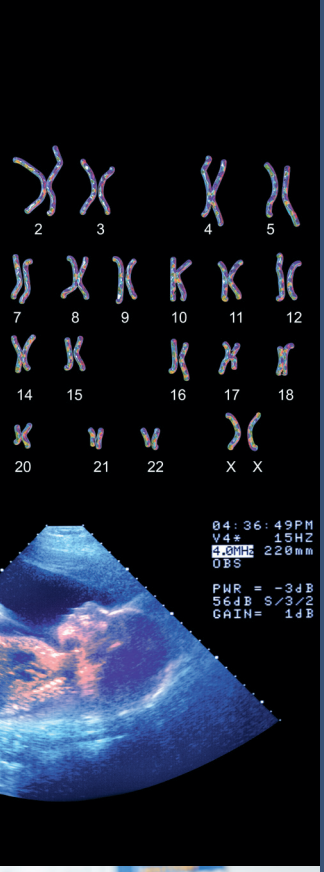

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High-Risk Pregnancy: Management Options

Cardiac Disease in Pregnancy

Mark W. Tomlinson, Rahul J. D'Mello, Lori M. Tam and Bernard Gonik

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Elements in High Risk Pregnancy: Management Options

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Abstract: Cardiac disease complicating pregnancy is present in a relatively small number of women; however, it accounts for a disproportionate share of maternal morbidity and mortality, especially in developing/emerging countries. The prevalence of cardiac disease in pregnancy is increasing and there are multiple underlying etiologies with wide-ranging severity. Normal adaptions during pregnancy often further challenge already compromised anatomic and physiologic compensatory mechanisms of the cardiovascular system, increasing the risk of adverse maternal and fetal outcomes. In this Element, the authors describe how these changes alter nonpregnant physiology with a variety of preexisting and newly diagnosed cardiac conditions. Maternal and fetal risks are reviewed. Diagnosis and management, from before conception through the postpartum period including appropriate contraception, is discussed. The goal of this review is to increase understanding of the importance of cardiac disease in pregnancy and encourage high-quality multidisciplinary care, and thus improve maternal and fetal outcomes.

Keywords: pregnancy, Marfan syndrome, myocardial infarction, hypertrophic cardiomyopathy, aortic stenosis

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Introduction: General Comments

Cardiac disease in pregnancy is associated with significant increased rates of morbidity and mortality in the birthing person (referred to in this Element as maternal) and fetus despite modern cardiac care. Cardiac disease complicating pregnancy is relatively uncommon; however, it is a leading cause of pregnancy-related complications and deaths, resulting in 21% of deaths in the USA and 14% in the UK.[1,2] The French Confidential Enquiry into Maternal Deaths evaluated 78 cardiac deaths from 2007 to 2015.[3] Only 32.9% had a known preexisting cardiac condition. Peripartum cardiomyopathy (PPCM), coronary artery disease, hypertrophic cardiomyopathy (HCM), and acquired pulmonary hypertension (PH) accounted for the majority of cases without a cardiac diagnosis before the acute event. The deaths in those with known cardiac disease occurred roughly equally throughout pregnancy and the postpartum period, while a majority of those with an undiagnosed cardiac condition occurred in the third trimester and postpartum (77.6%). Most (60.7%) were considered to be potentially preventable.

The prevalence is estimated to be between 1 and 4% of pregnancies and increasing.[4] This increase is likely due to multiple factors including more pregnancies in persons aged > 35 years and assisted reproductive technology increasing the age limits of childbearing, resulting in pregnant persons with more medical comorbidities; increasing prevalence of cardiovascular risk factors such as hypertension and diabetes in the reproductive-aged population; and improved medical and surgical therapies for persons with congenital heart disease (CHD).[5,6,7,8] The etiology of cardiac disease, like maternal mortality, varies regionally based on access and availability of health care resources. The prevalence of congenital and acquired heart disease is higher in developed countries and rheumatic heart disease (RHD) prevalence is higher in emerging countries.[9] Despite the potential for significant morbidity, most pregnant patients with cardiac disease can expect a satisfactory outcome with careful preconception, antenatal, intrapartum, and postpartum management by a multidisciplinary cardio-obstetrics team that includes obstetricians, maternal-fetal medicine (MFM) subspecialists, cardiologists, and anesthesiologists.[10–13] In this Element, we review the general impact of maternal cardiac disease on pregnancy outcomes; systematically present the epidemiology, pathophysiology, risks, and management of some of the more common and critical cardiac diseases in pregnancy; and summarize the role of the cardio-obstetrics team in optimal management of these patients.

General Pathophysiology

Normal physiologic pregnancy-related changes can aggravate underlying cardiac disease, leading to the associated morbidity and mortality. Total body water increases progressively during pregnancy by 6–8 L because an additional 500–900 mEq of sodium is retained.[14–16] As a result, plasma volume increases steadily throughout the first two trimesters and into the early third trimester, reaching a plateau at approximately 32 weeks.[17] In a singleton pregnancy at term, plasma volume is nearly 50% greater than that seen in nonpregnant women.[18] Maternal cardiac output starts to increase at approximately 10 weeks and reaches a plateau by the early third trimester at levels 30–50% above nonpregnant values.[19–22] This increased output results from increases in stroke volume and heart rate. The increase in heart rate peaks in the third trimester at 10–15 beats/minute above baseline.[20,22,23] These physiologic changes increase the demand on the heart, which can become critical if function is already compromised.

The pregnancy-related decrease in blood pressure may offset some of the increased work resulting from increased plasma volume. In some cases, however, the significant decrease in peripheral resistance can be deleterious; for example, it may reverse a left-to-right shunt, resulting in cyanosis. Normally, systolic and diastolic pressures fall throughout the first two trimesters, reaching a nadir between 24 and 28 weeks, before increasing to nonpregnant levels at term.[24] Systolic pressure decreases by an average of 5–10 mmHg, and diastolic pressure decreases by 10–15 mmHg.[25] Blood pressure and cardiac output may be further affected by maternal posture. Late in pregnancy, the gravid uterus may mechanically obstruct the aorta and vena cava in the supine position, leading to hypotension.[26] In addition, changes in cardiac output and blood pressure cause an initial decrease in systemic vascular resistance, followed by an increase toward nonpregnant values near term.[24] During cesarean section, fundal pressure used to facilitate delivery causes vena cava compression, resulting in decreased preload. Heart rate also decreases, possibly due to vagal stimulation. Aortic compression is usually not seen. The net effect of the changes in preload and heart rate is a decrease in cardiac output.[27] There can also be dramatic changes in venous return immediately following birth. If there is more than average blood loss, then venous return can be markedly reduced. Conversely, delivery of the placenta and the rapid contraction of the uterus can result in blood being squeezed out of the uterus and a sudden increase in venous return. This is particularly marked if the placenta is removed manually at cesarean section and uterotonics are given to make the uterus contract. Such manual removal is

probably best avoided. Finally, common uterotonics can have major effects on vascular tone (ergometrine producing an increase, and oxytocin producing a decrease). Although not clinically significant in normal pregnant women, the resulting changes in venous return may be important in those with limited cardiac reserve.

Colloid oncotic pressure is another important variable affected by pregnancy. Both plasma and interstitial colloid oncotic pressure decrease throughout gestation, with the latter decreasing to a greater extent.[28] There is an accompanying increase in capillary hydrostatic pressure.[29] Changes lead to the normal physiologic edema of pregnancy, most marked in the lower extremities. Any further increase in hydrostatic pressure or a decrease in plasma colloid oncotic pressure will produce increased edema formation, especially in late pregnancy. After delivery, an additional decrease in plasma colloid oncotic pressure occurs, reaching a nadir between 6 and 16 hours, with a return toward intrapartum levels after 24 hours.[30,31] The marked dependent edema commonly seen in normal pregnant patients can complicate the diagnosis of cardiac decompensation.

Maternal Risk

Awareness of complications, including death due to cardiac diseases in pregnancy, is gaining increasing attention. The CARPREG II (Cardiac Disease in Pregnancy) study reported complications in a Canadian cohort occurred in 16% of pregnancies with cardiac disease, most commonly arrhythmias (9%) and heart failure (6%), with rare cases of maternal cardiac death (0.3%).[32] The international Registry of Pregnancy and Cardiac Disease (ROPAC) reported heart failure in 11% of pregnancies with cardiac disease, arrhythmias in 2%, and maternal death in 0.6%, although this included non-cardiac causes of death.[33] Delivery was by cesarean in 44% and there were increased rates of preeclampsia and preterm birth. Obstetric complications occurred in 17% of pregnancies.[33]

Risk assessment for complications of cardiac disease in pregnancy is critical in order to aid in patient counselling and guide management.[34,35] A risk scoring system should be used by the multidisciplinary cardio-obstetrics team to identify pregnant persons with cardiac disease at higher risk of poor cardiac outcomes and to tailor the management plan to minimize risk, aiming to improve cardiac and perinatal outcomes.

Several risk assessment tools have been developed. One of the first came out of the CARPREG study published in 2001.[36] It used echocardiogram findings and clinical factors that were available at the first prenatal visit to

predict adverse maternal outcomes in women with both acquired and congenital heart disease. A primary event occurred in 13% of pregnancies, with the frequency ranging from < 5% when no predictive factors were present to 70% when two or more predictors were present. Due to the heterogenous population, complications were overestimated in those with CHD. To address this issue, the ZAHARA (pregnancy in women with congenital heart disease) study was published in 2010.[37] This retrospective review of a Belgian registry population found a cardiac complication rate of 7.6%. The modified World Health Organization (mWHO) classification was initially published by a group from the UK[38] and later validated in 2016 using the international ROPAC registry established in 2007.[9] The CARPREG II study from Canada reported cardiac complications in 16% of pregnancies with cardiac disease, most commonly arrhythmias (9%) and heart failure (6%). Maternal cardiac death was rare (0.3%). They proposed a risk assessment tool that included lesion-specific and delivery of care variables.[39]

When comparing the different risk scoring tools, several studies demonstrated the mWHO score was a more accurate predictor of cardiac outcomes in pregnancy compared to the CARPREG, ZAHARA, and/or CARPREG II risk scores.[4,34,40] Table 1 shows the updated mWHO classification of cardiac risk in pregnancy, including definitions and associated conditions.

Fetal Risks

Fetal and neonatal complications occur in 20% of pregnancies complicated by maternal cardiac disease, with fetal and neonatal death occurring in 2% of pregnancies (1% each).[41] Preterm birth, fetal growth restriction (FGR) or small-for-gestational-age birth weight, and respiratory distress are the most common perinatal complications.[41,42] There is also an overall increased risk for neonatal CHD (7%) in pregnancies complicated by CHD without the diagnosis of a genetic syndrome.[41] The increase in incidence ranges from 0 to 18%, depending on the specific lesion (Table 2). When the fetus is affected, approximately 50% have the same anomaly as the mother. The risk of a cardiac lesion in the fetus is also increased when other first-degree family members have a congenital heart lesion.[43] There are emerging risk scoring systems for predicting neonatal complications in pregnancies complicated by CHD.[42] However, these newer predictive risk scores need validation and confirmation studies.

Table 1 Modified WHO classification of maternal cardiac risk during pregnancy[4]

Risk class	Pregnancy risk definition	Cardiac condition	Maternal cardiac event rate	Pregnancy care and delivery	Minimal visits during pregnancy
I	No detectable increased risk of maternal mortality and no/mild increased risk in morbidity	• Small or mild pulmonary stenosis, PDA, or mitral valve prolapse (MVP) • Successfully repaired ASD, VSD, PDA, anomalous pulmonary venous drainage • Isolated atrial or ventricular ectopic beats	2.5−5%	Local hospital	Once or twice
II	Small increased risk of maternal mortality, or moderate increase in morbidity if patient is well and condition is uncomplicated	• Unrepaired ASD or VSD • Repaired tetralogy of Fallot • Most arrhythmias • Turner syndrome without aortic dilation	5.7−10.5%	Local hospital	Once per trimester

Table 1 (cont.)

Risk class	Pregnancy risk definition	Cardiac condition	Maternal cardiac event rate	Pregnancy care and delivery	Minimal visits during pregnancy
II–III	Intermediate increased risk of maternal mortality or moderate to severe increase in morbidity	• Mild LV impairment (EF >45%) • HCM • Native or tissue valve disease not considered WHO I or IV (mild mitral stenosis, moderate aortic stenosis) • Marfan or other HTAD syndrome without aortic dilatation • Aorta <45 mm in bicuspid aortic valve (BAV) pathology • Repaired coarctation • Atrioventricular septal defect	10−19%	Referral hospital	Bimonthly
III	Significantly increased risk of maternal mortality or severe morbidity. If pregnancy is continued,	• Moderate LV impairment (EF 30−45%) • Previous PPCM without any residual LV impairment	19−27%	Expert center for pregnancy and cardiac disease	Monthly or bimonthly

	extensive monitoring is required throughout pregnancy and postpartum	• Mechanical valve • Systemic RV with good or mildly decreased ventricular function • Fontan circulation. If otherwise the patient is well and the cardiac condition uncomplicated • Unrepaired cyanotic heart disease • Other complex CHD • Moderate mitral stenosis • Severe asymptomatic aortic stenosis • Moderate aortic dilatation (45−50 mm in Marfan syndrome or other HTAD; 45−50 mm in BAV; Turner syndrome ASI 20−25 mm/m2; tetralogy of Fallot <50 mm) • Ventricular tachycardia			
IV	Extremely high risk of maternal mortality or severe morbidity. *Pregnancy is*	• Pulmonary arterial hypertension	40−100%	Expert center for pregnancy and cardiac disease	Monthly

Table 1 (cont.)

Risk class	Pregnancy risk definition	Cardiac condition	Maternal cardiac event rate	Pregnancy care and delivery	Minimal visits during pregnancy
	contraindicated. Termination should be discussed.	• Severe systemic ventricular dysfunction (EF <30% or NYHA III–IV) • Previous PPCM with any residual LV impairment • Severe mitral stenosis • Severe symptomatic aortic stenosis • Systemic RV with moderate or severely decreased ventricular function • Severe aortic dilation (>50 mm in Marfan syndrome or other HTAD; >50 mm in BAV; Turner syndrome ASI >25 mm/m2; tetralogy of Fallot >50 mm) • Vascular Ehlers–Danlos • Severe (re)coarctation • Fontan with any complication			

ASD, atrial septal defect; ASI, aortic size index; EF, ejection fraction; HTAD, heritable thoracic aortic disease; LV, left ventricle; NYHA, New York Heart Association; PDA, patent ductus arteriosus; RV, right ventricle; VSD, ventricular septal defect

Table 2 Risk of CHD in offspring of women with CHD

Congenital heart defect	Neonatal risk (%)
Any defect	5–6
Atrial septal defect (ASD)	4–10
Ventricular septal defect	6–10
Tetralogy of Fallot	3–5
Transposition of the great arteries	0
Aortic coarctation	4
Aortic stenosis	4–18
Pulmonary stenosis	3–4
Ebstein anomaly	4–6

Data from references[43–48]

Management Options

Prepregnancy

Ideally, in patients with significant heart disease, pregnancy is a planned event. This assumes regular and reliable use of an effective contraceptive method. Before discontinuation of contraception, preconception evaluation and counseling should take place. The patient's cardiologist should be an active participant in this process. Only one-half of reproductive-aged persons with CHD recall discussing contraception with their cardiologist, and less than half received counseling before their first sexual encounter. As a result, they lack necessary contraception and pregnancy knowledge.[49] Maternal disease status should be determined and risk assessment performed to facilitate informed maternal decision-making. At a minimum, an electrocardiogram and echocardiogram should be performed. An exercise test should be considered if indicated.[4] An echocardiogram can be used not only to define the cardiac anatomy but also to describe ventricular function and estimate intracardiac pressure gradients.[50] Exercise testing demonstrating a pregnancy exercise capacity > 80% is associated with a more favorable pregnancy outcome because peak heart rate and oxygen uptake are predictive of maternal cardiac events in pregnancy.[51] Computed tomography (CT) and magnetic resonance imaging (MRI) can also be useful in visualizing the aorta in cases of aortic pathology.[4] Nuclear medicine scans, although helpful in the nonpregnant state, should be avoided during pregnancy.

A careful history is obtained to identify previous cardiac complications, including arrhythmias. The patient's functional status should also be

(cont.)

established. The New York Heart Association (NYHA) functional classification system (Table 3) is commonly used.[52] Ninety percent or more of patients are categorized as having Class I or II disease.[36,53–55] Outcomes are favorable in these two groups, but deterioration may occur. The reported frequency of adverse cardiac events varies from 3 to 69%, depending on patient risk factors.[36,53,54,56] Although few patients have Class III or IV disease, historically nearly 85% of maternal deaths occur in these groups.[57]

Management of the patient's cardiac disease should be optimized prior to pregnancy. Ideally, necessary cardiac surgery should be carried out before conception. Coexisting conditions that may aggravate preexisting cardiac disease, such as anemia, arrhythmias, and hypertension, should be appropriately treated and controlled. During the periconception period drug therapy should be carefully assessed and potential fetal effects considered. The US Food and Drug Administration replaced the A, B, C, D, X classification scheme for drug safety during pregnancy because it was felt to be confusing, overly simplistic, and not effective at communicating the risks a drug may have during pregnancy and lactation. It has been replaced with labeling containing more detailed and specific summary information.[58] Current evidence-based resources to efficiently evaluate drug safety during pregnancy include the National Institute of Child Health and Human Development Drugs and Lactation Databse (LactMed®) and MotherToBaby, a service of the nonprofit Organization of Teratology Information Specialists. Table 4 lists recommendations regarding commonly utilized medications in pregnancy and lactation along with indications and side effects.

Table 3 New York Heart Association cardiac functional classification

Class I	No limitations of physical activity; ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or angina pain
Class II	Slight limitation of physical activity; ordinary physical activity results in fatigue, palpitation, dyspnea, or angina pain
Class III	Marked limitation of physical activity; less than ordinary activity causes fatigue, palpitation, dyspnea, or angina pain
Class IV	Inability to perform any physical activity without discomfort; symptoms of cardiac insufficiency or angina syndrome may be present, even at rest; any physical activity increases discomfort

Table 4 Pregnancy and lactation considerations for common cardiac medications[59–64]

Medication	Use during pregnancy	Potential adverse effects	Indications	Use during lactation
Heart failure medications				
Loop diuretics (furosemide)	Compatible	Caution for hypovolemia or hypotension that may lead to decreased placental perfusion	For signs and symptoms of congestion and fluid overload	Compatible Caution: Over-diuresis can lead to decreased milk production
Beta-blockers	Most are compatible	FGR (particularly at higher doses and with atenolol); fetal bradycardia and hypoglycemia	For standard treatment of heart failure; consider treatment of women with history of cardiomyopathy with subsequent pregnancy	Compatible
Hydralazine	Compatible	Caution with hypotension	Use for afterload reduction during pregnancy (instead of angiotensin-converting enzyme	Compatible ACEI-I/ARB more typically chosen postpartum

Table 4 (cont.)

Medication	Use during pregnancy	Potential adverse effects	Indications	Use during lactation
			[ACE]-I/ angiotensin receptor blocker [ARB] or sacubitril-valsartan) when needed	
Nitrates	Compatible	Caution with hypotension	Use for afterload reduction during pregnancy (instead of ACE-I/ARB or sacubitril-valsartan) when needed	Probably compatible Limited data ACEI-I/ARB more typically chosen postpartum
Digoxin	Compatible	No associated congenital defects	Can be used with symptomatic heart failure during pregnancy or postpartum per guidelines	Compatible
ACE-I/ARB	Contraindicated	Anuria, oligohydramnios, fetal limb	Cannot use during pregnancy. After delivery, should be	Enalapril and captopril probably compatible

		contractures, craniofacial deformation, pulmonary atresia, fetal hypocalvaria, intrauterine growth restriction, prematurity, patent ductus arteriosus (PDA), stillbirth, neonatal hypotension, and death	used as part of guideline-directed medical therapy for afterload reduction and left ventricle (LV) remodeling	
Aldosterone receptor antagonists (spironolactone)	Avoid Limited human data, animal data suggests risk	Spironolactone has been associated with antiadrenergic activity, feminization of male rat fetuses and permanent changes in reproductive tract in both sexes	As per guideline-directed medical therapy for heart failure	Spironolactone probably compatible
Sacubitril-valsartan	Contraindicated	Same as ACE-I/ARB	As per guideline-directed medical therapy for heart failure	Avoid No human data Present in rat milk

Table 4 (cont.)

Medication	Use during pregnancy	Potential adverse effects	Indications	Use during lactation
Sodium-glucose cotransporter−2 (SGLT2) inhibitor	Avoid No human data	Dilatation of the renal pelvis and tubules, congenital anomalies and increased rate of miscarriage	As per guideline-directed medical therapy for heart failure	Avoid No human data Potential toxicity
Ivabradine	Avoid No human data Animal data suggest risk	Animal reproduction studies have shown adverse effects	As per guideline-directed medical therapy for heart failure	No human data Potential toxicity
Morphine	Use with caution	Neonatal depression and withdrawal	For treatment of pain	Probably compatible Use with caution
Dopamine	Compatible	May have vasoactive state on fetus, animal studies have shown adverse effects	For treatment of circulatory shock	Probably compatible No human data
Dobutamine	Probably compatible Limited human data Animal data suggest low risk		For treatment of cardiogenic shock	Probably compatible No human data
Milrinone	Probably compatible No human data		For treatment of cardiogenic shock	Probably compatible No human data

Anticoagulants

Low-molecular-weight heparin	Compatible	Caution at time of delivery and with neuraxial anesthesia; does not cross placenta; consider monitoring anti-Xa levels	For prevention and treatment of thromboembolic complications during pregnancy and as a bridge to warfarin postpartum	Compatible
Warfarin	Avoid. For exceptions (see Table 8)	Warfarin embryopathy and fetopathy	Prophylaxis during pregnancy in patients with mechanical heart valves (see Table 8) Pospartum prevention and treatment of thromboembolic complications	Compatible
Direct oral anticoagulants	Avoid	Association with miscarriage and possible fetal anomalies	For prevention and treatment of thromboembolic complications postpartum	Avoid No human data

Table 4 (cont.)

Medication	Use during pregnancy	Potential adverse effects	Indications	Use during lactation
Medications for ischemic heart disease				
Aspirin	81 mg formulation may be used at any time and does not require discontinuation prior to delivery	325 mg dose may be utilized until 32 weeks' gestation due to concern for premature closure of the fetal ductus arteriosus	For antiplatelet effect	Compatible when low dose is used
Clopidogrel	Probably compatible Limited human data	Must be discontinued five to seven days prior to delivery if neuraxial anesthesia is planned due to increased bleeding risk at delivery	For antiplatelet effect, often used as part of dual antiplatelet therapy in the first 6−12 months post percutaneous intervention	Probably compatible Limited human data
Statins	Contraindicated in first trimester	Risk of congenital anomalies	For treatment of hypercholesterolemia	Contraindicated
Nitrates (nitroglycerin and isosorbide dinitrate)	Compatible	Risk of hypotension and uterine and placental hypoperfusion	For antianginal effect	Probably compatible Limited human data

Medications for arrythmias

Beta-blockers (see earlier)			For rate control	
Verapamil	Compatible	Premature birth, FGR, fetal bradycardia	For rate control	Probably compatible Limited human data
Lidocaine	Compatible	Central nervous system depression, cardiac and vascular tone effects	Antiarrhythmic medication	Probably compatible Limited human data
Amiodarone	Alternative drug recommended when possible Human and animal data suggest risk	Congenital goiter, hypothyroidism, prolonged QT, neurodevelopmental abnormalities and premature birth	Antiarrhythmic medication	Contraindicated
Procainamide	Probably compatible Limited human and no animal data	Lupus-like syndrome, prolonged QT	Antiarrhythmic medication	Probably compatible Limited human data
Quinidine	Compatible	Fetal thrombocytopenia, prolonged QT	Antiarrhythmic medication	Probably compatible Limited human data

Data or experience to support use

Caution with using this medication

Prenatal

Unfortunately, few patients are seen for prepregnancy evaluation and most evaluation and counseling will be initiated at the first prenatal visit. Clinical screening for cardiac conditions at an initial prenatal visit can identify patients at risk of cardiovascular disease and reduce maternal morbidity and mortality.[10,12] Using a validated cardiovascular risk-assessment algorithm, such as the one developed by the California Maternal Care Quality Collaborative (www.cmqcc.org/quality-improvement-toolkits/cardiovascular-disease), helps stratify patients into low risk and high risk for cardiovascular disease.[12] When possible, cardiac surgery is best delayed until postpartum. When the maternal mortality rate is excessive, as in Eisenmenger syndrome, termination of the pregnancy should be discussed. With the growing restrictions on abortion care across the USA, the importance of reliable contraception and pregnancy planning is even more important.

During prenatal care, the patient should be routinely questioned and examined for signs or symptoms of worsening cardiac function. Cardiac deterioriation can progress rapidly and early intervention is key. Vital signs and weight gain should be closely monitored. Although symptoms such as shortness of breath, palpitations, chest pain, light-headedness, and fatigue are common in normal pregnancy, such complaints in a patient with known cardiac disease should lead to evaluation for PPCM and significant cardiac conditions. Cardiac testing with an electrocardiogram, B-type natriuretic peptide, or echocardiogram with cardiology consultation should be initiated.[12] In addition, cardiac risk early warning signs that are integrated into the medical record can be used to identify pregnant persons at risk of developing or having worsening cardiac disease.

Recent trends delaying childbearing and increasing obesity rates have resulted in women entering pregnancy at an older age and with more chronic medical conditions. As a result, heart disease is more frequently identified for the first time during pregnancy. The increased morbidity and mortality attributable to cardiac disease has drawn attention to those common symptoms often associated with normal pregnancy. The 2019 MBRRACE-UK report provides an infographic calling attention to the significance of chest pain and breathlessness in identifying at-risk women (www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/MBRRACE-UK%20Maternal%20Report%202019%20-%20Infographic%20v1.0.pdf).[65] The US Centers for Disease Control and Prevention has the HEAR HER campaign (www.cdc.gov/hearher/index.html), a patient education resource sharing warning signs and the need for care. The American College of Obstetricians and Gynecologists (ACOG) adds vital signs and physical findings to the symptoms and contrasts the more concerning findings with normal findings in pregnancy (Table 5).[10,66,67]

Table 5 Interpreting signs and symptoms of heart disease in pregnancy (adapted from references[10,66,67])

Clinical features	Low risk for heart disease – normal pregnancy	Moderate risk for heart disease	Severe risk with preexisting heart disease
History of cardiovascular disease	None	None	Yes
Symptoms			
Shortness of breath (including any asthma-like symptoms, persistent cough, paroxysmal nocturnal dyspnea or orthopnea, sleep apnea)*	None or does not interfere with daily living and activity or only with heavy exertion	With moderate exertion	At rest, or with minor exertion
Chest pain	None or noncardiac (e.g., reflux)	Atypical cardiac (e.g., tearing or pleuritic)	Typical compressional cardiac pain especially with exercise
Palpitations	Short-lived (seconds) and self-limiting	Brief, self-limited	Prolonged, especially associated with syncope
Syncope	None or dizziness with prolonged standing; postural hypotension	Vasovagal	Unprovoked or with exertion
Fatigue	Mild	Moderate	Severe
Physical signs			
Normal/sustained heart rate (beats/minute)* (100 beats/minute is an alternative recommended upper normal limit)	< 90	90–119	≥ 120
Systolic blood pressure (mmHg)	120–139	140–159	≥ 160 or symptomatic low blood pressure

Table 5 (cont.)

Clinical features	Low risk for heart disease – normal pregnancy	Moderate risk for heart disease	Severe risk with preexisting heart disease
Respiratory rate/ minute (≥ 30/minute is an alternative recommended 'Severe' threshold)	12–15	16–25	≥ 25
Jugular venous pressure ('not visible' is an alternative criterion for the first two columns)	≤ 2 cm	≤ 2 cm	> 2 cm
Heart sounds	Third heart sound, barely audible soft systolic murmur	Third heart sound, systolic murmur	Loud systolic murmur, diastolic murmur, fourth heart sound
Lungs	Clear	Clear	Wheezing, crackles, or effusion
Edema	Mild	Moderate	Marked
Oxygen saturation (the recommended "severe" threshold varies between < 94 and 96%) *	> 97%	95–97%	< 95%
Suggested action	Reassure patient	Needs nonurgent cardiac assessment if 4 or more of these	Needs urgent cardiac assessment

* The three references differ in the recommendations for these criteria.

Genetic counseling should be offered with parental testing when the parent has CHD that is known to be associated with genetic abnormalities, when there is thoracic aortic pathology, in cardiomyopathies and channelopathies, and when other family members are affected.[68] Fetal assessment with a first-trimester

ultrasound around the 12th week of pregnancy to screen for chromosome abnormalities and fetal CHD with a nuchal fold measurement is recommended. Pregnant persons with CHD should be offered fetal echocardiography between 20 and 24 weeks of pregnancy. When there is an increased risk of FGR, serial ultrasound examinations every two to four weeks in the third trimester allows assessment of interval fetal growth. Antenatal testing may begin at 32–34 weeks unless earlier surveillance is indicated because of compromised maternal or fetal status. Anesthesiology consultation should be obtained prior to delivery. Future fertility desires and contraceptive plans should be addressed in the antepartum period. Topics should include a discussion of sterilization, depending on future fertility desires, the maternal risk due to pregnancy, and the long-term prognosis.

Labor and Delivery

Ideally, women with significant cardiac disease should be delivered in a unit with 24-hour availability of expert obstetric, cardiology, anesthetic, and midwifery/nursing care because labor can start unpredictably at any time. However, in the most challenging cases, labor induction may be chosen to maximize the availability of a skilled multidisciplinary cardio-obstetric team. Implementing standard protocols with checklists and escalation policies for the management of cardiac sysmptoms is recommeneded.[12]

The key to successful labor and delivery management is to minimize cardiovascular stress, which can be achieved effectively with the use of regional anesthesia. Cesarean delivery subjects the mother to more stress than labor and a vaginal delivery. Therefore, cesarean delivery should not be undertaken simply because the mother has cardiac disease.[69] Vaginal delivery is the preferred mode of delivery for almost all women with cardiovascular disease with the exception of significant aortic dissection or in cases of fetal or maternal instability.[70] If induction with vaginal prostaglandin is used, we recommend starting with a low dose, because acute uterine hyperstimulation requiring either tocolysis or urgent delivery is particularly risky in a woman with significant cardiac disease. Labor should proceed with the patient in the lateral position to avoid aortocaval compression and possible hypotension. Intrapartum fluid balance should be closely monitored. Continuous maternal electrocardiographic monitoring may be used, as necessary, to detect arrhythmias. Invasive hemodynamic monitoring with an arterial line should be considered in particularly high-risk conditions or in patients with deteriorating cardiovascular status, because if the parturient becomes hypotensive, external blood pressure monitoring can be very difficult. A pulmonary artery catheter (PAC) may be considered in certain particularly high-risk cases, but its use has not been rigorously

evaluated during pregnancy, and some question the safety and utility of the PAC in critically ill and high-risk surgical patients.[71,72] Until more information is available on its safety and efficacy, a PAC should be used cautiously during pregnancy. Close fetal surveillance is needed throughout labor, and the fetal heart rate should be treated as an additional vital sign, correlating with tissue perfusion. Operative vaginal delivery is used more commonly in women with heart disease to shorten the second stage of labor and avoid the blood pressure changes associated with increased intraabdominal pressure and pushing. The majority of women do not require assistance and cesarean delivery can be reserved for obstetric indications in most situations.[69,73]

Postnatal

In the postpartum period, fluid balance must be monitored carefully. During the first 24–72 hours, significant fluid shifts occur and can lead to congestive heart failure in patients with cardiac disease. Careful attention should be paid to patients who do not have brisk spontaneous diuresis. In these patients, progressive reduction in oxygen saturation monitored by pulse oximetry often heralds the onset of clinical pulmonary edema.

Formulating an effective contraception plan can be challenging but is essential because of the potential maternal and fetal risks associated with an unintended pregnancy. The potential side effects and complications of various contraceptive methods must be considered in relation to the unique problems associated with specific cardiac conditions. The World Health Organization (WHO) provides a framework to aid in choosing an appropriate and effective contraceptive method based on known risks and contraindications.[74] This information is also accessible through a mobile app. The categories are presented in Table 6. In general, progestin-only pills, progestin implants, and emergency contraception are category 1 and can be used in all cardiac

Table 6 WHO contraceptive criteria[74]

Category	definition
1	A condition for which there is no restriction for the use of the contraceptive method
2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks
3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method
4	A condition that represents an unacceptable health risk if the contraceptive method is used

patients except those with ischemic heart disease. Depo-Provera can be used in the same group of patients, but should be avoided in patients on warfarin. Combined hormonal contraceptive methods present risks to some cardiac patients and should be avoided. Where the concern with intrauterine device (IUD) use is related to increased risk of bleeding or infection rather than insertion complications, the levonorgestrel-releasing intrauterine contraceptive system (Mirena) is probably acceptable, because its use of slow-release progestogen into the uterine cavity greatly reduces the risk of infection and heavy bleeding. The utility of these methods is reviewed for the individual conditions discussed here.

Cardiac Murmur

Maternal and Fetal Risks

Cardiac murmurs result from turbulent blood flow that causes vibration of the cardiac structures. Systolic murmurs are very common during pregnancy, with a reported incidence exceeding 90%.[75,76] The murmur is early to midsystolic and soft (grades I–II). The left sternal border is usually the area of maximal intensity, followed by the aortic and pulmonic areas.[77] These murmurs are rarely associated with cardiac pathology and are likely secondary to the increased intravascular volume and cardiac output.

Echocardiographic studies of pregnant patients who are referred for evaluation of nonspecific systolic murmurs show normal structure and function in > 90% of examinations. Most patients had the clinical characteristics of a benign flow murmur.[77,78] Most abnormalities were mild and were associated with a history suggesting pathology.[77,78,79] Clinically significant murmurs differ from the typical benign flow murmur. Systolic murmurs that are "loud or long" are suspicious and are more frequently associated with cardiac pathology. New diastolic murmurs are abnormal and require further evaluation.[4]

Management Options

A common benign flow murmur must be differentiated from a pathologic condition. A history that suggests cardiac disease or a pathologic murmur (late systolic, pansystolic, or diastolic) heard on physical examination should prompt evaluation with echocardiography. If a woman gives a history of repeated referrals because of an unusually loud but nonpathologic murmur, it can be helpful to give her a copy of her echocardiogram report, which she can show to future medical attendants, thus avoiding over-investigation and the development of cardiac neurosis.

Congenital Heart Disease

The reproductive-aged population with complex CHD is increasing due to advances in medical and surgical care resulting in improved survival. As a result, there are more individuals with CHD presenting for prenatal care. The following section summarizes important information for common CHD as it relates to pregnancy. Multidisciplinary collaboration accounting for an individual's anatomy, physiology, and personal beliefs is important to optimize outcomes.

Atrial Septal Defect

Maternal and Fetal Risks

Atrial septal defects are common and result from anatomic defects in the ostium primum, ostium secundum, sinus venosus defects (superior vena cava or inferior vena cava), and coronary sinus septum.[80] Ostium secundum atrial defects affect women more than men, and are one of the most common CHDs seen in pregnancy. Pregnancy is generally well tolerated and uncomplicated in patients with repaired ASDs (mWHO Class I). Unrepaired ASDs (mWHO Class II) have an increased risk of atrial arrhythmias, thromboembolic complications, preeclampsia, and FGR.[4] Supraventricular arrhythmias are more frequent with advancing age and may aggravate right-sided heart failure.[81] The risk of heart failure and paradoxical embolism is increased in patients with an unrepaired ASD and net left-to-right shunt (ratio of pulmonary blood flow to systemic blood flow [Qp:Qs]) of 1.5:1 or greater.[82] Pulmonary hypertension is uncommonly associated with ASD and is typically found in older patients.[83] The risk of fetal CHD increases from approximately 1% in the general pregnant population to as high as 10–14% in pregnant patients with ASDs.[84,85]

Management Options

Prepregnancy

The ASD should be evaluated for closure prior to conception and any secondary complications, such as supraventricular arrhythmias or PH, should be identified. Closure improves long-term outcomes, including fewer atrial arrhythmias, increased functional capacity, and decreased PH.[80] In cases of a newly diagnosed ostium secundum ASD, closure can be performed with a catheter-placed device during pregnancy with antiplatelet therapy but is rarely indicated.[4] Ostium primum, sinus venosus, and coronary sinus ASDs require surgical closure that should be completed prior to pregnancy.[80] The patient should also be referred for genetic counseling to discuss the risk of CHD in offspring.

(cont.)

Pregnancy is contraindicated, and effective contraception should be offered when significant PH is present (mWHO Class IV).[38] Combination hormonal methods are generally contraindicated due to the increased thromboembolic risk. The subdermal implant and IUD are considered safe and provide superior efficacy as long-acting reversible contraceptives (LARCs).[82] Depo-Provera is considered safe for patients with PH.[38] Permanent sterilization is also an option; however, surgical and anesthetic risks must be considered.

Prenatal

In patients with a repaired ASD, prenatal care is routine after a baseline echocardiogram and initial cardiology consultation.[82] In patients with an unrepaired ASD, consider aspirin 81 mg or prophylactic enoxaparin to reduce the risk of paradoxical embolism, and a follow-up echocardiogram at 28–32 weeks of gestation. However, in patients with an unrepaired ASD and a Qp:Qs $\geq$ 1.5, consider serial echocardiograms to monitor ventricular function and pulmonary pressures. A fetal echocardiogram should be recommended for all patients with an ASD because of the increased incidence of fetal CHD.

Labor and Delivery

Labor is generally well tolerated in patients with a repaired ASD or an unrepaired ASD with Qp:Qs <1.5. Patients should be monitored for arrhythmias. Blood pressure is carefully monitored to avoid systemic hypotension, which can transiently reverse the left-to-right shunt. Fluid intake and output are monitored to maintain euvolemia. In addition to pain control, epidural analgesia is encouraged because it reduces systemic vascular resistance and may reduce any left-to-right shunt. In patients with an unrepaired ASD with Qp:Qs $\geq$ 1.5, epidural analgesia is recommended.[82] Filtered IV lines are also recommended for all patients with an unrepaired ASD. Mode of delivery is determined by obstetric indication with vaginal preferred, unless the patient has severe PH, in which case, primary cesarean delivery may be considered.

Postnatal

In patients without secondary complications, postpartum management is routine. Postpartum management encourages ambulation to decrease the risk of deep venous thrombosis and paradoxical embolization.

Ventricular Septal Defect

Maternal and Fetal Risks

Isolated ventricular septal defects (VSDs) are common in the pediatric population, and most close spontaneously.[80] In adulthood, patients with an unrepaired VSD typically will have a small restrictive defect defined as a Qp:Qs < 1.5. However, a repaired VSD with a patch leak, or a moderately restrictive defect that has not been closed (Qp:Qs ≥ 1.5 and < 2), may also be seen. Rarely, a large nonrestrictive defect with Eisenmenger syndrome due to the right-to-left shunt occurs.[80] A VSD results in an increased volume load to the left heart. The magnitude of the hemodynamic impact is directly related to the size of the shunt and afterload. Maternal morbidity is similarly related to the size of the VSD, the presence of PH, and Eisenmenger syndrome. Patients with a repaired VSD (mWHO Class I) or small VSD (mWHO Class II) have a low risk of complications during pregnancy.[4,82] Paradoxical systemic emboli can also occur in patients with an unrepaired VSD. The risk of fetal CHD in pregnant patients with a VSD is roughly 10–14% and similar to that in patients with an ASD.[84,85]

Management Options

Prepregnancy

Before pregnancy, patients with an unrepaired VSD should be evaluated for PH since pregnancy is contraindicated in these patients. In the absence of severe PH, repair of an unrepaired VSD should be considered if there is a left-to-right shunt (Qs:Qp) ≥ 1.5.[80] Transcatheter device closure of muscular and perimembranous VSDs is feasible with good safety and efficacy.[80] Ventricular septal defect closure should not be performed when severe PH or Eisenmenger syndrome is present. Patients should be counseled about the increased risk of CHD in their offspring.

Prenatal

Prenatal care is similar for patients with a VSD and an ASD. A baseline echocardiogram and initial cardiology consultation can be followed by routine prenatal care in patients with a repaired VSD.[82] In patients with an unrepaired VSD consider aspirin 81 mg or prophylactic enoxaparin to reduce the risk of paradoxical embolism. A follow-up serial echocardiogram at 28–32 weeks of gestation should be scheduled to monitor for PH. A fetal echocardiogram should be recommended for all patients with a VSD because of the increased incidence of fetal CHD.

(cont.)

Labor and Delivery

Labor management is the same for patients with an ASD and a VSD, utilizing epidural for labor analgesia, monitoring volume status to maintain euvolemia, and avoiding hypotension to prevent transient reversal of the left-to-right shunt.

Postnatal

Volume status should continue to be monitored during the postpartum period because of fluid shifts and the potential for right heart failure. Ambulation is encouraged to reduce the thromboembolic risk. There are generally no postpartum contraception restrictions in the absence of PH.

Patent Ductus Arteriosus

Maternal and Fetal Risks

The ductus arteriosus is a fetal shunt between the aorta and the pulmonary artery that typically closes after birth. Patent ductus arteriosus is rare (0.3–0.8% of term infants) but more common in females.[80] Most PDAs are closed in infancy or childhood with catheter-based or surgical repair. Unrepaired lesions have traditionally accounted for < 5% of pregnancies complicated by CHD.[86] Maternal complications depend on the size of the ductus. Asymptomatic patients with a small PDA generally tolerate pregnancy without difficulty. Left-to-right shunting may decrease during pregnancy as a result of reduced systemic vascular resistance. A large lesion with a longstanding left-to-right shunt can lead to PH.[87] In this situation, the normal decrease in systemic vascular resistance during pregnancy can cause shunt reversal, with an increase in maternal mortality. The risk of fetal CHD in pregnant patients with a PDA is increased, from 1% in the general pregnant population to 3–7%.[84,85]

Management Options

Prepregnancy

Before pregnancy, the evaluation of patients with a PDA is similar to ASD and VSD. It is important to have an echocardiogram to determine the size of the PDA and identify PH. Patients should also receive genetic counseling due to the increased risk of CHD.

(cont.)

Prenatal

Prenatal care is routine in patients with a PDA after a baseline echocardiogram and initial cardiology consultation in the absence of PH.[82] A fetal echocardiogram should be recommended for all patients with a PDA because of the increased incidence of fetal CHD.

Labor and Delivery

Labor management is the same for patients with a PDA and for an ASD or a VSD. Consider labor epidural, monitor volume status to maintain euvolemia, and avoid systemic hypotension to prevent transient reversal of the left-to-right shunt.

Postnatal

Volume status should be monitored during the postpartum period because of fluid shifts and the potential for right heart failure. Ambulation is encouraged to reduce the thromboembolic risk. There are generally no postpartum contraception restrictions in the absence of PH.

Transposition of the Great Arteries

Maternal and Fetal Risks

Transposition of the great arteries (TGA) is a CHD consisting of discordance between the ventricles and the great arteries, in which the aorta arises from the right ventricle (RV) and the pulmonary artery originates from the LV. Two types exist, depending on the concordance of the ventricles and the atria. In the first type, or dextro-TGA (D-TGA), there is atrial concordance with the ventricles, and the arteries are switched. After delivery, two parallel circulations exist. The systemic venous return enters the right atrium, proceeds to the RV, and exits through the aorta, bypassing the pulmonary circulation. The pulmonary venous return enters the left atrium, continues into the LV, and returns to the lungs through the pulmonary artery. Thus, no oxygenated blood reaches the systemic circulation. Without an additional congenital shunt such as a PDA or a surgical procedure to redirect blood flow more appropriately, this condition is not compatible with extrauterine life. The Mustard or Senning operation, an atrial switch procedure, had been the most commonly used technique to repair D-TGA.[88] In this procedure, a baffle is placed between the right and left atria. Systemic venous return is redirected to the left side of the heart and to the lungs, while the oxygenated pulmonary venous blood is shunted to the RV and the

systemic circulation. Surgery allowed these patients to reach adulthood and contemplate pregnancy but left them with a systemic RV that often fails in the sixth decade because it is unable to cope long-term with the demands of supplying the systemic circulation (mWHO Class III). They are at increased risk of atrial arrhythmias (15%), heart failure (10%), worsening tricuspid regurgitation, and accelerated decline of their systemic ventricular function.[82,89] Today, the arterial switch operation is more common because it results in both ventricles performing their correct function and reduces the risk of complications during pregnancy (mWHO Class II and III). Patients with D-TGA corrected with the arterial switch operation have a lower risk of complications in pregnancy. Complications of arterial switch can be evaluated on echocardiogram and include stenosis at the arterial anastomoses, neoaortic root dilation, neoaortic valve regurgitation, and coronary obstruction.[80]

The second type of TGA is congenitally corrected TGA or levo-TGA (L-TGA). Both arterioventricular and atrioventricular discordance are present. The right atrium empties its systemic venous blood into the morphologic LV, which pumps the blood to the lungs. Oxygenated pulmonary venous blood returns to the left atrium, empties into the morphologic RV, and exits through the aorta. The major concern in patients with an unrepaired L-TGA is the ability of the morphologic RV to support the systemic circulation with the increased cardiac output occurring during pregnancy (mWHO Class III). The risk of significant morbidity is increased in patients with a systemic RV, similar to D-TGA with an atrial switch. Mortality is uncommon but reported. Cardiovascular complications include atrial arrhythmias (15%), heart failure (10%), worsening tricuspid regurgitation, and accelerated decline in systemic ventricular function resulting in myocardial infarction (MI).[88,82,90] There also appears to be an increased incidence of hypertensive disorders of pregnancy, reported in approximately 15% of pregnancies.[88,90] Long-term maternal cardiac function appears to be compromised in at least 10% of patients who proceeded with pregnancy.[4] Patients showed more compromise in RV function and a worsening of their NYHA functional class compared to patients who did not experience pregnancy.[89]

Surgically corrected transposition using an atrial switch operation is associated with a preterm birth rate of 30–60% and a rate of SGA of 20–30%.[88,90] The atrial switch operation was largely replaced in the 1980s by the arterial switch procedure. This surgery returns the morphologic LV to the role of the systemic ventricle. With an atrial switch operation, additional cardiac surgery after the initial procedure was common, and complications related to coronary artery stenosis affecting myocardial blood flow and aortic root dilatation were reported in the nonpregnant population. Although reports are limited, three small case series including 34 women and 63 pregnancies suggest pregnancy

is relatively well-tolerated and neonatal outcomes are generally good with the arterial switch operation. Maternal cardiac complications were variably defined and included heart failure, arrhythmias, aortic root dilation, and valvular dysfunction occurring in 22–43%. All were mild and easily managed. Delivery was by cesarean section in approximately 35% of pregnancies, mostly for typical obstetric indications, while a minority were done for aortic root dilatation. The majority of infants were born at term and were appropriately grown; however, the numbers are too small to draw firm conclusions. The risk of CHD in the offspring does not appear to be increased over the general population.[91,92, 93]

Management Options

Prepregnancy

As with all cardiac conditions in pregnancy, it is important to determine functional status using the NYHA functional classification. If a patient has chest pain symptoms, consider a baseline ischemic evaluation. Objective measurements from an echocardiogram to evaluate the function of the systemic RV are also recommended. Aortic root diameter, coronary arteries, and valvular function should be evaluated in patients with the arterial switch operation. Patients with NYHA functional Class III or IV, RV dysfunction (ejection fraction [EF] < 40%), or severe tricuspid regurgitation should be counseled against pregnancy.[4] A Holter or event monitor should also evaluate the patient for arrhythmias.[82] These patients should ideally be followed by a cardiologist with experience in treating CHD in adults. Often, pediatric cardiologists follow patients into adulthood. Unfortunately, pediatric cardiologists often have limited medical knowledge regarding pregnancy and contraception. A multidisciplinary team including MFM subspecialists, a cardiologist with expertise in adult CHD, and a high-risk obstetrician should see these patients preconceptionally, for counseling and pregnancy planning.

Prenatal

The multidisciplinary team should provide comprehensive prenatal care for these patients. Frequent (monthly or bimonthly) echocardiograms are needed to evaluate systemic RV function and identify arrhythmias.[4] Symptoms of heart failure should be evaluated quickly and treated with diuretics and other heart failure therapies, as indicated. Arrhythmias should also be managed with pregnancy-safe medications. An anesthesiologist should evaluate the patient before labor.

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Labor and Delivery

During labor, telemetry should be used to monitor for arrhythmias.[82] Volume overload should be avoided during labor and throughout the postpartum period. Adequate analgesia is important and can be provided with an epidural. A slow titration is recommended when significant systemic ventricular dysfunction is present. Delivery should be at a specialized center capable of caring for pregnant patients with cardiac disease. Vaginal delivery is preferred. Shortening of the second stage with forceps or a vacuum should be considered. Cesarean delivery is typically reserved for the usual obstetric indications, when decompensated heart failure is present and it may also be used in the presence of significant aortic root dilatation.[92]

Postnatal

The risk of postpartum heart failure is increased in D-TGA with atrial switch operation and L-TGA. Consider extended postpartum monitoring for 48–72 hours, with early outpatient follow-up.[82] Patients with D-TGA and an arterial switch operation are at low risk of postpartum arrhythmias or heart failure. Long-acting reversible contraceptive methods are preferred in patients with TGA. In addition, combined hormonal contraceptive methods can be used, provided there are no arrhythmias or cardiac dysfunction.[38]

Tetralogy of Fallot

Maternal and Fetal Risks

Tetralogy of Fallot (TOF) is the most common cyanotic heart disease, consisting of a VSD, overriding aorta, pulmonary stenosis, and right ventricular hypertrophy. In developed countries, nearly all patients undergo surgical repair in infancy. The majority of these patients are now alive during their reproductive years and leading normal lives. Nearly all patients with repaired TOF entering pregnancy not on cardiac medications and NYHA functional Class I tolerate pregnancy well (mWHO Class II).[4] However, maternal complications can occur in up to 8% of patients. Pulmonary regurgitation is the most common hemodynamic sequelae of TOF repair, seen in 70–85% of patients.[94,95] Moderate to severe pulmonary regurgitation and dysfunction of the RV are associated with an increased risk of arrhythmias (2–6%) and right heart failure (2%).[82] These complications also appear to be more common in patients with repair later in life.[95] Rare complications

include thromboembolism and endocarditis. Although survival to adulthood with uncorrected TOF is possible, pregnancy is rarely seen in these individuals owing to a shortened life expectancy as well as decreased fertility. When pregnancy does occur in uncorrected TOF, patients are at risk of serious maternal morbidity and mortality (see Table 1). Preexisting PH is a concern. In addition, increased cardiac output leads to increased venous return to the hypertrophic RV. These changes, together with decreased systemic vascular resistance, increase the right-to-left shunt. Oxygenation decreases, hematocrit increases, and cyanosis worsens, further stressing an already compromised cardiovascular system. Risk factors that worsen the prognosis include prepregnancy hematocrit > 65%, a history of congestive heart failure or syncope, cardiomegaly, right ventricular pressure >120 mmHg or strain pattern on electrocardiogram, or oxygen saturation < 80%.[96] Miscarriage, preterm delivery, and perinatal mortality do not seem to be increased.[90,94,95] There is an increased risk of offspring complications such as FGR and SGA newborns.[94,97] Congenital heart defect affects 3–5% of infants of mothers with TOF.[85,90]

Management Options

Prepregnancy

Surgery is recommended for patients with unrepaired TOF. Patients who underwent previous surgical repair should be evaluated for residual defects, such as pulmonary stenosis or residual VSD, by cardiac MRI, the gold standard for quantification of RV size and function in repaired TOF.[80] If defects are found, the need for repair should be evaluated and any necessary repair completed prior to pregnancy.[95] Pulmonary valve replacement should be performed prior to pregnancy if meeting criteria. Consider referral to a geneticist for maternal screening for 22q11 deletion and to discuss the increased risk of CHD in the offspring.[4]

Prenatal

Pregnancy in patients with a repaired TOF should be managed by a MFM specialist and a cardiologist with expertise in CHD.[82] A baseline echocardiogram should be performed to evaluate the pulmonary valve and RV function. If significant pulmonary valve or RV dysfunction is identified, serial echocardiograms are indicated to monitor for arrhythmias and signs of RV failure.[4] If RV failure occurs, treat with diuretics and bed rest. Preterm delivery or, rarely, transcatheter valve implantation can be considered. Patients with unrepaired TOF should be offered termination. In those who continue, the pregnancy hematocrit should be followed. Supplemental oxygen may be of benefit. Genetics consultation can be offered to discuss the

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increased risk of fetal transmission of conotruncal defects.[82] A fetal echocardiogram should be performed in all patients. In addition, serial obstetric ultrasound examinations should be done to monitor for FGR. Antenatal testing is started during the third trimester, as indicated.

Labor and Delivery

Patients with repaired TOF should be monitored by telemetry during labor and postpartum.[82] Epidural analgesia with slow titration for significant RV dysfunction is recommended. Hypotension should be prevented to avoid shunt reversal in unrepaired TOF. Vaginal delivery is the preferred mode of delivery. To prevent decreases in venous return with bearing down, operative vaginal delivery may be used to shorten the second stage of labor. This strategy is often applied in patients with corrected TOP, although it is probably unnecessary.[94]

Postnatal

Postpartum, there is an increased risk of right heart failure in patients with significant pulmonary valve or RV dysfunction. In patients with unrepaired TOF, volume status should be monitored during the early postpartum period. A reliable contraceptive plan should be made, with permanent sterilization a good alternative. All reversible forms of contraception can be used in patients with repaired and uncomplicated TOF.[38]

Coarctation of the Aorta

Maternal and Fetal Risks

Coarctation of the aorta (CoA) typically occurs adjacent to the remnant of the ductus arteriosus and the left subclavian artery. Coarctation of the aorta is also associated with other cardiovascular anomalies. A BAV is most common and found in 20–40% of patients. Ascending aortic aneurysms, VSDs, anomalies of the intercostal and subclavian arteries, and aneurysms of the circle of Willis may also be present. Pregnancy is seen almost exclusively in patients who have undergone some type of repair. When the lesions are corrected, maternal and fetal outcomes are not significantly different from those in the general obstetric population (mWHO Classes II and III).[4,82] Hypertension is the most common sequela of CoA, and in pregnancy can present as preeclampsia in up to 30% of patients.[82] Although data are limited, the physiologic changes associated with pregnancy may unmask and aggravate post-repair gradients. Aortic dissection is

rare, but more likely when hypertension is poorly controlled or if an ascending aortic aneurysm >50 mm is present.[80] Congential heart disease is seen in approximately 4% of offspring.[98]

Management Options

Prepregnancy

In a patient with a repaired CoA, magnetic resonance angiography (MRA) of the aorta is recommended to evaluate the CoA repair and for any aortic dilation.[82] If there is any residual coarctation (re-CoA) or recurrence, repair should be performed prior to pregnancy. If aortic dilation is ≥ 50 mm, then repair should be considered prior to pregnancy due to the increased risk of aortic dissection. Intracranial aneurysms are common (10%), with increasing age being a risk factor. Consider a baseline MRA brain to evaluate for berry aneurysms. Unrepaired CoA is a high-risk lesion (mWHO Class IV) and should be repaired prior to attempting pregnancy.[82] Until repair can be completed, pregnancy is contraindicated, and reliable contraception should be offered.

Prenatal

Termination may be considered in patients with uncorrected CoA, especially if it is associated with other anomalies, because of the increase in morbidity and mortality seen in adults. The majority of patients with a previous repair will require evaluation of the repair as well as screening for associated cardiac abnormalities at their first prenatal visit with a baseline MRA and echocardiogram. Close blood pressure monitoring and aspirin 81 mg should be considered to reduce the risk of preeclampsia and aortic dissection. Blood pressure goals should be personalized to avoid placental hypoperfusion in those with re-CoA.[4] The highest risk of aortic dissection is in patients with an aneurysm ≥ 50 mm. If there is aortic dilation ≥ 40 mm, serial noncontrast MRA or echocardiogram can be considered. Percutaneous intervention using a covered stent is possible during pregnancy but should only be performed for re-CoA with refractory hypertension or maternal or fetal compromise.[4] A fetal echocardiogram is recommended due to the increased incidence of fetal CHD.

Labor and Delivery

Hypertension should be controlled in both the intrapartum and the postpartum periods. There is an increased risk of postpartum hypertension with blood pressure peak between three to eight days after delivery. Epidural analgesia is recommended because it effectively controls pain

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and decreases systemic vascular resistance. Vaginal delivery is preferred for most patients with a repaired CoA. Consider cesarean delivery if the ascending aorta is ≥ 50 mm or there are signs or symptoms of acute aortic dissection or aneurysm.

Postnatal

Progesterone-only contraceptive methods, the subdermal implant, and IUDs can safely be used for contraception. In patients with repaired coarctation, combined hormonal methods are also considered safe in the absence of an aneurysm or hypertension.[38]

Fontan Circulation

Maternal and Fetal Risks

Fontan circulation or palliation results from the most common repair of single ventricle physiology.[80] The Fontan procedure is usually the last in a series of surgeries designed to improve circulation by allowing oxygen-poor blood from the lower body to bypass the heart and go directly to the pulmonary artery. Common conditions treated with Fontan circulation are hypoplastic left heart syndrome (most common), hypoplastic right heart syndrome, tricuspid atresia, pulmonary atresia with intact ventricular septum, L-TGA, unbalanced atrioventricular canal defect, severe Ebstein anomaly, and double inlet LV.[99] Fontan circulation results in elevation in central venous pressure (CVP) and reduced cardiac output. Patients with Fontan circulation are considered at high risk of cardiac complications during pregnancy (mWHO Class III).[4] In these patients, atrial arrhythmias, heart failure, thromboembolism, and NYHA functional class deterioration are not uncommon. Fontan circulation also predisposes to an increased risk of obstetric complications. Miscarriage rates are 26% in the first trimester and 16% in the second trimester.[100] There are very high rates of preterm birth (80%), FGR (70%), and neonatal death.[99, 100] Patients with Fontan circulation and evidence of Fontan failure, clinically significant cirrhosis, baseline hypoxemia (O_2 saturation <85%), moderate to severe aortic regurgitation, refractory arrhythmia, protein-losing enteropathy, or poor NYHA functional class are at very high risk of cardiac complications during pregnancy (mWHO Class IV), and should be counseled against pregnancy.[4,82] The live birth rate was 45% when there was evidence of Fontan failure. There is an increased risk of fetal CHD in patients with Fontan circulation, and referral to a geneticist for risk assessment should be considered.

Management Options

Prepregnancy

Prepregnancy evaluation and assessment of patients with Fontan circulation can be extensive.[82] These patients need a baseline echocardiogram and exercise testing. A right heart catheterization (RHC) is recommended every ten years in adults with Fontan circulation to directly measure systemic venous pressures, PA pressure and vascular resistance, and cardiac output.[101] Cardiopulmonary stress testing should be considered to assess functional capacity prior to pregnancy. Alternatively, a RHC can be done if a patient considering pregnancy has not had an evaluation in > 5 years.[102] Fontan revision surgery is indicated for adults with recurrent atrial tachyarrhythmias refractory to medication and catheter ablation, who have preserved systolic ventricular function and severe atrial dilation.[80] Liver function tests, renal function tests, liver imaging, and pulse oximetry should be performed. Consider evaluation for cardiac transplantation if signs and symptoms of protein-losing enteropathy.[80] A baseline endoscopy should be performed if evidence of portal hypertension is present to assess for esophageal varices.[82] If varices are identified, endoscopy should be repeated in the second trimester. If Fontan failure is suspected or multiorgan complications are present, pregnancy is contraindicated. Combination hormonal methods increase thromboembolic risk and should be avoided. Long-acting reversible contraceptive options are preferred, but all progesterone-only contraceptive options are acceptable in patients with Fontan circulation.[102] Permanent sterilization is also an option; however, surgical and anesthetic risks must be considered.[38]

Prenatal

Pregnancy requires coordinated care from a multidisciplinary team of cardiologist, MFM specialist, anesthesiologist, and neonatologist. During pregnancy, monthly echocardiograms are recommended to assess function and for arrhythmias, along with brain natriuretic peptide (BNP) level screening.[82,102] Elevated BNP concentrations are associated with adverse maternal cardiac events; a BNP <128 pg/mL has a negative predictive value of >95%.[103] Heart failure and atrial arrhythmias should be treated with pregnancy-safe medications or electrical cardioversion, if required.[4] There is an increased thromboembolic risk, and low-dose aspirin with prophylactic or therapeutic

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anticoagulation should be considered depending on the type of palliation, degree of cyanosis, and history of thromboembolism. This risk should be balanced with the increased risk of bleeding in pregnancy associated with Fontan circulation. The patient should be evaluated by anesthesia prior to anticipated delivery. Delivery should occur by 37 weeks' gestation. Pregnant patients with Fontan circulation and severe systemic ventricular dysfunction or failing Fontan circulation (reduced functional capacity, elevated peripheral vascular resistance, significantly reduced cardiac output, significant multisystem organ dysfunction) should be advised to have termination.[102] A fetal echocardiogram should be performed.

Labor and Delivery

In patients with Fontan circulation without complications, euvolemia is critical during labor, maintaining adequate hydration and treating hypotension or hemorrhage with fluid resuscitation.[82] Monitoring with telemetry and pulse oximetry is performed during labor and for 24 hours postpartum. Epidural analgesia is recommended with a slow titration due to the preload-dependent circulation. Intravenous (IV) filters are required. Vaginal delivery is preferred with cesarean for the usual obstetric indications. In patients with Fontan circulation with complications, labor should be in the left lateral decubitus position due to preload dependence. There should be a low threshold for assisted second stage of delivery to minimize Valsalva. Cesarean delivery can be considered in these cases using shared decision-making. Consider sending the placenta to pathology for evaluation of placental insufficiency.[104]

Postnatal

There is a high risk of postpartum hemorrhage.[102] Postpartum, patients remain at high risk for heart failure and thromboembolic events. If decompensated, they should recover in the cardiovascular intensive care unit (ICU). Observation in the hospital for 72 hours postpartum is suggested. Ambulation is encouraged to decrease the risk of deep venous thrombosis. In addition, aspirin and prophylactic enoxaparin are continued for 6–12 weeks postpartum. Follow-up is recommended in one week with cardiology and at two and six weeks with a MFM specialist. Contraception should be discussed at each encounter with an emphasis on planning future pregnancies to optimize Fontan circulation prior to conception.

Ebstein Anomaly

Maternal and Fetal Risks

Ebstein anomaly is rare, occurring in 0.005% of live births and accounts for < 1% of CHD cases.[80,105] It is characterized by apical displacement of the tricuspid valve leading to tricuspid regurgitation and right heart enlargement. Varying degrees of RV and LV dysfunction are also noted. Additional cardiac anomalies are often present, the most common being an ASD.[80] Right-to-left shunting can occur, resulting in cyanosis. There is an increased incidence of arrhythmias, particularly Wolff–Parkinson–White syndrome. Ablation of the accessory pathway has a lower success rate and higher recurrence rate in patients with Ebstein anomaly than in those without structural cardiac abnormalities.[105] This is likely because concealed accessory pathways, often multiple, are common in Ebstein anomaly.[80] Pregnancy is generally well tolerated in patients with Ebstein anomaly (mWHO Class II); however, serious complications can occur.[90] Arrhythmias and heart failure occur in 3–4% of pregnancies. The rate of preterm delivery is increased to approximately 25%. Oxygen saturation and cardiac output determine fetal and neonatal outcomes.[4] Congenital cardiac abnormalities are seen in 4% of offspring.[90]

Management Options

Prepregnancy

Most patients who require correction will have undergone surgery prior to adulthood. A baseline echocardiogram is important to evaluate ventricular function and the degree of tricuspid regurgitation. Cardiac MRI may be useful to assess RV volume and tricuspid valve morphology, displacement, and regurgitation.[106] However, even severe tricuspid regurgitation and heart failure can be managed medically during pregnancy. Worsening hemodynamics, progressive tricuspid regurgitation, or worsening RV function may require tricuspid valve repair, ASD closure, or ablation, which should be done before pregnancy.[80] Those who have not had surgical correction should be evaluated for this, and if indicated, it should be done prior to pregnancy.

Prenatal

The patient should be observed for arrhythmias. Serial maternal echocardiograms should be done to monitor cardiac function and evaluate for evidence of right heart failure. A fetal echocardiogram is indicated at 20–22 weeks to evaluate for fetal cardiac abnormalities. The patient should be

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educated and monitored for evidence of preterm labor. It may also be prudent to obtain serial ultrasounds for fetal growth, with antenatal testing if FGR is identified.

Labor and Delivery

Telemetry monitoring during labor should be considered to detect arrhythmias. Supplemental oxygen may be given, as necessary. Fluid balance should be monitored closely to avoid volume overload during labor and throughout the postpartum period. Adequate analgesia should be provided with an epidural. Shortening of the second stage with forceps or a vacuum may be considered. Cesarean delivery is reserved for the usual obstetric indications.

Postnatal

Long-acting reversible contraceptive methods are preferred. Combined hormonal contraceptive methods can be used in patients, provided there are no arrhythmias or cardiac dysfunction.[38]

Pulmonary Hypertension

Maternal and Fetal Risks

Pulmonary hypertension is defined by an elevation in the pulmonary artery pressure to ≥ 25 mmHg at rest on RHC.[107] Pulmonary hypertension is classified into primary and secondary PH. Primary PH is an idiopathic disease of the pulmonary vasculature that is seen primarily in females. Secondary PH has a number of underlying causes and associations. These include heritable, drug or toxin induced, connective tissue disease, HIV infection, portal hypertension, CHD, left heart diseae, and chronic lung disease. Historically, maternal mortality was reported to be as high as 50%. With current therapeutic approaches, mortality rates have decreased and are reported to be between 16 and 30%.[4] The ROPAC registry reported an overall mortality rate of 5.9% within six months of delivery among 151 patients with PH. The majority (74%) were associated with left heart disease, with the remainder associated with multiple other etiologies. In those with primary PH, the mortality rate was much higher (43%).[108] Fortunately, PH is rare, with a reported incidence of 1.6 per 100,000 deliveries in the USA.[109]

With primary PH, the most dangerous times are labor, delivery, and the early postpartum.[4] Intravascular volume changes are not well tolerated because of the

fixed pulmonary vascular resistance. Increases in cardiac output during labor or as a result of postpartum fluid shifts may lead to sudden right-sided heart failure. At delivery, excessive blood loss decreases preload, resulting in an inability to overcome high pulmonary vascular resistance. Both situations lead to a decrease in left ventricular preload and a dramatic decrease in left ventricular output. A direct consequence is myocardial ischemia, leading to arrhythmias, ventricular failure, and sudden death. Pulmonary thromboembolic events are usually fatal. There is an increased incidence of hypertensive disorders of pregnancy, further complicating the condition.[109] Additional risk factors for maternal death are the severity of PH, late hospitalization, and the use of general anesthesia.[110] In the fetus, the incidence of preterm delivery is increased, and chronic maternal hypoxia can lead to FGR.[108] There is an increased risk of fetal and neonatal mortality (0–30%), especially in the presence of reduced maternal cardiac output and hypoxia.[4]

Management Options

Prepregnancy

Evaluation of a patient with PH of reproductive age begins with a baseline echo, BNP, chest x-ray, six-minute walk test, and cardiac catheterization.[80] Despite improvements in pregnancy outcomes with a multidisciplinary team approach, maternal morbidity and mortality are high, and significant risks persist.[80,111] As a result, pregnancy is contraindicated, and LARC or permanent sterilization should be considered. A baseline echocardiogram and invasive RHC are recommended if the diagnosis is uncertain. Genetic counseling should also be offered to all familial cases.

Prenatal

Caution should be exercised in diagnosing PH during pregnancy. Cardiac catheterization is the gold standard for determining pulmonary artery pressures. In the nonpregnant patient, there is a significant correlation between echocardiography-derived pressures and those obtained by cardiac catheterization. In the pregnant patient, however, echocardiographic pulmonary artery pressures tend to be overestimated, with nearly one-third of those with elevated pressures found to be normal on subsequent cardiac catheterization.[112,113] If pregnancy occurs in patients with severe PH, termination should be offered to reduce maternal risks. If pregnancy is discovered in the second trimester and termination is chosen, dilatation and evacuation in experienced hands is preferred to induction. In a continuing pregnancy, the cardiologist, critical care specialist, and

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obstetrician must work closely together as part of a multidisciplinary team. An obstetric anesthesiologist should be consulted early in the pregnancy.[111] Thromboembolism prophylaxis is initiated early, typically with low-molecular-weight heparin. In the early third trimester, hospital admission with oxygen therapy and monitoring is often required because of increasing symptoms.[111] Pulmonary hypertension therapies such as prostacyclin analogs, phosphodiesterase inhibitors, sildenafil, nifedipine, and inhaled nitric oxide have all been used during pregnancy. Therapy should be individualized in consultation with a specialist experienced in the treatment of PH.[111] The use of the endothelin-receptor antagonist bosentan has also been reported; however, this agent should be used with caution in the antepartum period because animal studies have reported teratogenicity.[111]

Labor and Delivery

The majority of patients with PH deliver preterm because continuing pregnancy represents such a grave risk, and because 25% of babies have FGR. The optimal mode of delivery is somewhat controversial. Older evidence suggests that cesarean delivery is associated with increased maternal morbidity and mortality and should be reserved for obstetric indications, although some studies suggest that the proportion of patients being delivered by cesarean section is in fact increasing. This is probably due to the increasing recognition of the value of preterm delivery to avoid a third-trimester deterioration in maternal condition.[111,114] Some experts recommend scheduled preterm cesarean delivery around 34 weeks' gestation.[115] Despite the concern of increased morbidity and mortality associated with cesarean delivery, roughly 60% of patients with PH are delivered by cesarean.[108,109] Although the mortality rate was not reported in that study, a more recent small case series including 15 pregnancies in 14 patients with PH of various etiologies described a cesarean rate of 69%. The maternal mortality was 25% in those delivering vaginally and 22% in those delivered by cesarean.[116] Vaginal delivery remains an acceptable option and still accounts for the majority of births in some series.[117] When indicated, oxytocin or E series prostaglandins can safely be used for induction, provided great care is exercised to avoid uterine hyperstimulation. Oxygen flow is increased to 5–6 L/minute. Oxygen saturation is monitored continuously with pulse oximetry. A radial artery line is placed to allow continuous blood pressure monitoring and facilitate frequent

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blood gas sampling. Maintenance of stable blood pressure is important. A CVP catheter is also placed to monitor right heart pressures and assure adequate preload. A PAC is rarely necessary.[111]

Therapies directed specifically at PH, such as IV prostacyclin or inhaled nitric oxide, have been used during labor. Both drugs cause vascular dilatation and inhibit platelet aggregation, leading to improved oxygenation, decreased pulmonary vascular resistance, and a decreased risk of thromboembolism. Improvement in PH is similar between the two drugs in nonpregnant patients, and there seems to be no added benefit to a combination of the two agents. Inhaled nitric oxide avoids systemic hemodynamic changes, is easy to administer, and may cost less than other agents. Nitric oxide is typically used at a dose of 5–20 ppm. Elevated methemoglobin levels are a potential toxicity but have not been reported at these doses.[118]

An epidural catheter is placed early in labor and carefully activated when contractions become painful to avoid hypotension. Intrathecal narcotics can be added to decrease the hypotensive effect of local anesthetics. During labor and delivery, the patient is placed in the left lateral position to avoid supine hypotension. Vaginal delivery, with shortening of the second stage using forceps or a vacuum to decrease the need for pushing, is desirable. Blood loss at delivery is carefully monitored. Crystalloid solution can be used to replace volume and maintain preload if blood loss is greater than normal.

Postnatal

Antepartum and intrapartum management principles are continued into the postpartum period. Most maternal deaths occur in the first month postpartum due to thromboembolism, right heart failure, or sudden death.[82,115] Thromboembolism prophylaxis and oxygen therapy are continued. Excessive blood loss or right-sided heart failure as a result of fluid shifts can lead to sudden death and euvolemia should be maintained. The patient should be monitored closely during the first 24–48 hours in an ICU and with telemetry for 48–72 hours.[82] Discharge home can be delayed seven to ten days to facilitate continued monitoring for complications such as RV failure and to adjust the dose of pulmonary vasodilators. Long-term PH-specific therapies should be individualized and managed in conjunction with someone experienced in the use of these agents. Controlled diuresis is important during postpartum fluid mobilization to control

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preload and prevent worsening right-sided heart function. Pulmonary edema may develop rapidly in patients who do not have brisk spontaneous diuresis. Iron deficiency should also be treated promptly. Permanent sterilization should be considered in patients with severe PH. Depo-Provera or progesterone implants may be considered to avoid surgical and anesthetic risks. Intrauterine devices may be cautiously used. Combined hormonal contraceptives should be avoided because of the risk of thromboembolism.[38]

Eisenmenger Syndrome

Maternal and Fetal Risks

Eisenmenger syndrome is defined as PH resulting from an uncorrected left-to-right shunt of a VSD, ASD, or PDA, with subsequent shunt reversal and cyanosis. The increase in blood volume and decrease in systemic vascular resistance can lead to RV failure, with a decrease in cardiac output and sudden death. Maternal mortality with Eisenmenger syndrome is as high as 40% in pregnancies that continue past the first trimester.[119] In contrast, the 15-year survival rate is >75% in nonpregnant patients.[120] Postoperative fluid shifts associated with cesarean delivery pose an even greater risk, with mortality rates approaching 70%.

Fetal growth restriction is a common fetal complication. If the maternal arterial oxygen saturation is <85%, fetuses usually die in utero before reaching a viable gestation, and early miscarriage is very common. Preterm delivery is also frequent, occurring in up to 85% of pregnancies.[119] Despite the maternal and fetal complications, the neonatal survival rate of babies alive at birth approaches 90%.[90] Congenital heart defects are seen in approximately 5% of offspring.[90]

Management Options

Prepregnancy

Pregnancy should be discouraged and reliable contraception, preferably permanent sterilization, advised because of the extreme maternal risk associated with pregnancy. Depo-Provera or progesterone implants are nonsurgical alternatives.[38] Even first-trimester termination is associated with a maternal mortality rate of 5–10%.[121]

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Prenatal, Labor and Delivery, and Postnatal

Echocardiography is helpful in evaluating shunting, right ventricular function, and PH. Cardiac catheterization may be necessary to quantify PH. Pregnancy complications and outcomes are related to the degree of PH. Management of PH associated with Eisenmenger syndrome follows the same principles as those discussed in the pulmonary hypertension management sections.

Valvular Heart Disease

General

Maternal and Fetal Risks

Mitral valve prolapse, congenital stenosis or atresia, and RHD constitute the majority of valvular heart disease. The dramatic decline in the incidence and severity of RHD over the last several decades in developed countries is due to a number of factors including improved access to health care, primary prevention with early treatment of skin and throat infections, earlier diagnosis and treatment of acute rheumatic fever, and secondary antibiotic prophylaxis to prevent RHD.[122] As a result, RHD has become a disease affecting primarily underserved populations in low- and middle-income countries and First Nations people in developed nations.[123,124] There has been a renewed interest in reducing the global burden of RHD by using these same public health measures in high-risk populations. Although progress has been made, a number of challenges have prevented success to this point.[122,125] Women are affected by RHD approximately twice as often as men.[126] Acquired valvular disease is estimated to account for 15–30% of heart disease in pregnancy in developed countries and 65–90% in low- to middle-income countries.[36,126,127] Although the incidence of RHD in pregnancy is low in developed nations, it continues to be seen in immigrants as well as the First Nation peoples.

Rheumatic heart disease is a complication of rheumatic fever. Cardiac valve damage results from an immunologic injury initiated by a group A beta-hemolytic streptococcal infection.[128] During pregnancy, the increased maternal blood volume and heart rate can lead to heart failure and pulmonary edema. Arrhythmias particularly atrial fibrillation also complicate pregnancy.

Bacterial endocarditis is a concern often arising in patients with congenital or valvular heart disease. Recommendations regarding bacterial endocarditis antibiotic prophylaxis have varied among professional society guidelines based on the type of cardiac lesion and the procedure-related risk of bacteremia. Between 2006 and 2008, the American Heart Association (AHA) and the UK National Institute

for Health and Clinical Excellence (NICE) recommended against the routine use of antibiotic prophylaxis against infective endocarditis in obstetric procedures and childbirth.[129,130] Conversely, the Endocarditis Working Party of the British Society for Antimicrobial Chemotherapy recommends antibiotic prophylaxis at cesarean section for patients at high risk for endocarditis.[131] Routine antibiotic prophylaxis for the prevention of postoperative infection is well established as a standard of care, supported by many prospective, randomized trials.[132]

In patients with an uncomplicated labor and delivery, bacterial endocarditis is rare. In two series with a total of 906 pregnant women with cardiac disease, routine prophylactic antibiotics were not used and no cases of bacterial endocarditis were identified.[133,134] The incidence of positive blood cultures is low after uncomplicated vaginal delivery, with a reported range of 1–5%.[131] Bacteremia is more common with dental procedures, in which positive blood cultures are obtained in 60–90% of patients, depending on the procedure.[135] Recent focus has turned to bacteremia resulting from routine daily activities rather than procedure-related exposure. It has been estimated that over the course of a year, "everyday" exposure is 6 million times greater than that of a single tooth extraction.[131] Based on limited evidence suggesting that individuals with high-risk cardiac conditions may benefit from endocarditis prophylaxis, the AHA updated its guidelines in 2017, stating that prophylaxis is reasonable before dental procedures in patients with high-risk conditions. Individuals considered at high risk include those with a history of previous endocarditis, a prosthetic valve, a surgically conducted shunt or conduit, or complex CHD.[136] Genitourinary procedures including vaginal delivery are associated with a very low risk of endocarditis, and prophylaxis is not recommended.[129,130]

Prior to updated recommendations for infective endocarditis prophylaxis, Pocock and Chen evaluated the intrapartum use of endocarditis prophylaxis.[137] Only 12% of those receiving antibiotics had moderate- to high-risk cardiac conditions that would have potentially warranted therapy by the older recommendations. An appropriate antibiotic regime was given in only half of these cases, pointing out that even older recommendations were not being followed in clinical practice. The inappropriate use and overuse of antibiotics for infective endocarditis prophylaxis highlights the broader concerns related to increasing antibiotic use and its effect on child development.

Management Options

General management principles for patients with RHD are aimed at preventing cardiac failure and bacterial endocarditis. Volume status is monitored, and activity should be limited. Specific valvular lesions are discussed individually.

Mitral Valve Prolapse

Maternal and Fetal Risks

Mitral valve prolapse represents a range of valvular abnormalities that allow one or both mitral valve leaflets to extend above the plane that separates the atria and ventricles. There is a wide range in the reported prevalence of MVP depending on the method of diagnosis, the diagnostic criteria, and the population studied. The condition is common in women of reproductive age, and prevalence rates as high as 17% have been reported. However, standardized echocardiographic criteria and a better understanding of the shape of the mitral valve have dramatically decreased prevalence estimates.[138] The condition remains relatively common, with a prevalence of 0.5–3% in the general population.[139,140]

A midsystolic click with or without a mid to late systolic murmur is the classic auculatory finding defining MVP. Postural maneuvers have been used to aid in the auscultatory diagnosis. Activities that decrease left ventricular volume increase the degree of prolapse. Hydration affects the auscultatory findings of MVP.[141] Pregnancy may have similar effects, with changes in the timing of the click and shortening or softening of the murmur. Two-dimensional echocardiography has become the diagnostic gold standard. The diagnosis is made when the anterior and/or posterior valve leaflet is seen prolapsing into the left atrium 2 mm or more above the annular high points on the parasternal apical long-axis view.[139,140] Serial echocardiograms during pregnancy showed disappearance of MVP during pregnancy in a significant number of patients.[142]

Palpitations, arrhythmias, chest pain, syncope, fatigue, and panic attacks are reported in association with MVP. Together, they make up MVP syndrome, although the existence of a distinct syndrome has been questioned. The symptoms associated with MVP syndrome are very common and are seen with near-equal frequency in patients with and without an echocardiographic diagnosis of MVP.[139]

The majority of patients with MVP will have a benign course. However, there is increasing attention given to a small proportion of patients who develop severe complications including severe mitral regurgitation requiring surgery, infective endocarditis, cerebral ischemia, congestive heart failure, and sudden death. Identifying those at risk for such adverse events is an important area of reseach. Prediction models and new imaging techniques are being actively explored.[140,143] The severe complications are typically associated with older individuals, however they can be seen in reproductive-aged women. Using large nationally representative US administrative databases, of over 13.5 million pregnancy and delivery admissions, Wilke et al.[144] reported an incidence of

MVP of 16.9 women/10,000 pregnancy admissions. They found both maternal and fetal complications were increased in patients with a MVP diagnosis. Cardiac arrest and stroke were rare occuring in <0.1% of patients, but associated with adjusted odds ratios 4.4 and 6.9 respectively compared with those without MVP. Cardiac arrhythmia and heart failure were more common occurring in 4.6% and 3.2% of those with MPV with adjusted OR of 11.0 and 5.8 respectively. Preterm delivery and preeclampsia were also more common in MVP, both with an adjusted OR of 1.2.

Management Options

Prepregnancy

Prepregnancy management should document any associated mitral regurgitation by either echocardiography or evaluation by a cardiologist.

Prenatal, Labor and Delivery and Postnatal

Patients should be observed for cardiac arrhythmias.[140] Although these occur infrequently, the patient should be counseled to avoid caffeine, alcohol, tobacco, and beta-mimetic drugs. Arrhythmias are treated as indicated (see arrythmia section).

Mitral Stenosis

Maternal and Fetal Risks

Historically, mitral stenosis, either alone or in combination with other lesions, is the most common valvular disorder associated with RHD.[133,145] The international ROPAC reported on 273 women with mitral stenosis with or without associated mitral regurgitation during pregnancy representing 70% of those with RHD. The majority of women were from developing countries. In contrast, mitral regurgitation was the predominate lesion in 274 (45%) pregnant women from the First Nation peoples of Australia and New Zealand. The severity also varied between these two cohorts with more severe disease noted in the ROPAC study than in the Australaia/New Zealand report.[124,145] Rates of initial diagnosis during pregnancy varied widely and is likely related to health care access.[126] Although maternal mortality is higher than the general popluation, death is uncommon with a reported rate of <1–2% of women with mitral stenosis, even in developing countries.[124,133,145] Hemodynamically, mitral stenosis is a state of fixed cardiac output caused by left atrial outflow obstruction. Pressures in the left atrium and pulmonary vasculature are increased.

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Longstanding severe disease may be complicated by secondary PH and atrial fibrillation. In pregnancy, the increased intravascular volume can further elevate pressures and lead to pulmonary edema and arrhythmias, even in previously asymptomatic patients.[126] For this reason, any administration of IV fluid should be closely monitored and kept to a minimum. Maternal tachycardia should also be avoided due a decrease in left ventricular filling time, leading to a decrease in cardiac output.

Several risk factors for adverse maternal and perinatal outcomes have been identified. The severity of the stenosis is the best predictor of cardiac compromise. Other significant factors include PH, prior cardiac event including arrhythmia, and baseline NYHA functional classification. Use of cardiac medications have been found to be associated with both higher and lower risk of adverse outcomes.[32,124,146] The CORPREG II[32] and DEVI[146] pregnancy risk stratification tools both perform well clinically with the DEVI tool preforming slightly better.[147] The former was developed from a population with any cardiac condition and the latter from a population made up only of patients with RHD.

Rates of FGR and prematurity are increased with complicated RHD.[124,126,145,148] There also appears to be an increase in perinatal mortality.[124,126] Generally, with an optimal maternal baseline condition and avoidance of maternal decompensation, a good fetal outcome can be expected.[133]

Management Options

Prepregnancy

The goal of preconception care is to define the severity of cardiac compromise. Two-dimensional echocardiography and color-flow Doppler are used to determine cardiac function and the degree of stenosis. Together, these modalities allow noninvasive evaluation and decrease the need for cardiac catheterization.[149] Severe stenosis is variably defined by a valve area <1.5 cm2.[149] Percutaneous mitral balloon commissutomy (PMBC) is the recommended approach in symptomatic patients and asymptomatic patients with severely stenotic valves before conception due to the risk of decompensation during pregnancy. Surgical commissurotomy is recommended for those with contraindication to PMBC such as unfavorable valvular anatomy, atrial thombus and more than mild mitral reguritation.[149] Valve replacement is reserved for those requiring reintervention after a more conservative

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approach and some patients with mixed valvular disease. Satisfactory PMBC results persisted beyond 5 years in these reports, delaying and potentially avoiding the risks associated with prosthetic valves.[150]

Rapid advancements in transcather valve replacements have led to expanding indications for this approach. Safety and effectiness data in younger patients are limited. One small series used transcatheter mitral valve implantation (TMVI) in 12 women with failing bioprosthetic valves in women contemplating pregnancy. Four of these women had six successful pregnancies with one maternal valve thrombosis treated with anticoagulation and aspirin. Prematurity was common with four delivering between 32 and 36 weeks. Three of the 12 women had elective valve replacements between 6 and 54 months after TMVI.[151]

Prenatal

The goal of prenatal care is to avoid cardiac decompensation. Special attention should be paid to volume status. Weight gain should be closely monitored. Symptoms or physical findings associated with heart failure should be reported and evaluated promptly. Maternal tachycardia should be avoided to prevent a decrease in cardiac output. Restriction of physical activity can aid in this objective. Beta-blockers and calcium channel blockers may be used to control heart rate in sinus rythym or atrial fibrillation. Digoxin is a second line option. Ivabradine is listed as an option for medical management in the Australian, European, and US guidelines, although there is limited human data regarding safety. Loop diuretics are used for volume overload. Atrial fibrillation can be managed by cardioversion, as necessary. Long standing or persistent atrial fibrillation, atrial thrombus, or history of a thromboembolic event are all indications for anticoagulation.[149]

Serial echocardiography is indicated to follow cardiac function. Percutaneous mitral balloon valvulotomy is recommended to treat patients with significant functional deterioration or refractory pulmonary edema despite optimal medical management.[149] Several series have reported symptomatic improvement with good maternal outcomes in women managed with balloon valvulotomy for severe mitral stenosis during pregnancy.[152,153] In experienced hands, fluoroscopy time and fetal radiation exposure can be minimal.[153] More recent data suggests limited effectiveness of abdominal shielding and may actually increase exposure of the fetus to radiation due to inability for internal scatter to exit the abdomen.[154] Neonatal outcomes are also reported to be better when compared with

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closed mitral valvotomy or valve replacement.[152,155] Follow-up of 2–5 years has not identified any increase in developmental delay or adverse childhood outcomes following percutaneous valvuloplasty.[153,156,157]

Labor and Delivery

During the intrapartum and postpartum periods, volume status and cardiac output are critical concerns. In patients with NYHA functional Class III or IV disease, central hemodynamic monitoring has been used. Pulmonary pressures and cardiac output can be measured reliably. Although pulmonary capillary wedge pressure (PCWP) can warn of the potential for pulmonary edema, it does not accurately reflect left ventricular preload. The pressure gradient across the stenotic valve may necessitate a high-normal or even elevated PCWP to allow adequate left ventricular filling and maintain cardiac output. To prevent pulmonary edema after delivery as a result of postpartum fluid shifts, PCWP should be maintained as low as possible without compromising cardiac output. Fluid restriction or careful diuresis, with attention to cardiac output, may be used to obtain desirable pressures. Decreased diastolic filling time associated with tachycardia may also decrease cardiac output. Careful IV administration of beta-blockers may be necessary to control heart rate and maintain cardiac output during labor.[158]

Similar considerations accompany analgesia and anesthesia during labor and delivery. Epidural analgesia is both safe and effective. Slow administration of the anesthetic agent is necessary to avoid hypotension. Control of labor pain removes a stimulus for tachycardia. The increased venous capacitance can also moderate postpartum fluid shifts. Drugs such as atropine, pancuronium, and meperidine can cause tachycardia and should be avoided.

Traditionally cesarean delivery has been reserved for usual obstetric indications, however nearly 60% of women were delivered by cesarean with no difference in the rates based on the degree of severity.[145] European guidelines recommend cesarean delivery for patients with severe mitral stenosis, or PH, while the Austrailian and US guidelines do not make a recommendation.[149] If abdominal delivery is necessary, epidural is the anesthetic method of choice. Although assisted vaginal delivery is advocated to shorten the second stage of labor and reduce bearing down, it is not always required.[158]

Postnatal

Postpartum fluid shifts increase the risk of pulmonary edema. Fluid intake and output should be strictly monitored and diuretics should be used if necessary.

Combined hormonal contraceptive methods should be used only in patients with mild stenosis and no atrial fibrillation. All other hormonal or IUD forms of contraception are category 1 or 2 and can be used.[74]

Mitral Regurgitation

Maternal and Fetal Risks

Although mitral stenosis is almost exclusively caused by RHD, mitral regurgitation has several causes. In addition to rheumatic disease, floppy mitral valves in association with MVP, papillary muscle dysfunction, ruptured chordae tendineae, and left ventricular dilation can result in mitral regurgitation.[159] In women of reproductive age, however, RHD is the most common cause of hemodynamically significant regurgitation. It is the dominant lesion in approximately one-half of patients with RHD, and is commonly associated with mitral stenosis.[124,147] In patients without severe mitral regurgitation or ventricular dysfunction, pregnancy is generally well tolerated with few significant complications. The decrease in systemic vascular resistance associated with pregnancy has a beneficial effect. Severity of mitral regurgitation and the need for cardiac medication or anticoagulation were associated with adverse cardiac events.[124]

Management Options

Prepregnancy

New York Heart Association functional status should be determined (see Table 3). The degree of regurgitation, atrial size, and ventricular function should be established with echocardiography. If required, digoxin therapy should be optimized. Surgical intervention is indicated in symptomatic patients with severe regurgitation and in asymptomatic patients with ventricular dysfunction, left ventricular dilation or PH.[124,160]

Prenatal

In patients with NYHA functional Class I or II disease, restriction of activity to prevent fatigue should be all that is required. In patients who have symptoms, serial echocardiography is indicated. Heart failure medications, diuresis, and afterload reduction should be instituted if left ventricular failure develops.

If medical therapy is unsuccessful, cardiac surgery during pregnancy can proceed, if necessary.[124,160] Although the literature is limited, contemporary

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small case series suggest that adverse fetal outcomes are increased, but acceptable. Maternal mortality is increased when the surgery is performed emergently. Fetal complications including prematurity and death are also associated with emergent procedures as well as maternal comorbidities and early gestational age at the time of the surgery.[161,162,163] During cardiac bypass, fetal bradycardia and even cardiac arrest can occur as a result of maternal hypotension.[164] Fetal risks are minimized with high flow to maintain a mean maternal blood pressure >70 mmHg. Fetal heart rate can be monitored during the procedure and used as a guide to adjust flow rates. Hypothermia is also a concern because it is associated with fetal bradycardia, and therefore hypothermia should be avoided. Perfusion temperatures >30°C are generally well tolerated.[163,165] Uterine contractions are common, further complicating fetal heart rate abnormalities. In a larger review, however, neonatal outcome was not related to the evaluated variables associated with cardiac bypass, including duration of bypass, hypothermia versus normal temperature, and lowest temperature, provided the baby was born alive.[166]

Labor and Delivery and Postnatal

Volume status should be monitored, and increases in blood pressure should be avoided to prevent worsening of regurgitant flow. When the left atrium is enlarged, cardiac monitoring may aid in the early identification of atrial fibrillation. Regional anesthesia is the method of choice for pain control during labor and delivery because of the decrease in systemic vascular resistance. Monitoring for congestive heart failure and atrial fibrillation should continue into the postpartum period.

Combined oral contraceptive pills should be avoided in patients with severe regurgitation at risk for atrial fibrillation.[74,167]

Pulmonary Stenosis

Maternal and Fetal Risks

Pulmonary stenosis is one of the more common congenital heart defects seen in adults. It is often asymptomatic even in patients with severe stenosis. However, severe stenosis can be associated with right heart failure and arrythmias. Although reports on pregnancy outcome are limited, it appears that isolated pulmonary stenosis is not associated with significant adverse maternal or fetal

effects.[4,32,47,168] One report does suggest, however, that there may be an increased incidence of hypertensive disorders of pregnancy and thromboembolic events.[46] In patients entering pregnancy with good functional status, maternal deterioration is uncommon. There is not an increased incidence of spontaneous preterm delivery or FGR. Severe stenosis does not increase the risk of adverse obstetric outcome.[47] The risk of CHD in the offspring is approximately 3–4%.[46,47]

Management Options

Prepregnancy and Prenatal

Maternal functional status and the degree of stenosis should be determined by echocardiography. Balloon valvotomy is done in patients with cardiac symptoms including exertional dyspnea, angina, or syncope when the gradient across the valve is > 30 mmHg. It should also be considered in asymptomatic patients when the gradient is > 40 mmHg.[4,32] Because significant problems during pregnancy are rare even with severe stenosis, balloon valvotomy can usually be delayed until after the postpartum period.[168] This will reduce the risk of thromboembolic complications associated with the hypercoagulable state during pregnancy.

Labor and Delivery and Postnatal

Cesarean section should be reserved for obstetric indications.[168] Patients should be monitored for signs of right heart failure during the postpartum period, although this is uncommon. There are no contraceptive restrictions.[167]

Aortic Stenosis

Maternal and Fetal Risks

Aortic stenosis is the most common cardiac valve lesion in the USA and Europe. Etiologies include congenital or RHD, and age-related calcification of the aortic valve. All are uncommon in women of reproductive age, with congenital aortic stenosis being the most frequent of these conditions seen during pregnancy and is often associated with a BAV.[4] Aortic stenosis of rheumatic origin is uncommon in pregnancy, accounting for approximately 5% of cases and is usually seen in conjunction with mitral valve disease.[133,146,147]

The normal aortic valve area is 3–4 cm.[2] The pressure gradient across the valve increases rapidly as the valve area is reduced to <2 cm,[2] and this increase is associated with left ventricular outflow obstruction.[169] Aortic dilation can be

seen in patients with a BAV, however >90% of cases are normal or only mildly dilated (< 45 mm). Moderate dilation (diameters of 45–49 mm) was seen in 7% of patients and there were no cases of severe dilation (> 50 mm). Risk of aortic dissection appears to be much lower than in Marfan syndrome.[4,170] Mild to moderate congenital stenosis (valve area > 1 cm2) is relatively well tolerated in pregnancy, and cardiac complications typically do not occur.[171,172] Even patients with asymptomatic severe aortic stenosis generally do well. Maternal mortality is rare, although cardiac complications occur in approximately 10% of patients.[4,171,172] During two-year follow-up, 36% of patients had progression of the cardiac condition that required surgery.[171] In these patients, cardiac output is fixed. Increased left ventricular pressure leads to hypertrophy and subsequent atrial enlargement. Tachyarrhythmias and atrial fibrillation may further complicate the condition. A decrease in cardiac output may result in inadequate coronary artery and cerebral perfusion, followed by sudden death.

With severe stenosis, the rate of preterm delivery and low birth weight is increased.[172] If maternal disease is congenital, the incidence of CHD in the fetus has been reported to be as high as 18%.[32]

Management Options

Prepregnancy

Before pregnancy, the severity of aortic stenosis should be determined by echocardiography. In the presence of a BAV, aortic diameter should be measured. Pregnancy should be discouraged with a diameter >50 mm. Severe stenosis should be corrected surgically before conception.[4,32]

Prenatal

Patients should be observed for signs of congestive heart failure or arrhythmias. Physical activity should be limited when symptoms of heart failure develop. Diuretics should also be used when there is evidence of congestive heart failure. Serial fetal ultrasound should be undertaken to detect FGR.[4] Surgery is indicated during pregnancy in patients when medical therapy fails. Percutaneous balloon valuloplasty is the first-line therapy.[4] Transcather aortic valve implantation has emerged as a preferred approach for many older patients requiring valve replacement. The experience in younger patients is limited however.[173] Information in pregnancy is limited to a small number of case reports. It is currently seen as an emerging option in select clinical scenarios.[4,154]

(cont.)

Labor and Delivery and Postnatal

Fluid management is the critical component of intrapartum care. Volume overload can lead to pulmonary edema. Of greater concern, however, is hypovolemia or hypotension, with decreased venous return and cardiac output. Patients should labor and deliver in the lateral position to avoid aortocaval compression. Regional anesthesia is administered slowly and cautiously, after adequate volume loading, to avoid hypotension. A narcotic epidural can decrease the occurrence of hypotension. Blood loss should be monitored closely and replaced as necessary. If pulmonary edema develops, overaggressive diuresis is avoided to prevent a decrease in preload. Oxygen supplementation, morphine, and inotropic agents, such as dopamine or dobutamine, may be needed to maintain cardiac output. The European Society of Cardiology[4] recommends early delivery by cesarean in patients with decompensated heart failure where percutaneous valvuloplasty was not possible. Close monitoring of volume status is essential in the postpartum period.

Continued follow-up after the postpartum period is important, because the condition is typically progressive. Many patients require surgical intervention within two years of pregnancy.[174]

Combined hormonal methods and standard IUDs need be avoided only in patients with severe stenosis. The risk of thrombosis with atrial fibrillation is a concern with the oral contraceptive pill, and the potential for a vasovagal event is of concern with IUD insertion. These methods, as well as progestin-only contraception, can be used in patients with mild stenosis.[74,167]

Aortic Regurgitation

Maternal and Fetal Risks

Like aortic stenosis, aortic regurgitation is uncommon in women of childbearing age. Aortic regurgitation may be due to RHD, although any condition that causes aortic root dilatation, including connective tissue disorders such as Marfan syndrome and syphilitic aortitis, can result in aortic regurgitation.

With progressive aortic insufficiency, cardiac output is usually maintained by left ventricular dilatation and hypertrophy as a result of increased preload and stroke volume. Because the condition is progressive, severe disease, with ventricular dilatation, hypertrophy, and widened pulse pressure, typically has

not yet developed in women of reproductive age and is not likely to be seen in pregnancy.[175] The decreased systemic vascular resistance and increased heart rate associated with pregnancy may improve the hemodynamics of aortic insufficiency because of decreased resistance to forward flow and decreased time for regurgitant flow during diastole. As a result, pregnancy is generally well tolerated.[176] Patients with severe regurgitation and left ventricular hypertrophy can show cardiac decompensation during the later part of pregnancy or postpartum, however.[177]

Management Options

Prepregnancy

Before conception, the extent of disease should be defined by echocardiogrpahy. In symptomatic patients, cardiac function should be optimized with digoxin and afterload reduction, as necessary. If indicated, valve replacement should be done before pregnancy.

Prenatal

Cardiac status should be optimized, as in the nonpregnant state, and patients should be followed for signs of congestive heart failure. If medical management is inadequate, valve replacement can be performed during pregnancy with generally good maternal outcomes but an increased risk of fetal mortality, as previously noted.[155,161,162,165]

Labor and Delivery and Postnatal

Vaginal delivery with epidural anesthesia is the goal. A shortened second stage of labor should be considered in more severe disease. Volume status should be followed during labor and delivery and into the postpartum period while the patient is observed for congestive heart failure.[4] Invasive hemodynamic monitoring is usually unnecessary unless other valvular disease is present. Pain control is best achieved with lumbar epidural anesthesia, which decreases regurgitant flow by reducing afterload.

Combined hormonal contraceptive methods can be used, as the benefit generally exceeds the risk (WHO category 2).[74,167]

Prosthetic Heart Valves

Maternal and Fetal Risks

Surgical valve replacement has allowed many patients with severe valvular heart disease to survive and lead near-normal lives. There are two broad

categories of replacement valves. Mechanical valves are made of nonbiologic materials. Bioprosthetic valves are either heterografts, made of porcine valves, bovine pericardium, or homografts, which are human aortic valves. The optimal choice for women of reproductive age is difficult and controversial. Mechanical valves have the advantage of durability, but require long-term anticoagulation to prevent valve thrombosis. Bioprosthetic valves do not require long-term anticoagulation, beyond aspirin, however they suffer from progressive deterioration requiring reoperation when used in young women.[178] Prioritizing longevity, valve replacement in young women has favored mechanical valves. Reported rates of mechanical valves in pregnancy over the last 10–30 years range from 74 to 83%.[179,180] That trend may be changing, with one report of nearly 12,000 reproductive-aged women with aortic and mitral valve replacments between 1990 and 2015 reporting bioprosthetic valve use increasing from 13 to 44% in the mitral position and from 15 to 57% in the aortic position.[179]

De Santo and coworkers followed 267 women with mechanical mitral valves for more than 3,700 patient-years.[181] Survival was 90% at five years and 72% at 25 years. Only 6% of patients experienced a thrombotic complication within five years of surgery, with 25% experiencing it by 25 years. Fourteen percent of patients required reoperation by 25 years of follow-up. The incidence of major thromboembolism in nonpregnant patients with mechanical valves averages 8%. Anticoagulation reduces this risk by 75%.[182] Valve thrombosis causes pulmonary congestion, poor perfusion, and systemic embolization. Rapid clinical deterioration often follows. Most embolization involves the cerebral vessels. Patients with atrial fibrillation or left ventricular dysfunction are at increased risk of embolic events.[181] Bleeding complications due to anticoagulation also occur.[183,184]

Progressive valve deterioration occurring in younger patients with bioprosthetic valves eventually requires reoperation. At 15–20 years, bioprosthetic aortic valves reoperation rates increased from 29 to 62%.[173] Pregnancy itself may accelerate deterioration and the need for reoperation. Comparison of women with mechanical and bioprosthetic valves to similar women who had never been pregnant using time to event analysis and propensity matching showed that pregnancy was associated with roughly a 2.5-times higher incidence of reoperation regardless of valve type. In patients with a mechanical valve requiring reoperation after pregnancy, 43% occurred within one year after delivery. Most involved the mitral valve and had a valve thrombosis. In those with bioprosthetic valves, median time from delivery to reoperation was 4.8 years and likely related to increased hemodynamic stress of pregnancy.[179]

The Ross procedure is an alternative for young women requiring aortic valve replacement. The patient's own pulmonary valve is transplanted into the aortic valve position and an aortic or pulmonary homograft is used to replace the transplanted pulmonary valve. The advantages of this procedure include the fact that the valve can grow with the patient and anticoagulation is not required. A major disadvantages of the operation is its technical difficulty limiting its availability to specialized centers. Long-term follow-up has been promising, with most centers reporting >90% survival at 15 years and >75% at 20–25 years after the procedure. These same centers report reoperations rates from 4 to 30% out to 25 years with most around 10%.[173]

A small series of five women with 12 pregnancies after the Ross procedure reported no significant cardiac complications during pregnancy. There was a suggestion of an increased risk of preterm delivery, although the numbers were small. One patient required reoperation for complications of both the aortic and the pulmonary valves nine years after the original operation and five years after the last pregnancy.[185]

During pregnancy women with both mechanical and bioprosthetic valves are at 10–20-fold higher risk of maternal complications when compared to pregnant community controls.[179,180,186] Reported morbidty associated with mechanical and bioprosthetic valves is inconsistent. Table 7 compares reported outcomes in pregnancy between bioprosthetic and mechanical valves reported from ROPAC and two large administrative databases. Two found higher rates of pregnancy loss, severe maternal morbidity, and hemorrage in patients with mechanical valves,[179,187] while the third found no difference in these outcomes between valve types.[180] In addition to pregnancy loss,[183,188] increased rates of prematurity and low birth weight are reported in patients with mechanical valves.[184,189]

In patients with mechanical valves, anticoagulation is required throughout pregnancy, however there is no concensus on optimal therapy. Heparin use, both LMWH and unfractionated (UFH) formulations, has been associated with an increased incidence of valve thrombosis compared with warfarin.[183,184,188] Many of the cases are associated with inadequate heparin dosing or lack of adequate monitoring using anti-factor Xa levels.[190] In a series of 18 patients in whom levels were closely followed and anti-factor Xa levels were maintained between 1.0 and 1.2 U/mL there was no valvular thrombosis, with only minor bleeding episodes experienced by two patients.[191] Osteoporosis and fractures are also potential risks of long-term UFH therapy. Low-molecular-weight heparin has the advantage over UFH of more predictable therapeutic effect and lower risk of bleeding complications

Table 7 Maternal and fetal outcomes in women with mechanical and prosthetic heart valves

	Registry study[188]		Administrative database study[181]	
Outcome	**Mechanical (%; n=212)**	**Bioprosthetic (%; n=2,620)**	**Mechanical (%; n=4,152)**	**Bioprosthetic (%; n=874)**
Maternal mortality	1.4	0.2	< 0.2	0
Valve thrombosis	4.7	0	0.2	< 0.2
Bleeding complication	23.1	4.9	5.5	5.0
Heart failure	7.5	13.2	0.9	0
Arrythmia	3.3	3.5	11.2	12.1
Miscarriage/abortion	15.6	2.8	11.2	12.1
Fetal loss	2.8	0.6	0.6	0

as well as lower risks of osteoporosis and thrombocytopenia. Conversely, warfarin is associated with increased fetal risk in pregnancy, both early and late, compared with heparin.[188] A specific embryopathic pattern is seen when warfarin is used between six and nine weeks. Fetal warfarin syndrome is characterized by nasal hypoplasia, stippled epiphyses, cardiac malformations, microcephaly, and neurodevelopmental abnormalities.[178] The incidence of fetal complications has been reported to be related to the warfarin dose, with a substantially increased risk noted in patients requiring >5 mg/day.[181,192,193] Others have reported increased fetal loss rates despite low-dose warfarin therapy.[194] Miscarriage was more common in women on a vitamin K antagonist (28.6%) compared with heparin (9.2%). The same was true for late fetal death (7.1 vs. 0.7%).[187] Because it crosses the placenta, warfarin can also cause fetal anticoagulation and bleeding, particularly if taken within two weeks of labor.[195] It is associated with an increased risk of neurologic abnormalities in the baby, probably related to intracerebral bleeding. Guner et al.[196] compared various anticoagulation options including low-dose warfarin (≤5 mg/day) throughout pregnancy, LMWH throughout pregnancy, high-dose warfarin (>5 mg/day) throughout pregnancy, LMWH in first trimester with warfarin through second and third trimesters, and warfarin throughout pregnancy. When feasible, low-dose warfarin showed the lowest rate of maternal and fetal complications. There were more early pregnancy losses and fewer stillbirths compared to LMWH regimes. There were also fewer valve thrombosis and fewer overall maternal complications in the low-dose warfarin group with no difference in bleeding. The study was limited by small cohort sizes (21–51 patients) and 65% of patients receiving LMWH did not have anti-factor Xa monitoring.

The European Society of Cardology[197] recommends low-dose warfarin throughout pregnacy when feasible and LMWH with dose adjusted to maintain therapeutic levels in the first trimester followed by therapeutic warfarin and IV UFH at delivery. The Society of Maternal-Fetal Medicine[178] has similar recommendations except for a switch to LMWH at 35–36 weeks followed by UFH at delivery. Therapeutic dose adjusted LMWH throughout pregnancy is also an option in patients who decline warfarin therapy. Low-dose aspirin (75–100 mg/day) should be added to these regimens to further decrease the risk of thrombosis. Unfractionated heparin is not recommended outside of the peripartum period. Table 8 shows the recommended dosing regimes.

Table 8 Anticoagulation dosing options in pregnancy[178]

Regimen	Dosing	Monitoring	Therapeutic goal
LMWH throughout pregnancy	Begin with 1 mg/kg enoxaparin every 12 hours	Anti-factor Xa trough level immediately before the dose and a peak level four hours after dose every one to two weeks	Trough >0.6 U/ml Peak Aortic: 0.8 −1.2 U/ml Mitral: 1.0 −1.2 U/ml
Warfarin throughout pregnancy	≤5 mg/day	International normalized ratio (INR)	2.5−3.5
LMWH until 13 weeks; warfarin from 14 weeks to planned delivery or swtich back to LMWH at 36 weeks	LMWH/heparin every 12 hours Warfarin daily	As earlier for LMWH INR	As earlier for LMWH 2.5−3.5
Aspirin added to all previous regimens	75−100 mg daily	None	Aspirin added to all previous regimens
UFH perpartum	Titrated IV Discontinue four to six hours before anticipated delivery of scheduled cesarean section	Anti-factor Xa levels every six hours activated partial thromboplastin time every six hours if anti-factor Xa levels unavailable	0.7−1.0 u/ml Two-times normal level

Management Options

Prepregnancy

As with other cardiac lesions, NYHA functional status is determined. Baseline echocardiography is indicated. Patients with bioprosthetic valves should be informed of the symptoms of valve deterioration. Low-dose aspirin (75–100 mg/day) should be continued or started.[4,178] Warfarin

(cont.)

embryopathy must be discussed with patients who have a mechanical valve. An informed decision should be made about the potential use, timing, and duration of heparin treatment.[4,32,178]

Prenatal

Patients with bioprosthetic valves should be followed for signs of valve deterioration. Those with mechanical valves must maintain adequate anticoagulation. In patients who are able to continue treatment with low-dose warfarin (typically < 5 mg/day), the INR is maintained in the therapeutic range. If LMWH is used, the anti-factor Xa peak and trough levels level should be monitored and maintained in the therapeutic range (Table 8). Although it is rare in pregnancy, monitoring for heparin-induced thrombocytopenia should be undertaken.[198] At term, if warfarin has been used, it is discontinued and heparin initiated.[32]

An anesthetic consultation is recommended. The Society for Obstetric Anesthesia and Perinatology provides guidelines for women receiving anticoagulants during pregnancy.[199] Type and dose of heparin as well as time since last dose affect when regional anesthesia may be administered. With UFH, regional anesthesia can be placed more than four to six hours since the last dose if the dose is 5,000 U three-times daily or less. If the dose is between 7,500 and 10,000 U twice daily, initiation should be delayed at least 12 hours after the last dose, and for higher doses, a 24-hour delay is recommended. A normal aPTT would allow an initiation in shorter time frames. With low-dose LMWH, regional anesthesia should be delayed at least 12 hours, and at least 24 hours with high dose.

Labor and Delivery

Intravenous UFH at therapeutic doses may be given until four to six hours before anticipated vaginal or planned cesarean delivery. A normal aPTT should be present before using regional anesthesia/analgesia and before removing an epidural.[178] If necessary, protamine can be used to reverse IV heparin anticoagulation at a dose of 1 mg/100 units of heparin up to a maximum dose of 50 mg. The dose is decreased as the time since heparin withdrawal increases. Another approach is to give prophylactic doses of heparin (5,000–7,500 U q12h) subcutaneously.

Patients with bioprosthetic valves may benefit from operative vaginal delivery to shorten the second stage of labor and avoid the additional hemodynamic stresses of pushing.

(cont.)

Postnatal

Warfarin is initiated in the postpartum period in patients with mechanical valves. While bridging to therapeutic warfarin levels, therapeutic IV UFH started four to six hours after delivery and >1 hour after epidural removal is recommended over LMWH due to easier management of postpartum bleeding. Breastfeeding during anticoagulation with warfarin is not contraindicated, because the levels of warfarin in the breast milk are too low to be significant.[178]

Patients with bioprosthetic valves and no other complications generally can use combined hormonal contraceptive methods (WHO category 2) and IUDs. Those with mechanical valves should generally avoid combined hormonal methods, Depo-Provera, and standard IUDs.[167] The levonorgestrel-containing IUD may be acceptable.

Marfan Syndrome

Maternal and Fetal Risks

Marfan syndrome is a connective tissue disorder resulting from a mutation in the *FBN1* gene leading to alterations in fibrillin 1, a protein found in the extracellular matrix. The characteristic findings include skeletal, ocular, and cardiovascular abnormalities. Cardiac manifestations include MVP, mitral regurgitation, and aortic root dilatation. Aortic pathology is associated with an increased incidence of aortic regurgitation, dissection, and rupture, leading to significant morbidity and mortality.[200] Pregnancy in Marfan syndrome with aortic root diameter ≥ 45 mm is considered high risk (mWHO Class III).[82] In pregnant patients, morbidity and mortality rates increase with aortic root diameter ≥ 40 mm, and dissection rates are reported to be 10%, compared with only about 1% if the aortic root is of normal dimensions.[201,202] Limited data support a recommendation to avoid pregnancy in Marfan patients with aortic root diameter ≥ 45 mm or in patients with a history of dissection (mWHO Class IV).[82] If aortic dissection occurs, mortality rates as high as 25–50% have been reported. Even with a normal aortic root diameter and after successful aortic root replacement, maternal mortality has been reported likely due to dissection risk of other vessels.[4] The elevated risk seen in pregnancy may be related to the increased cardiac output, placing additional stress on the relatively stiff aorta. Hypertensive disorders of pregnancy, such as preeclampsia, may further aggravate the condition.[203] Several reports have suggested a better prognosis when

there is minimal cardiovascular involvement. These patients had no increase in adverse maternal outcomes and no accelerated dilatation of the aorta compared with similar patients with Marfan syndrome who were not pregnant. Patients without aortic root dilatation usually tolerate pregnancy well.[201,204] Pregnancy does not appear to be associated with an increased rate of progression of aortic root dilatation in patients with a prepregnancy diameter <40 mm. Pregnancy is associated with a slightly increased rate of dilatation in those with an initial diameter ≥ 40 mm.[204]

There is an increased incidence of adverse pregnancy outcomes noted in women with Marfan syndrome. Incompetent cervix and preterm delivery occur in 15% of pregnancies, and perinatal mortality was reported to be 7%.[204] The syndrome is inherited by autosomal dominant transmission, so there is a 50% chance that the fetus will be affected. Referral to a geneticist is recommended for patients planning pregnancy.

Management Options

Prepregnancy

Genetic counseling is an essential part of family planning in Marfan syndrome because of the autosomal dominant inheritance. In about 80% of women (or affected men), a specific gene abnormality can be identified, allowing the possibility of prenatal diagnosis (either by preimplantation genetic diagnosis or by chorionic villus sampling in the first trimester). An echocardiogram to evaluate the aorta is performed to define maternal risk status. In nonpregnant adults, 50 mm is the critical aortic root diameter at which prophylactic repair is recommended.[200] Pregnancy is contraindicated in patients with aortic root dilatation ≥ 45 mm. If pregnancy is desired, prophylactic repair should be performed for aortic root dilation ≥ 40–45 mm if moderate to severe aortic regurgitation is present or if rapid dilation (≥ 2–3 mm/year) is documented.[82] Aortic repair is not completely protective against complications, however. Those with previous dissections are at risk for future events.[201,204] Initiation of beta-blockade should be considered if not already utilized.[39,202] Although information on its use in pregnancy complicated by Marfan syndrome is limited, studies of long-term use outside of pregnancy show that it slows the progression of aortic dilatation.[200]

Prenatal

Serial echocardiography to follow the aortic root diameter should be performed every trimester for aortic root diameter <40 mm or every four

(cont.)

to eight weeks for aortic root diameter ≥ 40 mm.[39,82,201,202] If not initiated before conception, the addition of beta-blocker therapy should be considered. Little information is available to guide management in patients with progressive aortic root dilatation during pregnancy. Hypertension should be avoided because of the increased risk of aortic dissection. Although it is best postponed until postpartum, aortic root repair may be considered in extreme cases. Genetic counseling and prenatal diagnosis should be made available for all patients.

Labor and Delivery

Epidural anesthesia during labor should be recommended. Adequate oxygenation must be maintained, and hypertension should be avoided. Vaginal delivery is desirable, with shortening of the second stage of labor with the use of a vacuum or forceps to avoid Valsalva.[39,201,202] Cesarean delivery is indicated in patients with an aortic root diameter of ≥ 40 mm or with a history of aortic dissection.[39,82]

Postnatal

Both patient and physician must remain vigilant because the risk of aortic dissection persists for six to eight weeks postpartum.[201,202] Long-acting reversible contraceptives are preferred, but other progesterone-only contraceptives are recommended. Combined hormonal contraceptives can be used in patients without aortic dilatation but should be avoided in those with dilatation.[38,74]

Peripartum Cardiomyopathy

Maternal and Fetal Risks

Cardiomyopathy is uncommon in women of reproductive age, however it is the most common cause of maternal death between one week and one year postpartum.[205] Women may enter pregnancy with a preexisting cardiomyopathy or develop PPCM. Peripartum cardiomyopathy is a subset of cardiomyopathy defined by onset of heart failure in the last month of pregnancy or the first five months postpartum, with no other etiology of heart failure identified and a LV EF of < 45%.[206,207] The reported frequency of the condition varies widely. The reasons for such variations are unknown. In Nigeria, PPCM occurs in up to 1 in 100 deliveries.[208] In Haiti, the incidence is as high as 1 in 300 live births,[209,210,211] whereas in the USA, it is between 1 in 3,000 and 1 in

4,000.[209,211] In the USA, the incidence varies by race, being more common in black women, in whom the incidence is reported to be approximately 1 in 1,400 births.[209,212] Despite the rarity of the condition, it accounts for a significant proportion of maternal mortality in the USA. Important racial disparities exist with cardiomyopathy, as well as it being the second leading cause of maternal mortality in black mothers.[213]

The etiology of pregnancy-associated heart failure is unknown, although a number of pathologic theories exist. Evidence of varying degrees of inflammation has been found through serum markers and on endomyocardial biopsy.[214,215,216,217] The inflammation has been associated with evidence of viral infection in some cases,[214] as well as autoimmune mechanisms.[217] Hypertensive disorders and black African descent are significant risk factors.[209,212,218,219] A systematic review and metaanalysis found that 22% of women with PPCM also had preeclampsia, and suggested that these two conditions may share common pathogenic features.[218] A number of other risk factors have been reported, including older maternal age (>30 years), multiparity, multigestational pregnancy, and tocolytic use.[61] The existence of PPCM as a distinct pathologic entity is debated. The marked hemodynamic stress of pregnancy may unmask patients with genetic prediposition or preexisting susceptibility.[61] To minimize confounding by exacerbation of unrecognized preexisting heart disease, the National Institute of Health work group emphasized the importance of limiting the diagnosis of PPCM to within a defined six-month window.[219] A report of pregnancy-associated cardiomyopathy diagnosed more than one month before the end of pregnancy found no difference in risk factors, present course, and outcome, suggesting that there may be a continuum of the disease process during pregnancy.[220]

Regardless of the etiology, cardiomyopathy during pregnancy is associated with significant morbidity and mortality. Reported complication rates vary widely and likely reflect different patient populations and variations in diagnostic criteria. Long-term outcome data in the USA report mortality at 7–20% in patients with PPCM.[61] Persistent cardiac dysfunction is seen in 50–80% of patients.[210,221,222] Left ventricular thrombus is seen in up to 17% of initial echocardiograms and 5–9% of patients have thromboembolic complications.[61] A number of echocardiographic findings at initial presentation have been reported to predict persistent dysfunction. These include a decreased fractional shortening to < 20%, a left end-diastolic dimension of > 6 cm, a left end-systolic dimension of > 5.5 cm, an EF of < 27%, and a left ventricular thrombus.[221–223] Maternal mortality reports vary widely, with rates up to 15% in Haiti,[210] and 1–4% in larger population-based studies in the USA.[209,212] Temporary mechanical circulatory support with devices such as an intraaortic balloon pump,

a percutaneous ventricular assist device, and extracorporeal membrane oxygenation may be necessary in patients with persistent cardiogenic shock despite inotropic support.[61] Left ventricular assist device placement is also now increasingly used in patients with severe heart failure and ongoing cardiogenic shock. Some survivors may require cardiac transplant.[221,223] The rate of recurrence in subsequent pregnancies is as high as 85%.[219] Patients with severe left ventricular dysfunction during the index pregnancy or persistent dysfunction are at increased risk of recurrent or progressive heart failure and death in subsequent pregnancies.[224,225] Elkayam and colleagues found in their cohort that 44% of patients with residual LV dysfunction developed heart failure symptoms during the subsequent pregnancy and 19% of these patients died, compared with no mortality in women who had normalization of LV function following the initial pregnancy.[226] Although those with normal cardiac function six to 12 months postpartum fare better, they are still at risk for heart failure and a recurrent decrease in EF that may not recover after another pregnancy.[226] Patients whose cardiomyopathy clinically resolved had decreased contractile reserve with provocative testing.[227] This lack of reserve may cause cardiac decompensation as a result of the hemodynamic stress of a subsequent pregnancy and may contribute to the morbidity after a previous return to normal cardiac function.

Maternal cardiomyopathy is associated with increased rates of SGA infants and preterm birth.[211]

Management Options

Prepregnancy

Pregnancy is strongly discouraged in patients with a history of PPCM, particularly those with residual cardiac dysfunction. In those with normal cardiac function, pregnancy is less contraindicated. The patient should be informed of the potential for worsening cardiac function during pregnancy, which may not completely resolve postpartum.[226] Combined hormonal contraceptives should be avoided in patients with residual ventricular dysfunction. Depo-Provera or IUDs can be safely used.[167] Permanent sterilization may also be considered.

Prenatal

If pregnancy occurs, echocardiography should be performed to document ventricular size and function as well as the presence of mural thrombi. Termination should be offered, especially to patients who have persistent echocardiographic abnormalities, because of the high associated maternal

(cont.)

morbidity and mortality. If the pregnancy is continued, a multidisciplinary should collaborate to optimize outcome. Decreased activity and potentially even bed rest are recommended, along with salt restriction. Diuretics and afterload reduction with hydralazine should be used, as necessary. Beta-blockers, most commonly metoprolol, can be used although there is potential risk for FGR, fetal bradycardia, and fetal hypoglycemia. Digoxin can be used if indicated. Given the hypercoagulable state of pregnancy, the AHA published a scientific statement noting moderate consensus for a treatment recommendation of anticoagulation in patients with PPCM and LVEF < 30%. Prophylactic heparin is recommended as warfarin generally should not be used.[228] Bromocriptine is a prolactin blocker and studies have demonstrated improved recovery of the EF in PPCM.[229] The European Society of Cardiomyopathy work group on PPCM recommends bromocriptine for treatment of women with an EF of < 25% or in cardiogenic shock.[4] However, given that bromocriptine can have a pro-thrombotic effect, it should be combined with at least low-dose UFH or LMWH, especially in the context of the hypercoagulable state of pregnancy.[230]

Labor and Delivery

Patients are watched closely for signs of heart failure and pulmonary edema. Cardiac monitoring is instituted early in labor. Fluids are restricted, and central hemodynamic monitoring may be considered if decompensation occurs. A flow-directed PAC is rarely required, but if one is used, care must be taken during insertion. Positioning may be difficult because of dilated chambers and decreased EF. Arrhythmias may also be precipitated during insertion. Heparin can be discontinued prior to a planned delivery or during early labor and resumed in the early postpartum period. Adequate pain control is important, and epidural anesthesia works well. Patients with significant cardiac dysfunction may need to labor in a sitting position to reduce or prevent shortness of breath.

Postnatal

Monitoring of volume status must continue through the postpartum period, with fluid restriction as necessary. Diuretics may be used as necessary, and the patient should be given guideline-directed medical therapy for afterload reduction and left ventricular remodeling, These medications may include: an ACE inhibitor, ARB, or sacubitril-valsartan for afterload reduction, aldosterone receptor antagonists, beta-blockers, and SGLT2 inhibitors.[61,219] Cardiac

(cont.)

MRI may be performed to evaluate for evidence of myocarditis or infiltrative cardiomyopathy. Although uncommonly performed, endomyocardial biopsy may be considered to exclude treatable causes of cardiomyopathy. Some patients with certain types of myocarditis found on biopsy respond favorably to immunosuppressive therapy.[219] There are no contraceptive restrictions in patients whose cardiac function has completely recovered. Combined hormonal methods should not be given in the early postpartum period or to those with persistent ventricular dysfunction.[167]

Cardiac Arrhythmias

Maternal and Fetal Risks

Cardiac arrhythmias are relatively common during pregnancy. Most are benign and include sinus bradycardia, sinus tachycardia, and atrial and ventricular premature contractions. These patients are often asymptomatic, but may have palpitations, although the correlation between symptoms and the actual arrhythmia is poor. Shotan and associates evaluated symptomatic pregnant patients who were referred to a cardiac clinic and compared them with asymptomatic pregnant patients who were referred for evaluation of a cardiac murmur.[231] The incidence of premature atrial and ventricular contractions was 50–60% in each group. Although the frequency of arrhythmias was higher in symptomatic patients, only 10% of symptoms occurred in conjunction with the arrhythmia. Healthy, asymptomatic patients without underlying pathologic arrhythmias can often be managed with reassurance and observation.[232] Nearly all women in labor will have tachycardia and isolated premature atrial beats at some point.[233] Basal resting heart rate can increase by 10–20 beats/minute during pregnancy.[234] In patients with pacemakers, it may be necessary to ensure that rate-responsive programming is in place to match the physiologic increase in heart rate that occurs in pregnancy.[235]

Pregnancy may be associated with an increase in the incidence and severity of arrhythmias.[231,236,237] Briller et al. found that 10.7% of maternal deaths were related to arrythmia.[238] Pregnancy can be associated with physiologic changes that increase the risk of arrhythmia, including increased plasma catecholamine concentrations, chronotropic effects of relaxin, increased atrial stretch from increased cardiac output, increased ventricular end-diastolic volume due to intravascular volume expansion, and hormonal changes.[235] Underlying structural heart disease, thyroid abnormalities, and electrolyte derangements can increase the risk of more sustained arrhythmias.[239]

Supraventricular tachycardia is a common sustained arrhythmia seen in younger women and can be more often seen in pregnancy. Ventricular tachycardia and multiform premature ventricular complexes are much less common but may be recognized for the first time during gestation. Atrial fibrillation is usually associated with underlying cardiac disease.[240] With any of these arrhythmias, cardiac decompensation can occur, resulting in pulmonary edema. This is particularly common with underlying structural heart disease, in which cardiac reserves may be limited. Sudden death is a concern in the presence of significant preexisting cardiac conditions. Women with a prior history of significant arrhythmias have a high incidence of recurrence during pregnancy. Atrial arrhythmias occur in approximately half of these patients, whereas ventricular arrhythmias recur in a quarter.[240]

Long QT syndrome is a genetic condition associated with a prolongation of the QT interval along with syncope and sudden cardiac death. Beta-blockers are the mainstay of therapy. Women who continue therapy during pregnancy are at low risk of complications.[236,241] An increase in cardiac complications as a result of long QT syndrome has been noted during the postpartum period.[236] Some may benefit from the surgical implantation of a pacemaker. Prematurity is increased in the presence of many arrhythmias.[240] In addition, fetal exposure to drugs used for maternal therapy is a potential concern. Direct electrical cardioversion is safe and effective and is recommended over chemical cardioversion in hemodynamically unstable patients.[238] Symptomatic and sustained arrhythmias may require appropriate antiarrhythmic therapy. Generally benign arrhythmias such as premature atrial and ventricular complexes are best treated conservatively and with reassurance. Beta-blockers can be used in patients with persistent arrhythmias after conservative management.[237] These agents have been associated with an increased incidence of FGR in women with heart disease.[242] Metoprolol is generally preferred over atenolol given the more significant issues with FGR.[243] In patients with long QT syndrome, beta-blockers are continued to reduce the incidence of cardiac events.[236] Digoxin can be used safely to control the ventricular rate in atrial fibrillation, atrial flutter, and some supraventricular tachycardias.[244] Vagal maneuvers should be attempted in cases of supraventricular tachycardia but if that fails, IV adenosine may be used.[238] Adenosine has a rapid onset and very short duration of action. It is used acutely during pregnancy to treat supraventricular tachycardia and is the drug of choice.[244] Esmolol and verapamil can be used intravenously in the acute management of supraventricular tachycardia. Quinidine is used to treat some atrial and ventricular arrhythmias. Lidocaine is used acutely to control ventricular arrhythmias. Procainamide can also be used to treat ventricular arrhythmias but can result in maternal side effects, including cardiac rhythm disturbances,

lupus-like syndrome, and blood dyscrasia. Amiodarone is used to treat life-threatening ventricular arrhythmias when first-line agents are unsuccessful. It is associated with neonatal hypothyroidism, hyperthyroidism, and possibly FGR, fetal bradycardia, and neurologic abnormalities.[232] Catheter ablation may be considered for arrhythmias refractory to medical therapy but it is preferable to delay until the second trimester to limit radiation exposure during early development.[238] In cases with severe symptomatic and unstable bradyarrhythmia, including high-grade heart block or sick sinus syndrome, pacemaker placement can be done during pregnancy.[238] However, patients with stable congenital aortic regurgitation block can be managed conservatively without need for pacemaker placement.[238]

Management Options

Prepregnancy

All patients with a sustained arrhythmia should undergo a baseline electrocardiogram to determine whether the rhythm abnormality originates from the atrium or the ventricle. This is followed by a search for an underlying etiology. Patients with unexplained sinus tachycardia or premature atrial or ventricular contractions are questioned about tobacco, caffeine, and illicit drug use. They are also evaluated for anemia and hyperthyroidism. If a contributing factor is identified, behavior modification is attempted, as appropriate. Medical conditions should be treated before conception. Ambulatory monitoring is considered when patients have symptoms that suggest a rhythm disturbance but no objective evidence on examination. Patients who may benefit from ablative therapy should be identified and treated before conception.[244]

Prenatal, Labor and Delivery, and Postnatal

Management during pregnancy consists of maintenance therapy to control arrhythmias. Drug levels should be monitored, as indicated, because of pregnancy-associated changes in volume of distribution and protein binding. Vagal maneuvers can be tried initially in supraventricular tachycardia during pregnancy.[244] Cardioversion can be used safely during pregnancy in unstable patients or when medical therapy is unsuccessful.[244,245] In patients with atrial fibrillation, ventricular rate should be controlled with beta-blocker, digoxin, or a calcium channel blocker. Prophylactic anticoagulation is warranted in patients with atrial fibrillation with elevated stroke risk as per the CHA_2DS_2VASc scoring system or considered in patients with mitral stenosis that increases clot risk.[238] Anticoagulation

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options include heparin (LMWH or UFH) with monitoring of anti-factor Xa levels or vitamin K antagonists (warfarin) may be used after the first trimester.[238] Direct oral anticoagulants are contraindicated during pregnancy and breastfeeding.[238] In the stable patient, medical cardioversion with quinidine or procainamide may be tried. Electrical cardioversion should be done in those who are hemodynamically unstable.[246] Continuous cardiac monitoring may be necessary intrapartum and postpartum for symptomatic or complex arrhythmias.

Occasionally, surgical implantation of an automatic defibrillator can be life-saving in patients with a high risk for recurrent ventricular arrhythmias. In patients with cardiac implantable electronic devices, baseline interrogation should be performed in the first trimester. In patients undergoing surgery such as for cesarean section, there can be the potential risk for electromagnetic interference (EMI) from an electrosurgery unit that can disrupt the operation of the cardiac device. Bipolar electrocautery reduces the risk of EMI compared to unipolar electrocautery. Moreover, the grounding pad should be placed as far away as possible from the cardiac device.[235] To decrease potential for EMI-related inhibition of pacing, patients who are pacemaker-dependent can have their pacemaker converted to a continuous asynchronous pacing mode by reprogramming or placement of a magnet over the device. Care should be made to ensure that appropriate program settings are restored after delivery and before discharge.[235]

Myocardial Infarction and Cardiac Arrest

Maternal and Fetal Risks

Myocardial infarction is uncommon in women of reproductive age, with an incidence ranging from 2.8 to 8.1 per 100,000 births and mortality rates of 4.5–7.3%;[247] although with the current epidemic of obesity and rising maternal age, it is likely to become increasingly important. Pregnant women are at a three- to four-times higher risk of acute MI compared to nonpregnant women of similar age.[247] Ischemic etiologies of MI include: atherosclerosis, thromboembolism, spontaneous coronary artery dissection (SCAD), and MINOCA (MI in the absence of obstructive coronary artery disease). A study of acute MI in pregnancy found that the mechanisms of MI were as follows: 43% coronary dissection, 27% atherosclerotic disease, 17% clot without angiographic evidence for atherosclerotic disease, and 14% normal coronary anatomy.[248]

MINOCA is used when there is an acute MI with no lesion ≥ 50% of the lumen diameter in a major epicardial vessel,[249] and may include conditions such as coronary vasospasm, microvascular dysfunction, and supply-demand ischemia.

Elkayam and colleagues found that 75% of the patients with acute MI during pregnancy presented with ST-segment-elevation MI (STEMI) and the remainder with non-STEMI. The majority of these cases occurred during the third trimester of pregnancy or the postpartum period. Complications of acute MI included heart failure or cardiogenic shock (38%), ventricular arrhythmias (12%), and recurrent angina or acute MI (20%).[248] Maternal mortality is in the range of 5–7% in contemporary studies.[248,250] Mortality has been reported to be approximately 20% when the MI occurs in the peripartum period. This is roughly twice the rate during the antepartum period.[251,252] Prematurity is reported to be 43% in patients with an antenatal MI. Fetal outcome is ultimately related to maternal status and outcome.[251]

Risk factors associated with MI in pregnancy include increasing age, cigarette smoking, hyperlipidemia, chronic hypertension, diabetes, hypertensive disorders of pregnancy, thrombophilia, postpartum infection, and multiparity.[248,251,253] Obesity is associated with an increased incidence of several of these risk factors. Although MI was reported to be more common in black women, race was not an independent risk factor after controlling for other comorbidities.[251,253] Transfusion has also been identified as a risk factor for MI and may represent a surrogate marker for postpartum hemorrhage.[253] Karpati and colleagues[254] demonstrated elevated troponin I levels, electrocardiographic changes, and decreased cardiac contractility compatible with myocardial ischemia in half of the 55 patients they managed with severe postpartum hemorrhage.

Acute MI is defined as myocardial injury determined by the elevation of cardiac troponin, with at least one value above the 99th percentile upper reference limit and at least one of the following: ischemic symptoms or electrocardiographic changes, development of pathologic Q waves, imaging evidence of new loss of viable myocardial or regional wall motion abnormalities consistent with ischemia, and identification of a coronary thrombus by angiography or autopsy.[255]

Criteria for the diagnosis of MI do not change during pregnancy. The diagnosis remains a challenge, in part because the index of suspicion is often low. Physiologic changes of pregnancy may mimic the symptoms of MI and delay the diagnosis. During labor, the diagnosis is further complicated by the fact that creatinine phosphokinase and the cardiac-specific MB fraction may normally be elevated,[256] although the most commonly used biomarker for myocardial injury in current times is the cardiac troponin. Cardiac troponin I and cardiac troponin T are specific markers for cardiac injury that do not

increase during normal labor and delivery, making it a useful tool in the diagnosis of MI in the pregnant woman.[64,257] However, up to 4% of asymptomatic postpartum women will have elevated high sensitivity cardiac troponin T so the diagnosis of acute MI should be made in the context of symptoms and clinical evidence of ischemia in addition to biomarker elevation.

Spontaneous coronary artery dissection is a non-iatrogenic dissection of the epicardial coronary artery that is not due to atherosclerosis or trauma.[258,259] The resulting intramural hematoma or intimal disruption results in coronary artery obstruction.[259] Risk factors for SCAD include: pregnancy or early postpartum period, fibromuscular dysplasia, connective tissue disorders (including Marfan's and Ehlers–Danlos), systemic inflammatory conditions, hormonal therapy, history of fertility treatment, drug use, Valsalva-type activities, and intense exercise or emotional stress.[259] A Mayo Clinic registry found that patients with peripartum SCAD more frequently presented with STEMI (57%) and more often had left main or multivessel SCAD and a left ventricular function of ≤ 35%, with the majority of the peripartum SCAD events occurring within one month postpartum.[260] Multiparity, history of fertility therapies, and preeclampsia were more often seen in women with peripartum SCAD. In the absence of ongoing ischemia or hemodynamic instability, the preferred management approach with SCAD is conservative medical therapy as percutaneous intervention with catheters and guidewires may result in propagating the dissection and extension of the false lumen. Among patients with minimal ongoing ischemia with distal coronary involvement or preserved coronary flow, 95% of conservatively treated patients with SCAD will heal within 30 days.

Cardiac arrest is a feared complication of MI. In addition to cardiac causes, other common etiologies during pregnancy include hemorrhage, amniotic fluid embolism, and sepsis. Cardiac arrest occurs in approximately 1 in 12,000 delivery hospitalizations. This rate has not changed since the late 1990s. Nearly 60% of women survive the event and leave the hospital.[261]

Management Options

Prepregnancy

Since the underlying condition is rare, pregnancy after MI is uncommon. Unfortunately, it is even more uncommon for these patients to seek preconception counseling.[262] When possible, cardiac evaluation should be done, including echocardiography and stress testing if indicated. Even if the patient has no cardiac dysfunction, pregnancy should be planned cautiously.[262] Medication should be optimized and statins should ideally be stopped before conception. Oligohydramnios and neonatal renal failure

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are associated with ACE inhibitors used in the second or third trimester. An alternative drug should be used, beginning before conception or in early pregnancy. Beta-blockers can be used. Atenolol is a cardioselective beta-blocker that has been associated with FGR, but can be used with caution. Low-dose aspirin is not associated with adverse effects. There is limited information during pregnancy for clopidogrel, an antiplatelet agent. Animal studies suggest low risk. It is believed to cross the placenta and, in theory, could pose a bleeding risk to the fetus.[60] For this reason, it should be used with caution near delivery. Because as many as half of women with ischemic heart disease will be obese, dietary advice and support in achieving weight reduction are important.

Prenatal

Patients should rest and avoid strenuous activity. They should also be monitored for evidence of arrhythmias or congestive heart failure. If an MI occurs during pregnancy, management principles are similar to those for nonpregnant patients.[252] Nitroglycerin, oxygen supplementation, morphine, heparin, and continuous cardiac monitoring are initiated. Lidocaine, dopamine, calcium channel blockers, and beta-blockers can be used, as indicated. Coronary angiography can be utilized as clinically indicated during pregnancy. Percutaneous angioplasty and stent placement are being used more frequently in pregnant patients with favorable outcomes.[252,253] Coronary artery bypass surgery has also been reported in pregnancy; however, the number of cases is small and conclusions regarding outcomes are limited.[252] Pregnancy is considered a relative contraindication to thrombolytic therapy because of the theoretical increased risk of maternal and fetal bleeding; however, safe and effective use during pregnancy has been reported, as well as cases of significant maternal bleeding and abruption. The increased incidence of coronary artery dissection also urges caution with the use of thrombolytic therapy because bleeding may worsen the dissection.[253] In fact, once SCAD is diagnosed, anticoagulation with heparin or LMWH is discontinued as anticoagulation can worsen the intramural hematoma and dissection.[258,259]

In cases of cardiac arrest, cardiopulmonary resuscitation proceeds with some notable modifications to the procedure used in the nonpregnant patient. These include left lateral displacement of the gravid uterus to prevent aortocaval compression and improve venous return. Early intubation is recommended. In an intent to prevent aspiration, historically

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cricoid pressure has been requested but this is no longer routinely recommended. For chest compressions, the heel of the first hand is placed in the middle of the chest over the lower half of the sternum. There is no change in the recommendations for defibrillation.[263] If initial attempts at resuscitation are unsuccessful, perimortem cesarean section is indicated. Although a final heroic effort, the procedure is potentially life-saving for a viable fetus, and improved effectiveness of the resuscitation may also be life-saving for the mother. Due to the rarity of the event, evidence defining the ideal time from decision to delivery associated with optimal maternal and neonatal outcomes is limited to case reports and small case series. Past guidelines based on these reports advocated initiating the cesarean section within four minutes of the arrest to accomplish delivery within five minutes.[264,265] A more contemporary review including events occurring since 1980 found this goal was achieved in <5% of cases. An arrest-to-delivery interval of <10 minutes was associated with improved maternal outcomes. Improved neonatal survival was associated with in-hospital arrest but not the time to delivery, although there was a shorter arrest-to-delivery interval for survivors compared to nonsurvivors (14 vs. 22 minutes). The current AHA guideline acknowledges that the decision to perform a perimortem cesarean section is complex, and a specified time interval is no longer included. Shorter arrest-to-delivery intervals are associated with better outcomes, and the procedure should be considered at approximately four minutes if resuscitative efforts have been unsuccessful.[263] Simulation has demonstrated improvements in team performance.[266]

Labor and Delivery

Vaginal delivery is believed to be acceptable in patients who have had an MI. In cases of SCAD, if possible, it is preferable to wait two weeks before delivery. Cesarean delivery should be reserved for the usual obstetric indications as well as for those who have had a MI in close proximity to labor or are unstable. External cardiac monitoring is necessary. Supplemental oxygen should be given, and epidural anesthesia is used for pain control. Operative vaginal delivery to shorten the second stage of labor is also recommended, especially in the case of patients with a history of SCAD to allow for passive descent and minimizing Valsalva effort.[252,259]

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Postnatal

Volume status is monitored in the postpartum period, and the patient should avoid strenuous exertion. A reliable plan for contraception should be made. Combination oral contraceptives, patches, rings, or injectables are usually contraindicated (category 4). Although the risk of atherosclerosis is not increased, estrogen increases thrombotic risk, especially when other risk factors are present. Continued use of progesterone-only methods including the progesterone-only pill, Depo-Provera, and implants should generally be avoided because they may have adverse effects on lipid profiles (category 3). Systemic hormonal contraception with either estrogen or progesterone is generally not recommended in patients with a history of SCAD given the presumed pathophysiological association with female sex hormones.[258] If permanent sterilization is not desired, the copper-containing IUD is a reasonable alternative but this may be associated with increased risk of cramping and menorrhagia, particularly in women receiving aspirin or dual-antiplatelet therapy. Intrauterine devices with local delivery of progestin (levonorgesterel 20 μg/day) are generally acceptable in patients with history of SCAD given that the effect is mostly localized to the endometrium.[258]

Hypertrophic Cardiomyopathy

Maternal and Fetal Risks

Hypertrophic cardiomyopathy is an autosomal dominant condition characterized by left ventricular hypertrophy without chamber dilatation and no other etiology to explain the hypertrophy. It is classically associated with left ventricular outflow obstruction, but this is not found in all patients. As a result, older names for this condition, such as idiopathic hypertrophic subaortic stenosis and hypertrophic obstructive cardiomyopathy, have been generally replaced. In the general population, the frequency of this condition is approximately 1 in 500.[267]

The presentation and prognosis are clinically variable. Most patients have a normal life expectancy without limitations; however, HCM is a common cause of sudden cardiac death in young people. The annual mortality rate is estimated at 1%, substantially less than the rate reported in older series, primarily because of the identification and inclusion of patients with more benign forms of the disease.[267,268] Clinical risk factors for sudden death include a family history of sudden cardiac death, previous syncope, and documented ventricular tachycardia. Maki and colleagues identified an inadequate increase

in systolic blood pressure associated with exercise, defined as <24 mmHg on treadmill testing, as a risk factor in patients younger than 50 years.[268] A left ventricular wall thickness of >30 mm may be a risk factor in young adults. Septal myectomy in nonpregnant individuals has not only improved the outflow obstruction but also resulted in significant regression of the ventricular hypertrophy.[269] Implantable cardiac defibrillators are used successfully in high-risk patients and can be used in pregnant patients.[270]

Maternal mortality is generally low in HCM. In ROPAC, there were no maternal deaths reported among 60 patients with the condition, although fetal loss was reported to be 5%. In this cohort, 23% of patients developed heart failure and arrythmias. Patients with signs of heart failure and decreased functional status (NYHA functional Class II or greater) prior to pregnancy were associated with increased occurance of complications. The majority of these outcomes occurred during the third trimester or in the postpartum period.[271] In the ROPAC registry, there was no significant difference in pregnancy outcome between women with obstructive and nonobstructive HCM, but the CARPREG II study reported a 10% incidence of adverse maternal cardiac events in patients with a left ventricular outflow tract (LVOT) gradient of >30 mmHg.[32]

Physiologic changes associated with pregnancy have variable effects on the condition. Adequate preload and systemic vascular resistance are important factors in maintaining end-diastolic volume and cardiac output. A decrease in end-diastolic volume increases outflow obstruction. The increased blood volume associated with pregnancy has a beneficial effect, whereas the decrease in systemic vascular resistance can worsen outflow obstruction. The increased heart rate can also adversely affect maternal condition due to the resulting decreased diastolic filling time. Mitral regurgitation can be seen in the setting of LVOT obstruction due to systolic anterior motion of the mitral valve.[272] Despite these concerns, maternal complications are uncommon and are confined primarily to women with specific risk factors.[273,274] The autosomal inheritance pattern gives the fetus a 50% chance of having the condition, although there can be variable phenotypic expression.

Management Options

Prepregnancy

Genetic counseling is indicated if either parent is affected. A careful history should be taken to identify patients with historical risk factors. An echocardiogram should be done. Patients should also be seen by a cardiologist who has experience with patients having this condition to

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determine the need for exercise testing and the role of Holter monitoring. High-risk patients may be evaluated for septal myectomy.

Prenatal

Activity is limited to avoid tachycardia. Adequate hydration should be maintained. The CARPREG II study found that cardiac arrhythmias were more likely to occur in the second trimester and heart failure more commonly presented in the third trimester or postpartum.[32] Although it is not necessary in all patients, beta-blockade may be used in symptomatic patients, to decrease the risk of arrhythmias, increase left ventricular diastolic filling time, and reduce LVOT obstruction.[267]

Labor and Delivery and Postnatal

Volume status is monitored to avoid dehydration and hypotension during labor. Regional anesthesia may be used, but should be administered with care after adequate volume loading, again to prevent hypotension. If tachycardia develops and the patient becomes symptomatic, beta-blocking agents may be used to control the heart rate. The patient should be observed for excessive blood loss and tachycardia in the postpartum period. Volume replacement is given as indicated.

Summary

Serious cardiac disease is uncommon in pregnancy, however it can be associated with significant maternal and fetal morbidity including death. Diagnosis and management are complicated by dramatic physiologic changes that can exacerbate existing disease and symptoms that are common in normal pregnancy. With a multidisciplinary approach to care and close follow-up, a good outcome can be expected in most cases.

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High-Risk Pregnancy: Management Options

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