregnancy has increased, the overall numbers of affected patients remain small, and prospective, randomized studies are rare. Therefore, care for pregnant patients with CHD is guided largely by retrospective case series and expert opinion. Common recommendations published for this population include the following: Patients with moderate to complex disease are best managed by multidisciplinary teams at specialized centers, and preconceptual counseling is recommended for all patients. Assessing the patient prior to pregnancy allows caregivers the opportunity to review functional status and medications, discuss risks, and, if indicated, order additional studies.

Maternal Risk Assessment

Given the physiologic demands of pregnancy, it is not surprising that women with underlying CHD are at increased risk of complications. Adverse cardiac outcomes have been reported to occur in 7.6% to 25.0% of such pregnancies, and the most common cardiac events diagnosed are congestive heart failure (CHF) and arrhythmias.[16-18] Less common complications include myocardial infarction, cerebrovascular accidents, and death.[18] Two considerations are worth mentioning. First, CHD is a heterogenous disease, and the complexity of the population studied will affect the outcomes observed. Second, the incidence of cardiac complications may be underestimated because the diagnosis of heart failure early in pregnancy is a common reason for termination.[18]

Table 1. CARPREG Risk Index[19]

Prior cardiac event or arrhythmia (*heart failure, transient ischemic attack or stroke before pregnancy, or arrhythmia*)
NYHA functional class >II or cyanosis
Left heart obstruction (*mitral valve area <2 cm^2, aortic valve area <1.5 cm^2, peak LVOT gradient >30 mm Hg*)
Systemic ventricular dysfunction (*ejection fraction <40%*)
Assign one point for each predictor present, the risk estimation of cardiovascular complications is as follows:
0 points: 5%
1 point: 27%
>1 point: 75%

Abbreviations: CARPREG, cardiac disease in pregnancy; NYHA, New York Heart Association; LVOT, left ventricular outflow tract.

Several instruments have been developed to estimate the risk of pregnancy in this population. The most common is the CARPREG risk index (Table 1). The CARPREG investigators identified 4 predictors of primary cardiac events, with increasing maternal risk for each additional predictor identified.[19] Although the CARPREG index has been validated in other studies,[16,20] its application in the CHD population is limited because the index was developed in a cohort that included patients with acquired disease and primary electrical disease.[17] In addition, several important patient populations (those with aortic pathology, pulmonary hypertension, and complex CHD) were underrepresented.[7,17]

The CARPREG risk index was validated in a single-center, retrospective study of patients exclusively with CHD, and 2 additional risk factors were identified—depressed subpulmonary ventricular function and/or severe pulmonary regurgitation.[16] In a similar study, the ZAHARA investigators also evaluated pregnant patients with CHD. In addition to the risk factors identified by the CARPREG risk index, the investigators discovered that the presence of a mechanical valve, pulmonary or systemic atrioventricular (AV) valve regurgitation, and cardiac medication prior to pregnancy also increased risk of adverse maternal cardiac events.[17] Using their findings, the ZAHARA investigators proposed an alternative risk score, but to date, it has not been validated by other studies.

Although not exclusive to the CHD population, recently published guidelines by the European Society of Cardiology endorse the use of the modified World Health Organization risk classification for stratification of cardiovascular risk in pregnancy (Table 2). The European Society of Cardiology recommends the use of the World Health Organization classification because it integrates all known

Table 2. Modified WHO Classification of Maternal Cardiovascular Risk *[7, 21]*

Risk Class	Risk of Pregnancy	Conditions Corresponding to Risk Class
I	No detectable increased risk of maternal morbidity and mortality	*Risk class I* Uncomplicated, small or mild pulmonic stenosis, patent ductus arteriosus, mitral valve prolapsed Successfully repaired simple lesions (eg, atrial septal defect, ventricular septal defect, patent ductus arteriosus) Isolated ventricular or atrial ectopic beats
II	Small increased risk of maternal morbidity and mortality	*Risk class II* Unoperated atrial septal defect or ventricular septal defect Repaired tetralogy of Fallot Most arrhythmias *Risk class II or III (depending on individual)* Mild left ventricular impairment Hypertrophic cardiomyopathy Native or tissue valvular disease not considered WHO class I or IV Marfan syndrome without aortic dilation Repaired coarctation
III	Significant increased risk of maternal morbidity and mortality	*Risk class III* Mechanical valve Systemic right ventricle Fontan circulation Cyanotic heart disease Other complex congenital heart disease Aortic dilatation 40-45 mm in Marfan syndrome
IV	Extremely high risk of maternal mortality and severe morbidity; pregnancy is contraindicated	*Risk class IV* Pulmonary artery hypertension of any cause Previous peripartum cardiomyopathy with residual impairment Severe systemic ventricular dysfunction (LVEF < 30%, NYHA III or IV) Marfan syndrome with a dilated aorta >45 mm Native severe coarctation

Abbreviations: WHO, World Health Organization; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

maternal cardiovascular risk factors as well as the contraindications to pregnancy not included by other instruments.[7]

Pregnancy represents a prolonged, physiologic challenge to women with CHD. Cardiopulmonary exercise testing may help further identify women at risk for adverse cardiac outcomes. In a retrospective, observational study of women with CHD, poor chronotropic response to exercise testing before pregnancy correlated with adverse pregnancy outcomes. Adverse cardiac events occurred in 18% of patients, with CHF and arrhythmias being the most common.[22] Not surprisingly, patients who experience cardiac complications during pregnancy also appear to be at increased risk of adverse cardiac events in the months following delivery.[23]

Neonatal Risk Assessment

Adverse neonatal events occur with greater frequency in pregnancies complicated by CHD and are closely tied to maternal complications and the severity of the underlying disease. Rates of preterm delivery are elevated—complicating 16% to 19% of pregnancies. Related comorbidities, such as neonatal intensive care unit admission, intraventricular hemorrhage, small for gestational age, and neonatal mortality are also more common.[18,24,25]

In the absence of genetic syndromes, the offspring of women with CHD have a 3% to 10% incidence of heart defects,[26,27] which is 10-fold greater than that of the general population. In patients with inherited disorders, for example, Marfan's syndrome, the rate of affected offspring may be as high as 50%. As such, patients with CHD should have a second trimester fetal echocardiographic evaluation for screening and diagnosis, and they should be counseled on the risks to their descendants. Genetic testing may be useful in select patients.

Anesthetic Management and Considerations

Specific decisions regarding the type of anesthesia and appropriate monitoring for delivery should be tailored to

the individual patient and the planned procedure. In general, vaginal delivery is preferred for patients with CHD, and cesarean delivery is reserved for obstetric indications. There are, however, important exceptions: patients with substantial aortopathy, patients who are acutely unstable, or those on warfarin anticoagulation (because of the risk of neonatal bleeding).[28] In an effort to avoid hemodynamic fluctuations associated with maternal pushing, a passive or assisted second stage is frequently advocated in patients with CHD, although there is no evidence of improved outcomes with this practice.[29] Whether an active or passive second stage is planned, good analgesia will benefit the parturient by controlling pain and limiting the catecholamine release that can result in tachycardia, hypertension, increased cardiac output, and increased myocardial oxygen demand.

Most obstetric anesthesiologists prefer to use neuraxial techniques for labor analgesia and cesarean deliveries. Neuraxial techniques used in this population include single shot spinal, continuous lumbar epidural, combined spinal–epidural, sequential low-dose combined spinal–epidural, and continuous spinal anesthetic.[30] The addition of opioids in neuraxial techniques will improve the quality of the block and reduce the local anesthetic requirements and hemodynamic impact. When placing epidural catheters, practitioners should evaluate the risk of paradoxical air embolus or hemodynamic instability from epinephrine and modify their loss of resistance and/or test dose technique accordingly.[29,30] Cautious administration, careful monitoring, and an understanding of the patient's unique physiology are critical to the safety and success of the chosen technique.

Anticoagulant medications may complicate the timing and placement of neuraxial techniques in these patients. Women with CHD may be anticoagulated because of mechanical valves, or as thromboprophylaxis in high-risk populations, like those with Eisenmenger's syndrome or Fontan physiology. To limit the risk of spinal hematoma, coagulation function should be assessed before performing any neuraxial anesthetic in patients receiving anticoagulants during pregnancy (Table 3). Published guidelines by the American Society of Regional Anesthesia and Pain Medicine recommend the following: (*a*) schedule the delivery when possible; (*b*) transition from oral anticoagulants to low-molecular-weight heparin or unfractionated heparin no later than 36 weeks' gestation; (*c*) stop low-molecular-weight heparin at least 36 hours before induction or scheduled cesarean delivery and if needed, maintain the patient on intravenous or subcutaneous unfractionated heparin; (*d*) 4 to 6 hours before the anticipated delivery, stop intravenous unfractionated heparin; and (*e*) in the postpartum period, low-dose prophylactic anticoagulation may be resumed 12 hours after vaginal delivery and epidural catheter removal, but therapeutic anticoagulation should be withheld until 24 hours after delivery.[31] Pregnant patients with mechanical valves are at high risk for thrombotic complications and practice guidelines state that in the absence of significant bleeding, it is reasonable to resume unfractionated heparin and warfarin 4 to 6 hours after delivery.[32] Thus, anticoagulation in the puerperium should be carefully coordinated and individualized to each patient.

Common monitors for laboring patients include pulse oximetry and noninvasive blood pressure. Patients with CHD may benefit from the addition of electrocardiography (ECG) and intra-arterial blood pressure monitoring. Central venous catheters and pulmonary artery catheters are rarely used in this patient population, but they may be helpful in selective cases. Some patients with CHD, such as those with shunt lesions or Fontan circulation, have complex anatomy, and central access should only be attempted by practitioners familiar with these patients. Finally, in patients who undergo general anesthesia for cesarean delivery, transesophageal echocardiography may be used to monitor volume status and ventricular function. However, patients with CHD may have unusual anatomy and training in complex CHD is necessary to accurately interpret the images.[33]

Recommendations for Specific Conditions

Isolated Shunt Lesions

Shunt lesions are common congenital defects, and they may occur in isolation or in combination with other malformations. Shunt lesions include atrial septal defects (ASDs), ventricular septal defects (VSDs), atrioventricular septal defects (AVSDs), and patent ductus arteriosus (PDA). Most pregnant patients with simple shunt lesions will have left-to-right flow. However, over time, shunt defects may increase right-sided pressures and lead to pulmonary arterial hypertension (PAH) and reversal of the shunt (Eisenmenger's syndrome). The presence of PAH or right ventricular (RV) failure is a contraindication to pregnancy because of the significant risk of fetal and maternal mortality.

Atrial septal defects. ASDs are a common congenital lesion in older patients as defects may not be diagnosed until well into adulthood. Patients with a repaired ASD have limited risk of complications, although arrhythmias are more common than in the general population. A retrospective review comparing pregnancy outcomes in women with repaired and unrepaired ASDs found similar cardiovascular outcomes in both groups, with arrhythmias the most frequent complication.[34] In addition to arrhythmias, patients with an unrepaired ASD are at increased risk of

Table 3. Timing and Evaluation of Anticoagulants

Medication	Discontinuation	Laboratory Evaluation
Warfarin	No later than 36 weeks' gestation, or 4 to 5 days before the anticipated delivery or procedure	A normal (or near-normal) prothrombin time (PT) and/or international normalized ratio (INR) should be obtained before the placement of neuraxial anesthesia or catheter removal.
LMWH	Therapeutic (high dose) LMWH should be stopped for 24 hours, and prophylactic (low dose) LMWH should be stopped 12 hours, before placement of neuraxial anesthesia	Although anti-Xa levels may be used in the antepartum period to monitor patients, they are not predictive of bleeding risk and should not be used to guide neuraxial anesthesia placement
UFH	UFH should be stopped with the onset of labor or 12 hours before a scheduled procedure. In high-risk patients, intravenous UFH may be continued until 4-6 hours before the anticipated delivery or procedure	A normal aPTT and/or a blood heparin concentration near zero should be obtained before neuraxial anesthesia placement or catheter removal

Abbreviations: PT, prothrombin time; INR, international normalized ratio; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin; aPTT, activated partial thromboplastine time.

paradoxical embolus,[3,7,35] and obstetric complications of preeclampsia, small-for-gestational age births, and fetal mortality.[34]

Ventricular septal defects. Although ventricular septal defects (VSD) are the most common congenital heart defect at birth, they are encountered less frequently during pregnancy because of early diagnosis and repair, or spontaneous closure during childhood. Women with isolated, small VSDs and no pulmonary hypertension or ventricular failure have no significant increase in cardiovascular risk with pregnancy[3,7] but do appear to be at increased risk of preeclampsia.[7,36] Women with large shunts and PAH may experience arrhythmias and progression of their disease.[3]

Atrioventricular septal defects. AVSDs may also be known as AV canal defects or endocardial cushion defects. The primary lesion is the presence of a common AV connection with abnormalities in the fibrous skeleton of the heart, and a septal defect that may be above the AV valves or extend below the AV valves. AVSDs may be subdivided into 2 categories: partial defects with 2 distinguishable AV valves or complete defects with a single common AV canal.[37] Most patients with AVSD have had surgical repair in childhood with good results, but late postoperative complications, such as left ventricular outflow tract obstruction and/or left AV valve regurgitation or obstruction, occur in 5% to 10% of patients.[3]

Although patients with a complete repair and no significant residual lesions will tolerate pregnancy well, patients with AVSDs are at higher risk of cardiovascular complications during pregnancy than patients with isolated VSDs or ASDs. In a retrospective review of 26 pregnant women with AVSD in which 84% of patients had a history of repair, cardiovascular complications affected almost 40% of completed pregnancies. Complications included deterioration of functional status, increased left AV valve regurgitation, and arrhythmias.[38] Patients with severe preexisting AV valve regurgitation and/or ventricular dysfunction may deteriorate during pregnancy, and surgical repair prior to pregnancy should be considered.[7]

Patent ductus arteriosus. A PDA is a persistent connection between the aorta and the pulmonary artery. Most clinically significant PDAs are diagnosed and ligated in childhood, but patients with moderate or large uncorrected shunts may present as adults with signs and symptoms of RV failure and PAH. Patients with a silent or small PDA, or those with larger defects with good ventricular function and no PAH have no significantly increased risk associated with pregnancy.[35,39]

Management. In the absence of ventricular dysfunction and/or PAH, the management for pregnant patients with simple left-to-right shunts is similar to that of the general population. Patients should be evaluated by a cardiologist in the first trimester, with additional follow-up individualized to the patient and her underlying pathology.

Low-risk patients do not need any special monitoring during labor, although those with a history of arrhythmias may benefit from continuous ECG monitoring. Patients with residual lesions are at risk for paradoxical embolism—particularly with a Valsalva maneuver or a reduction in SVR following regional anesthesia. Intravenous lines should be carefully de-aired. To minimize pain-associated sympathetic stimulation, early neuraxial analgesia is recommended, and gradual titration of the block is suggested to avoid sudden drops in SVR.

Congenital Heart Disease–Associated Pulmonary Arterial Hypertension

Pulmonary arterial hypertension is defined as mean pulmonary artery pressures greater than 25 mm Hg at rest, or

greater than 30 mm Hg with exercise. Patients with CHD are at increased risk for the development of PAH, compared with the general population, with an estimated prevalence of 30% in patients with unrepaired lesions and 15% in patients with repaired lesions.[40] PAH associated with CHD (CHD-PAH) may involve several different scenarios, but the most common etiology is from a large, unrepaired systemic-to-pulmonary shunt,[3] which will be the only form of CHD-PAH discussed in this review. Longstanding systemic-to-pulmonary shunts result in vascular remodeling and increased vascular resistance in the pulmonary circulation. Eventually, these changes lead to bidirectional flow or right-to-left shunting, and oxygen-unresponsive hypoxemia (Eisenmenger's syndrome).

Classically, patients with Eisenmenger's syndrome present with symptoms of dyspnea and/or palpitations in the second decade of life. In some patients, the physiologic changes of pregnancy may precipitate the first symptoms.[40] Patients with Eisenmenger's physiology have progressive disease and significant morbidity. Common complications include "paradoxical" emboli with brain abscesses, altered hepatic function, hemoptysis, hypoxemia-related erythrocytosis with intravascular sludging, and RV ischemia.[3,40]

Pregnancy is contraindicated in patients with Eisenmenger's syndrome because of poor maternal and fetal outcomes. In 1979, one of the first clinical series published on this patient population reported a maternal mortality rate of 52% and a perinatal mortality rate of 28%.[41] A recent article analyzed pregnancy outcomes in a total of 29 patients with CHD-PAH from case reports and case series published between 1997 and 2007. Although maternal mortality improved from previously published reports, it remained prohibitively high at 28%. All the maternal deaths occurred in the postpartum period, and severe RV failure was the most common cause of death. The authors suggested that the modestly improved outcomes might be related to advanced therapies now available to treat PAH but concluded that pregnancy is best avoided in this patient population.[42]

During pregnancy, a reduction in SVR will worsen right-to-left shunts, decrease pulmonary blood flow, and increase cyanosis. In addition, intravascular volume expansion and elevated cardiac output place pregnant patients with Eisenmenger's physiology at increased risk of cardiovascular failure and complications. Therapies for pregnant patients with Eisenmenger's syndrome are limited. Oxygen may improve cyanosis or PAH in some patients, but others will not be oxygen responsive. Patients may benefit from bed rest and gentle diuresis. Anticoagulation is widely used in patients with Eisenmenger's physiology to prevent thromboembolic events and most recommend continuing anticoagulation in pregnancy.[7,43] However, this approach is not without risk, as these patients are also at risk of thrombocytopenia and hemoptysis.

Vasoactive modulators, such as intravenous prostacyclin or oral sildenafil, beraprost, and bosentan, have improved hemodynamics and exercise capacity in adult patients with CHD-PAH, but few studies have been performed exclusively in patients with Eisenmenger's physiology.[40] In general, if vasoactive modulators are used prior to pregnancy, continuation throughout pregnancy should be considered. However, the safe administration of these medications in pregnancy has not been well established, and some, such as bosentan, are contraindicated in pregnancy.[42]

Intravenous prostacyclins have known platelet antiaggregatory effects, and neuraxial anesthesia should be used with caution in patients receiving these medications. Intravenous prostacyclins have a circulatory half-life of 2 to 5 minutes and antiplatelet effects are short-lived, lasting 20 to 30 minutes once the intravenous prostacyclin is discontinued.[44] Abrupt withdrawal of the medication may precipitate rebound pulmonary hypertension and is not advised. Because antiplatelet effects are not seen clinically with nitric oxide or aerosolized prostacyclins,[44,45] the transition to an inhaled formulation during the peripartum period has been described as a technique to maintain hemodynamic stability while minimizing the risk of bleeding complications.[45]

In addition to oxygen and pharmacologic therapies, management of pregnant patients with Eisenmenger's physiology should include care at a tertiary center with expertise in these patients, and hospitalization and/or delivery if maternal deterioration is identified. The optimal route of delivery has not been established. An assisted vaginal delivery may be a better option than cesarean delivery, which is associated with an increased risk of postpartum infection, pulmonary comorbidity, peripartum fluid shifts, and metabolic demands.[46]

The primary goals of anesthetic management include maintenance of SVR and intravascular volume and avoiding an increase in PVR from pain, sympathetic stimulation, hypercarbia, acidosis, or worsening hypoxemia. Suggested monitors include continuous pulse oximetry for detection of increasing right-to-left flow, ECG, and an arterial line for close monitoring of systemic pressures and acid–base status.[43] A central venous line may be useful to monitor filling pressures or to facilitate administration of inotropes and vasoactive medications. Pulmonary artery catheters are rarely used because of the risk of arrhythmias, difficult placement, and limited utility.

If an assisted vaginal delivery is chosen, it should take place in an intensive care unit.[43] Epidural anesthesia should be performed in early labor but carefully and slowly titrated to minimize SVR reduction and cyanosis. Cesarean delivery may be necessary, and epidural anesthesia has become the technique of choice.[47,48] Slow titration of local anesthetics while counterbalancing the hemodynamic changes with

vasoactive medications is critical in this population. The use of neuraxial opioids or a low-dose combined spinal–epidural block have been advocated to improve the quality of the block and provide analgesia postoperatively.[47,49]

The postpartum period is a critical time for patients with Eisenmenger's physiology; the majority of deaths occur within 30 days after delivery.[42,50] Blood loss should be promptly replaced with crystalloid or blood products, as guided by the clinical situation and laboratory values, without giving excessive volume to the patient. Although atony should be aggressively treated, rapid intravenous oxytocin bolus administration has been associated with hemodynamic instability and death in these patients.[51,52] A continuous intravenous infusion of oxytocin is associated with greater hemodynamic stability.[53] A slow oxytocin infusion of 40 units over 4 hours, in combination with uterine massage, has been used successfully in patients with severe cardiac disease.[51] After delivery, anticoagulation should be resumed, and patients should remain in the hospital for several weeks.[43]

Aortic Diseases

Several congenital and inherited conditions affect the thoracic aorta. Patients with these disorders are at increased risk of morbidity and mortality during pregnancy and delivery. Aortic diseases were reported to be a leading cause of maternal death in the 2003-2005 report of the UK Confidential Enquiry into Maternal and Child Health.[7] The hormonal and hemodynamic changes that occur with pregnancy place women with aortic disease at increased risk of dissection—particularly in the third trimester and in the puerperium. These conditions include Marfan's syndrome (MS), Ehler–Danlos syndrome type IV, Loeys–Dietz syndrome (LDS), Turner's syndrome, and coarctation of the aorta. Patients with a bicuspid aortic valve and a dilated aorta are also at risk of aortic dissection during pregnancy but will not be discussed in this review.

Marfan's syndrome. MS is an autosomal-dominant connective tissue disorder affecting multiple organ systems, but the most common problems involve the skeletal, ocular, and cardiovascular systems. Eighty percent of affected individuals will have cardiovascular manifestations, which include mitral valve prolapse, mitral regurgitation, aortic regurgitation, and aortic dilatation (primarily affecting the ascending aorta).[54] The most common cause of premature death in patients with MS is type A aortic dissection or rupture from aortic root dilation.[55]

Pregnancy has been shown to increase the risk of aortic dissection in patients with MS.[56,57] Increases in heart rate, intravascular volume, and stroke volume, combined with hormonally mediated histologic changes in the aorta, are believed to contribute to the elevated risk of cardiovascular complications. In a retrospective study of 91 pregnancies in 36 women with MS, significant aortic events occurred in 6 women during pregnancy. Four of the 6 women had an acute dissection and 2 died of complications; the remaining 2 patients had progressive dilatation without dissection. The women were followed for a mean of 10 years after their last pregnancy; an additional 5 had an aortic dissection with one fatality, and 3 had an elective root replacement. The remaining 22 women had an aortic root dimension of <4.3 cm at the time of publication.[56] More recent studies have examined unselected pregnant patients with MS to better estimate the actual risk of complications. The overall expected risk of aortic dissection in pregnancy is approximately 3%. Patients with an aortic root <4.0 cm have an estimated risk of 1%, whereas patients with an aortic root >4.0 cm, rapid dilation, or a previous dissection of the aorta are estimated to have a 10% risk of complications.[58] In addition to cardiovascular complications, patients with MS are at increased risk of obstetric complications, such as preterm delivery, preterm premature rupture of membranes, and increased neonatal mortality.[59]

Patients with MS need careful surveillance throughout their pregnancies. Beta-blockers have been shown to be beneficial in patients with MS and their continuation during pregnancy is recommended.[60] Pregnant patients with MS and an aortic root <4.0 cm in diameter should be followed with transthoracic echocardiography each trimester and again prior to delivery. If no dilatation is detected during pregnancy, patients may have an assisted vaginal delivery, and cesarean deliveries should be reserved for obstetric indications.[61] In patients with an aortic root diameter >4.0 cm or risk factors for dissection (progressive dilatation or a history of dissection), a transthoracic echocardiography should be performed every 4 to 6 weeks and an elective cesarean delivery performed to minimize the hemodynamic changes associated with delivery.[54] Although limited data are available, most experts agree that patients with an aortic root measuring >4.5 cm should be discouraged from attempting pregnancy.[7,62] In patients in whom there is an acute event after 24 to 28 weeks' gestation, cesarean delivery of the fetus prior to cardiopulmonary bypass and surgical repair is recommended.[54,61]

During labor, epidural anesthesia controls pain, minimizes sympathetic activation, and limits fluctuations in blood pressure. For these reasons, early neuraxial analgesia is recommended for vaginal delivery in patients with MS.[54,61,63] For patients having a cesarean delivery, the successful use of both regional techniques[64] and general anesthesia have been described.[65] An arterial line is helpful for tight hemodynamic control of patients with a dilated aorta or dissection. Several additional caveats to the anesthetic management of these patients should be mentioned. First, careful vasopressor administration in response to hypotension is

warranted. Hypertension and tachycardia increase shear forces on the aorta. Titration of an alpha-agonist such as phenylephrine, may be a better choice than an indirect sympathomimetic like ephedrine.[63] Second, patients with MS and other aortopathies need tight hemodynamic control during delivery and throughout the postpartum period, as hypertension and tachycardia increase the risk for cardiovascular complications. Lastly, dural ectasia, or ballooning of the lumbosacral dural sac, is present in 63% to 92% of patients with MS. The increased CSF volume associated with dural ectasia, may increase the rate of failure with intrathecal techniques.[66]

Ehlers–Danlos syndrome type IV. The Ehlers–Danlos syndromes are a group of inherited disorders of connective tissue. Type IV is the most severe; the median age of survival is 48 years, with arterial dissection and rupture accounting for most deaths.[67] Recent guidelines have stated that pregnancy is contraindicated in patients with Ehlers–Danlos syndrome type IV,[7] as it is associated with a maternal mortality of around 12% from uterine rupture, vascular rupture, and hemorrhage.[68] When vascular injury occurs, the proximal branches of the aortic arch and descending thoracic aorta are commonly affected. Unfortunately, aortic dissection may occur without preceding aortic dilation, making management more difficult.[7]

There are no clear recommendations on the timing or mode of delivery, although some have advocated elective Cesarean deliveries at 32 to 34 weeks to minimize the risk of uterine rupture and fluctuations in cardiac output and blood pressure.[7,69] Information on anesthetic management is limited in the literature, but principles similar to those outlined for MS may be applied.

Loeys–Dietz syndrome. LDS is an autosomal dominant connective tissue disorder. It is characterized by the triad of arterial tortuosity and aneurysms, hypertelorism, and bifid uvula or cleft palate.[70] LDS has been subdivided into 2 groups that form a clinical continuum: type I, which is characterized by craniofacial manifestations and more severe vascular disease, and type II, in which characteristic cutaneous findings are seen and craniofacial manifestations are absent.

Regardless of type, the clinical history of LDS is marked by aggressive arterial aneurysm formation and a high incidence of pregnancy-related complications.[71] In the original series, the average age at death was 26 years, and the primary cause of death was progressive dilation of the aorta, dissection, and rupture.[70] Patients with LDS may have arterial involvement at any level of the vascular tree, and dissection can occur in the absence of significant root enlargement[72] making management difficult. Current recommendations for all patients with LDS include vascular imaging at 6- to 12-month intervals, and surgical intervention with an aortic diameter >4.2 cm (internal diameter) by transesophageal echocardiography or >4.4 cm (external diameter) by computed tomography or magnetic resonance imaging.[73]

Limited information is available to guide the care of pregnant patients with LDS. In the original case series, a total of 21 pregnancies in 12 women were followed: 6 women had a major complication (aortic dissection in 4 and uterine rupture in the remaining 2) during pregnancy or in the immediate postpartum period.[70] Antepartum management should be similar to patients with MS, with the understanding that aortic dissection and rupture may not be preceded by root dilation. Several authors reported performing an elective cesarean delivery at 34 weeks to minimize the risk of vascular and uterine rupture,[74] but no formal recommendations have been established. Neuraxial anesthesia techniques for delivery have clear advantages in patients with LDS: good pain control, minimal sympathetic activation, and limited fluctuations in blood pressure. If general anesthesia is necessary, it should be noted that up to 50% of patients with LDS have cervical spine instability.[71,72]

Turner syndrome. Turner syndrome is caused by complete or partial monosomy of the X chromosome. It is the most common genetic defect at conception, but occurs in only 1/2000 live female births. Congenital cardiac defects account for many lost pregnancies and are common in surviving girls and adults. The 2 most common lesions in this population are bicuspid aortic valve (30%) and coarctation of the aorta (12%).[75] Recently, these patients have been recognized to be at increased risk of aortic dissection, even in the absence of structural defects.[76]

Advances in reproductive technology have enabled more women with Turner syndrome to get pregnant. Although many women with Turner syndrome will have an uneventful pregnancy, up to 2% have died from aortic dissection or rupture, a rate 100 times greater than the general population.[77] Women at greatest risk of aortic dissection are those with aortic dilation.[7] Because women with Turner syndrome are of small stature, aortic dilation should be normalized to body surface area. Women with aortic diameters >25 mm/m^2, a history of aortic surgery or dissection, aortic coarctation, or uncontrolled hypertension are at increased risk for aortic dissection, and pregnancy is considered to be contraindicated.[77]

Management of Turner syndrome patients is similar to the management of those with MS. Hypertension is common and should be aggressively controlled with beta-blockers. Patients should be followed carefully with echocardiography performed at the end of the first two trimesters, and each month during the third trimester.[77] Most patients with Turner syndrome will need a cesarean delivery because of cephalopelvic disproportion. Those that are candidates for vaginal delivery may benefit from an

assisted second stage.[77] The objectives of anesthetic management are similar to those with MS or other conditions that increase the risk of aortic dissection and rupture. An increased incidence of difficult airway and ventilation have also been described in patients with Turner syndrome.[78]

Coarctation of the aorta. Coarctation of the aorta is a discrete narrowing of the descending aorta and it accounts for 6% to 8% of CHD.[79] It may be an isolated finding, or be associated with other malformations such as biscuspid aortic valve, subaortic stenosis, Turner's syndrome, intracranial aneurysms, or a VSD.[3] The most common location is distal to the left subclavian artery, and clinical manifestations include proximal hypertension, distal hypotention, and distal hypoperfusion. Most cases of coarctation are diagnosed in infancy or childhood, and the best outcomes are associated with early surgical intervention.[80] The mean survival of patients with untreated coarctation is 35 years, with 75% mortality by 46 years of age.[3,62] Patients who have had a repair are also at risk of complications, including re-coarctation, aneurysm formation at the site of repair, persistent hypertension, cerebrovascular events, and premature atherosclerotic disease.[80]

In pregnancy, an uncorrected, isolated coarctation is associated with a mortality risk of 3%, and aortic rupture is the most common cause of death.[46] In the pregnant patient with a hemodynamically significant coarctation of the aorta, blood pressure management is extremely important. Maternal hypertension is present in up to 30% of patients and is more common in women with higher coarctation gradients.[81] Beta-blockers have been recommended for blood pressure control in patients with uncorrected lesions,[3] and their use may be continued during pregnancy. To avoid placental hypoperfusion, maintaining a lower limb systolic blood pressure of >100 mm Hg has been recommended.[80]

Although cardiovascular complications are uncommon in patients with corrected coarctation and no residual gradients, they are at increased risk for hypertensive disorders of pregnancy and early pregnancy loss.[79] Patients with corrected coarctation of the aorta are candidates for a vaginal delivery with epidural anesthesia, and an assisted second stage may provide some additional benefit.[15] Patients with an uncorrected lesion, residual coarctation, significant hypertension, or a dilated aorta, may benefit from a cesarean delivery.[81] Although aortic coarctation represents a fixed obstructive defect, both general anesthesia[82] and epidural anesthesia[80] have been described as successful techniques in patients with significant lesions necessitating cesarean delivery. Careful control of blood pressure, heart rate, and intravascular volume are important, and the use of an arterial line may be beneficial. Before placing an arterial line, it is important to know the location of the coarctation; in pregnant patients, some favor placing the line below the level of the coarctation to better estimate uterine perfusion pressure.[80]

Cyanotic Heart Disease

Congential heart disease may be broadly divided into cyanotic and acyanotic diseases. Acyanotic diseases involve left-to-right shunting or an obstruction to flow. Cyanotic diseases, by definition, are a group of lesions where systemic venous return bypasses the pulmonary circulation and is shunted to the left side of the heart.[83] The result is a decrease in arterial oxygen saturation and cyanosis. Cyanotic CHD is a heterogeneous group of diseases, often with multiple defects resulting in right-to-left shunting. Most children born with cyanotic heart defects will require surgical palliation or repair to reach adulthood, although some patients with mild disease may present later in life. Repaired patients may have residual disease or late complications related to their repair.

A complete discussion of cyanotic CHD and pregnancy is beyond the scope of this article. Instead, this review will focus on 2 common cyanotic lesions, tetralogy of Fallot (TOF) and transposition of the great arteries (TGA), and a third group of patients with single-ventricle physiology who have been palliated with a Fontan operation.

Tetralogy of Fallot. TOF is a common cyanotic lesion at birth with a reported incidence of 10%.[83] It is characterized by 4 components: a large VSD, a right ventricular outflow tract (RVOT) obstruction, an overriding aorta, and RV hypertrophy. The RVOT obstruction is variable in location and causes increased right-sided pressures with resultant RV hypertrophy and right-to-left shunting. Without repair, the prognosis for individuals born with this disease is poor.[84] Patients who have not had surgical correction of their defects are advised against pregnancy.[3,7]

Almost all infants born with TOF will have surgical repair or palliation. Palliative procedures are performed on symptomatic neonates to increase pulmonary blood flow and bypass the stenotic lesion.[84] A common example of a palliative procedure is a modified Blalock–Taussig shunt, in which a synthetic graft connects the subclavian artery to the pulmonary artery. Primary repair usually occurs within the first year of life and involves closure of the VSD and relief of the RVOT obstruction. Pulmonary regurgitation is the most common complication found in adults who have had a repair.[3] Other common problems include atrial or ventricular arrhythmias, aortic root dilation with aortic valve regurgitation, RV dilation or failure, residual VSD, or recurrent RVOT obstruction.[3,84,85]

Although pregnancy is well tolerated in most patients with a repaired TOF, cardiac complications have been reported in 7% to 12% of pregnancies.[7,86] The most common cardiac complications in this population are arrhythmia

and CHF.[18,87] The hemodynamic burden of pregnancy in combination with residual defects put these women at increased risk. In a single center, retrospective study of pregnancy complications in 43 women with a confirmed diagnosis of TOF, 7% of patients experienced cardiovascular complications during pregnancy. Patients who had cardiovascular complications had preexisting RV dilation or dysfunction, pulmonary hypertension, or RVOT obstruction.[86] These findings are consistent with other retrospective studies that identified subpulmonary ventricular dysfunction and severe pulmonary regurgitation as risk factors for adverse maternal cardiac events in patients with CHD.[16,85] In contrast, a retrospective, multicenter study of 123 pregnancies in 69 women with surgically corrected TOF, found no association between the severity of PR and adverse cardiac outcomes. Instead, cardiovascular complications were strongly associated with the use of cardiac medication before pregnancy.[87]

All patients with TOF should be followed during pregnancy by a cardiologist familiar with adult CHD, and a comprehensive cardiac evaluation is recommended before conception.[3,7] Most patients with surgically corrected TOF are candidates for a vaginal delivery with or without an assisted second stage, and cesarean delivery should be reserved for obstetric indications.[7] For laboring patients, the establishment of early neuraxial anesthesia is recommended. In patients having a cesarean delivery, there is no clear evidence to support either neuraxial or general anesthesia as the better choice. In a case series of 27 deliveries involving 20 women with repaired TOF, all patients received neuraxial anesthesia for their deliveries with no reported complications.[29] The use of ECG and invasive hemodynamic monitoring should be individualized to the patient and planned procedure. If an arterial line is used in patients with a history of a Blalok–Taussig shunt, it should be placed on the contralateral side.

Transposition of the great arteries. TGA accounts for 5% of CHD. In TGA, there is ventriculoarterial discordance: The aorta arises from the RV, and the pulmonary artery arises from the LV. There are 2 basic types of TGA. The first and less common, is congenitally corrected TGA (CCTGA). With CCTGA there is a double discordance: ventriculoatrial discordance (the RA is connected to the LV, and the LA is connected to the RV) in addition to ventriculoarterial discordance. The end result of CCTGA is "corrected" physiology with a subaortic (systemic) RV.

The second variant is complete TGA or dextro-TGA (d-TGA) in which there is ventriculoatrial concordance (the RA is connected to the RV and the LA to the LV) but ventriculoarterial discordance. Patients born with d-TGA will require surgery to redirect blood flow. The earliest procedures (Mustard and Senning) used intra-atrial baffles to separate the 2 streams of blood return and provide a physiologic repair, allowing the deoxygenated blood to flow from the RA through the LV and into the pulmonary circulation, and the oxygenated blood to flow from the LA to the RV and then out to the body. Surgical management has since evolved and the corrective procedure performed today is the arterial switch operation (ASO), in which the aorta and pulmonary artery are connected to the correct ventricles, returning blood flow to a normal physiologic configuration with a subaortic (systemic) LV. A small number of patients with d-TGA and a VSD will have had a Rastelli procedure, in which oxygenated blood is directed through the VSD via a synthetic graft to the aorta; the advantage of this repair is that the left ventricle is the systemic ventricle.

Complications associated with TGA are usually related to a systemic RV or sequelae of the corrective surgery. Patients with a systemic RV (CCTGA or those who have had atrial switch procedures) commonly have RV dysfunction and dilation, annular dilation and tricuspid regurgitation, and arrhythmias.[39] Although uncommon, obstruction of the inferior vena cava, superior vena cava, intra-atrial baffle is possible, and pulmonary hypertension is present in up to 7% of women with a history of Mustard or Senning repair.[88] The ASO first gained popularity in the 1980s and thus, longterm cardiac complications in adults are not as well established. The early outcomes for most adults with a history of ASO appear to be good; however, reduced exercise capacity, coronary events, neoaortic valve regurgitation, dilation of the aortic root, RVOT obstruction, and arrhythmias have been described.[89,90]

The pregnancy-related changes in the cardiovascular system may place an additional hemodynamic burden on these patients. The presence of a systemic right ventricle is independently associated with adverse cardiac and pregnancy outcomes.[91,92] Women who have had atrial switch procedures appear to have a high incidence of cardiac and pregnancy complications. In a retrospective review of outcomes following an atrial switch procedure in 28 women who had 49 completed pregnancies, clinically significant arrhythmias were seen in 11 (22%) pregnancies, NYHA (New York Heart Association) class deterioration occurred in 17 (35%) patients and persisted postpartum in 4 patients. Hypertensive disorders of pregnancy complicated 9 (18%) pregnancies, and patients had elevated rates of preterm delivery and postpartum hemorrhage.[93] Another retrospective review of 54 completed pregnancies in 40 women who had an atrial switch repair documented similar outcomes. During pregnancy, 6 women developed heart failure in the third trimester and 7 others developed heart failure in the immediate postpartum period. One woman died suddenly 6 weeks postpartum, and another remained hospitalized until heart transplant could be performed. Arrhythmias and obstetrical complications were common.[94]

Women with CCTGA may have less risk than those who had atrial switch procedures. In a retrospective review of 22 women who had 50 completed pregnancies, only 2 patients had cardiovascular complications: 1 patient developed CHF in pregnancy necessitating valve replacement postpartum, and another woman with multiple pregnancies had CHF in 3 of her pregnancies and a single-vessel myocardial infarction during another.[95] Less is known about the pregnancy outcomes in women following an ASO as they are just reaching reproductive age. In a retrospective study of 9 women who had 13 completed pregnancies, there were no significant obstetrical complications, but 2 women had cardiac complications: ventricular tachycardia in one patient, and postpartum valve thrombosis in a patient with a mechanical mitral valve.[89]

All women with a history of TGA should have a comprehensive cardiac evaluation prior to conception, and patients with evidence of moderate to severe RV failure, or severe tricuspid regurgitation should be counseled against pregnancy.[7] Most pregnant patients with a history of TGA are candidates for a vaginal delivery, with or without an assisted second stage. Patients in labor should receive early neuraxial analgesia to control pain and minimize the sympathetic response. Acute increases in SVR and volume overload should be avoided. Afterload reduction may help patients with impaired subaortic ventricular dysfunction, and neuraxial analgesia and anesthesia is generally well tolerated.[30] Patients should be monitored with continuous pulse oximetry. ECG, an arterial line, and central venous catheter may be considered in patients with an arrhythmia or risk of ventricular failure. Following delivery, women with a systemic RV and/or evidence of ventricular dysfunction should be carefully monitored for signs of congestive failure.

Fontan circulation. Originally described for the treatment of patients with tricuspid atresia, the Fontan procedure is a palliative treatment in patients with a functional or anatomic single ventricle unsuitable for reconfiguration into biventricular circulation.[84] The Fontan procedure separates the pulmonary and systemic circulations by providing a direct connection between the systemic venous return and pulmonary artery. Initially, this was accomplished by connecting the right atrium to the pulmonary artery (atriopulmonary connection or classic Fontan circulation), modern techniques involve the anastamosis of the inferior and superior vena cava directly to the pulmonary artery (cavopulmonary connection). In bypassing a subpulmonary ventricle, pulmonary blood flow is non-pulsatile and driven by venous return. Thus, blood flow through the pulmonary circulation is driven by central venous pressure, augmented by negative intrathoracic pressure from spontaneous respiration, and hindered by increases in PVR.[96]

Ten-year survival after a Fontan procedure is now 80% to 90%,[3] but patients are at risk of short- and long-term complications such as arrhythmias, peripheral edema, ventricular dysfunction, thrombosis, a need for reoperation, and protein-losing enteropathy.[97] Older techniques incorporated portions of the right atrium into the circulation, predisposing patients to atrial dilation; as a result, atrial arrhythmias are a common complication, affecting up to 40% of patients 10 years after surgery.[97] The underlying lesion may impact the likelihood of ventricular dysfunction. A morphologic RV, or an undetermined primitive ventricle, may fail after years of systemic loading,[97] a process that may be exacerbated by the physiologic changes associated with pregnancy.[91,98]

Women with Fontan physiology may have increased rates of infertility related to ovarian dysfunction.[84,99] For women who do get pregnant, there is very limited information available to help predict outcomes and guide care. In a study of 21 patients who had 33 pregnancies, 15 pregnancies resulted in live births, 5 had therapeutic abortions for noncardiac reasons, and 13 had spontaneous first-trimester pregnancy loss. Two patients required treatment for cardiovascular problems: One developed supraventricular tachycardia, which was successfully managed with medications, and the second was treated for CHF in the postpartum period.[100] In another study of 6 women who had 10 pregnancies, there were 4 live births, 5 miscarriages, and 1 ectopic pregnancy. The pregnancies that resulted in live births were complicated by arrhythmias, worsening functional status, preterm delivery, postpartum hemorrhage, small-for-gestational-age infants, and 1 neonatal death.[99]

Women with Fontan circulation should be evaluated by a cardiologist familiar with adult CHD prior to becoming pregnant, and once pregnant, they should be managed by a multidisciplinary team with experience and expertise in complex CHD.[3,7,101] Many patients with Fontan palliation are chronically anticoagulated with warfarin to prevent thrombosis. Pregnancy is a procoagulant state and continued anticoagulation with unfractionated heparin, low-molecular-weight heparin, or warfarin should be considered.[7,102]

Pregnant patients who reach viability with good functional status are eligible for a vaginal delivery with or without an assisted second stage. In laboring patients, early placement of neuraxial anesthesia will blunt the sympathetic response to pain, and provide an effective alternative to general anesthesia with positive pressure ventilation should urgent cesarean delivery be necessary. The goal of anesthetic management is to preserve pulmonary blood flow by maintaining intravascular volume, SVR, and sinus rhythm, and minimizing PVR. Patients should be monitored with continuous pulse oximetry and ECG, and an arterial line should be considered, for tight hemodynamic control and intermittent blood gas evaluation. Both regional and general techniques have been used with success for cesarean delivery[103,104]; however, when

possible, slow and careful titration of regional techniques may be advantageous in this patient population.

Summary

Patients born with CHD are surviving longer and reaching childbearing age in greater numbers. Patients with CHD who desire pregnancy should be evaluated prior to conception and counseled on their risk. Those who become pregnant need careful management by a multidisciplinary team familiar with their underlying disease, their surgical repair or palliation, and the increased cardiovascular demands associated with pregnancy. Anesthesiologists play an important role in the care of these patients by understanding the unique physiology of each patient, and using this knowledge to provide careful labor analgesia or surgical anesthesia to ensure the best possible outcome.

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