20 Cardiac diseases in pregnancy

Saravanan Kuppuswamy and Sudarshan Balla

INTRODUCTION

Major hemodynamic alterations in the cardiovascular system occur during normal pregnancy, labor, and delivery. With advances in surgical techniques and improved diagnostic and therapeutic alternatives, greater numbers of women with congenital and acquired heart disease are surviving to the childbearing years. Therefore, management of the pregnant patient, especially those with underlying cardiovascular disease, requires a thorough understanding of both the normal cardiovascular adjustments to pregnancy and the predicted response of the abnormal cardiovascular system to the hemodynamic stresses of pregnancy.

NORMAL CARDIOPULMONARY ADJUSTMENTS DURING PREGNANCY

Symptoms and Signs

Table 1 summarizes the cardiovascular symptoms and signs in normal pregnancy and findings that need further investigations.

Cardiovascular Hemodynamics in Pregnancy

Table 1 Normal and Pathologic Findings in Pregnancy

Normal findings seen in pregnancy

Fatigue, dyspnea, and decreased exercise tolerance

Peripheral edema

Apical impulse will be laterally displaced

First heart sound (S1) will have an increased amplitude and a wide splitting of the two components (mitral and tricuspid) due to early closure of the mitral valve

The second heart sound (S2) is little affected

Majority of patients (84%) will develop a third heart sound (S3)

Continuous murmurs due to cervical venous hum and mammary soufflé

Pathologic findings warranting evaluation (1)

Paroxysmal nocturnal dyspnea

Hemoptysis

Diastolic murmurs

Continuous murmurs

Loud systolic murmurs (louder than grade 2 on the six-point scale)

Pansystolic murmurs

Murmurs associated with symptoms or an abnormal electrocardiogram

Table 2 Cardiovascular Changes in Pregnancy

Parameter	Modification	Magnitude	Peak
Oxygen consumption (VO ₂)	Increases	+20% +40–60%	Term
Oxygen delivery (DO ₂)	↔ ↑	700–1400 mL/min	Term
Plasma volume	↑ ↑	+45–50% ^a	32 weeks
Red blood cell volume	↑	+25–32%	30–32 weeks
Total body water	↑	+6–8 L	Term
Systemic vascular resistance	↓	–20%	16–24 weeks
Pulmonary vascular resistance	↓	–34%	34 weeks
Blood pressure			
Systolic	↓	–9% ^b	28 weeks
Diastolic	↓	(slightly more on diastolic)	
Heart rate	↑	+20–30%	Term ^c
Contractility (SV)	↑	+11–32%	Term
Cardiac output	↑	+30–50%	Term ^c
Uteroplacental circulation	↑	+>1000%	Term

^aCorrelates positively with the number of fetuses. ^bPosition dependent; lower for systolic and diastolic in left lateral decubitus. ^cIf measured in left lateral decubitus; otherwise peaks between 28 and 32 weeks. Abbreviation: SV, stroke volume. Source: From Ref. 2.

Alterations During Normal Labor and Delivery

Numerous cardiovascular changes take place during labor and delivery, and these changes are affected by a wide range of variables including anesthesia, analgesia, pain sensation, and mode of delivery.

During labor, transient increases in cardiac output occur with each uterine contraction, as well as increases in blood pressure, both systolic and diastolic. These changes are attenuated by anesthesia, with the minimum alterations occurring with spinal or epidural anesthesia, and with the greatest alterations seen during balanced general anesthesia.

Changes in blood volume during delivery are primarily a function of blood loss, with greater loss occurring after cesarean section rather than vaginal delivery. After delivery of the fetus, preload may increase dramatically due to the decompression of the vena cava and the return of uterine blood into the systemic circulation.

The point at which cardiac changes regress to preconception levels is debatable; normal levels have been reported from 5 to over 12 weeks postpartum (3,4).

PRECONCEPTIONAL CARE

The woman with heart disease should be considered a high-risk patient even before she becomes pregnant (5). Thorough planning, beginning even before conception, is the key for a successful pregnancy. Ideally, the timing of pregnancy should be a decision that the woman should decide after a detailed discussion with her obstetrician and the cardiologist. The following are the key points to be discussed before conception:

1. The natural history of the patient's disease. Pregnancy may be postponed for the medical treatment of a condition, for example, remission in the case of lupus or acute phase of myocarditis or for the surgical repair of structural abnormalities, such as valvular disease or shunts (2).
2. The expected outcomes of pregnancy in terms of maternal and perinatal morbidity and possible mortality of these conditions (6,7). Table 3 summarizes the maternal risk in commonly encountered heart diseases in pregnancy and can serve as a guide for counseling.
3. The frequency of office visits, multiple specialty consultations, medications, and peripartum management should also be discussed. This discussion prepares the patient or the couple for economic and other social issues (10).
4. The risk for transmitting the cardiac condition or syndrome to offspring (11–13). Accurate estimates of the risk for cardiovascular defects in the offspring of affected parents are difficult to obtain. Frequently, the risk is quoted as approximately 5%, which is six times higher than the risk in the general population (14). More recent studies have observed risks in the range of 13% to 16% (Table 4) (12,15,16).

Preconceptional Risk Stratification

Risk stratification is based on three main factors: (i) the cardiac lesion, (ii) the baseline functional compromise, and (iii) the possibility and probability of complications during gestation based on the published literature. The spectrum of risk ranges from small to prohibitive. Table 5 summarizes some of the conditions that are indications for strong consideration of termination of pregnancy, and patients with these conditions should be strongly advised against pregnancy.

A thorough discussion and informed decision before conception minimize the need for a difficult decision like termination of pregnancy. After conception, the decision to terminate or continue the pregnancy is that of the woman. For some of these patients, there may be only one chance for a

successful pregnancy (19). The team should provide the patient with the best information possible and to continue to assist her regardless of her decision (20).

PRENATAL CARE

Management of the pregnant woman with heart disease should be coordinated by an obstetrician experienced in high-risk cases, with a multidisciplinary team of cardiology and anesthesia (21).

Most patients with cardiac disease are aware of their cardiac condition, but in some, cardiac disease is suspected and confirmed subsequently (22). Between 16% and 25% of the patients referred for the suspicion of cardiac disease have significant structural heart disease (23). The reasons for referrals are for the evaluation of murmurs (43%), arrhythmias (35%), and congenital (15.6%) and acquired heart disease (7%) (23,24). A previous successful obstetric outcome does not exclude a significant cardiac pathology, for example, rheumatic heart disease may not manifest until second or third pregnancy (25). In addition, patients with already diagnosed heart disease may have acquired new lesions that may complicate their usual symptomatology (Table 6) (26).

A targeted ultrasound to evaluate for fetal congenital anomalies (the fetal heart and major vessels) should be scheduled between 16 and 20 weeks of gestation in women with defined clinical syndromes at risk for complications and in women with a history of congenital heart disease (16,27).

Prenatal Risk Stratification

Assessing the risk of maternal and fetal mortality and morbidity is a continuous process throughout the pregnancy. A clinically relevant tool to assess the risk would be to use Cardiac Disease in Pregnancy (CARPREG) risk index. A retrospective study examined the risks and predictors of pregnancy-related cardiac complications in women with heart disease (28). The findings were then validated by the CARPREG investigators in a prospective study (29).

Four predictors of cardiac events were identified as follows:

- Poor functional class [New York Heart Association (NYHA) class III or IV] or cyanosis
- Previous cardiac event (e.g., heart failure (HF), transient ischemic attack, stroke) or arrhythmia
- Left heart obstruction (mitral valve area of $<2\text{ cm}^2$, aortic valve area of $<1.5\text{ cm}^2$, peak left ventricular outflow gradient $>30\text{ mmHg}$)
- Left ventricular systolic dysfunction (ejection fraction $<40\%$)

The presence of none, one, or more than one risk factor was associated with 3%, 30%, and 66% rates of cardiac events (pulmonary edema, arrhythmia requiring treatment, stroke, cardiac arrest, or death) during gestation, respectively. In the presence of one or more risk factors, the score was 91% sensitive and 61% specific for the occurrence of cardiac events (28).

GENERAL PRINCIPLES FOR MANAGEMENT OF CARDIAC DISEASE DURING PREGNANCY

A multidisciplinary approach is key to a successful outcome. The frequency of assessment and the types of investigations needed depend on individual conditions. High-risk pregnancies

Table 3 Maternal Mortality Risk Groups of Cardiac Disease Associated with Pregnancy

Risk group	Conditions	Mortality
Low	Atrial septal defect Ventricular septal defect (uncomplicated) Patent ductus arteriosus (uncomplicated) Pulmonic/tricuspid disease Corrected tetralogy of Fallot Bioprosthetic valve Asymptomatic AS with low mean gradient (less than 25mmHg and valve area greater than 1.5cm ²) in presence of normal LV systolic function (EF greater than 0.50) NYHA functional class I or II AR with normal LV systolic function NYHA functional class I or II MR with normal LV systolic function MVP with no MR or with mild to moderate MR with normal LV systolic function Mild MS (MVA greater than 1.5cm ² , gradient less than 5mmHg) without severe pulmonary hypertension	<1%
Moderate	Mild to moderate pulmonary valve stenosis Mitral stenosis with atrial fibrillation Artificial valve Coarctation of the aorta (uncomplicated) Uncorrected tetralogy of Fallot Previous myocardial infarction	5–15%
High	Mitral stenosis, NYHA II, III, and IV Severe aortic stenosis with or without symptoms AR with NYHA functional class III–IV symptoms MR with NYHA functional class III–IV symptoms Aortic and/or mitral valve disease with severe LV dysfunction (EF less than 0.40) Marfan syndrome with normal aorta Pulmonary hypertension Coarctation of the aorta Marfan syndrome with aortic involvement	25–50%

Abbreviations: NYHA, New York Heart Association; AR, aortic regurgitation; MR, mitral regurgitation; EF, ejection fraction; LV, left ventricular; AS, aortic stenosis; MS, mitral stenosis. *Source:* From Ref. 8,9 ACC guideline document does not have moderate risk category.

should be managed in a tertiary care center, where immediate access to specialists is readily available. The following pages summarize the management of the different conditions.

SPECIFIC CARDIOVASCULAR ABNORMALITIES OF LOW RISK TO THE PREGNANT PATIENT (FIG 1)

Atrial Septal Defect

Ostium secundum atrial septal defect (ASD) is the most common congenital cardiovascular defect seen in pregnancy. Most women are asymptomatic and pregnancy is usually well tolerated in the pregnant patient with an ASD.

Numerous reports suggest that pregnancy is safe (30), although there are reports of the development of congestive HF and arrhythmias in these patients (31). If circumstances allow, ASDs should be closed before pregnancy. For a secundum defect, catheter device closure can be performed during pregnancy if necessary (with transesophageal or intracardiac echocardiographic guidance). In most instances, in pregnant women diagnosed with an ASD during pregnancy, closure can be deferred for 6 months after delivery (32).

A small proportion of patients with an ASD may develop Eisenmenger syndrome and should be considered as high-risk pregnancy. The management of high-risk patients is discussed below.

Ventricular Septal Defect

Women who reach childbearing years with an uncorrected ventricular septal defect (VSD) generally have smaller defects

that are well tolerated, since the clinical picture is largely determined by the size of the defect; larger defects often require repair in childhood. Physical exam is characterized by a harsh holosystolic murmur.

Pregnancy is usually very well tolerated in women with a VSD (33). Morbidity and mortality is related to the presence of pulmonary hypertension, with a higher complication rate in those patients with Eisenmenger's physiology (31). Management of Eisenmenger syndrome is discussed below.

Patent Ductus Arteriosus

With improved pediatric surgical techniques, most patients with a patent ductus arteriosus (PDA) are surgically corrected during infancy and childhood, so it is a rare finding in pregnancy. Many patients are asymptomatic unless there is associated pulmonary hypertension. The physical examination is characterized by a "machinery" or continuous murmur in the second intercostal space. As with other shunt lesions, echocardiography is useful in defining chamber dimensions and shunt detection.

The patient with a PDA generally tolerates pregnancy well, whether surgically corrected (34) or uncorrected (30,31), but the presence of pulmonary hypertension increases the morbidity and mortality.

Mitral Regurgitation

The causes of mitral regurgitation (MR) are myriad, but in young women of childbearing age, the most common

Table 4 Maternal and Fetal Outcomes in Cardiac Lesions

Maternal lesion	Number of pregnancies	Number of abortions	Maternal mortality (%)	Maternal cardiovascular complications (%)	Live births (%)
Mitral stenosis	408	0	1.5	16	—
	339 ^a	0	0.3 (0–0.5)	—	—
Aortic stenosis	38 ^b	9	11	—	68
	59	0	3.4 (0–5.3)	—	
Severe aortic stenosis	16	0	6.3	69	94
Hypertrophic cardiomyopathy	67 ^b	11	1.5	27	98
	54	11	0	22	100
Ebstein anomaly	153	30	0	1.3	98
Aortic coarctation (unrepaired)	32	18	0	50	93
Aortic coarctation (repaired)	21	2	0	4.8	100
Fallot (corrected)	62	14	0	8.1	100
TGA (Mustard)	15	2	0	0	92
TGA (Fontan)	33	18	0	6.1	100
Marfan syndrome	74 ^b	10	22	5.4	86
	105	23	1.0	8.6	98
Transplanted heart	30	5	0	>40	100
Pulmonary hypertension (primary and secondary excluding Eisenmenger)	25	Up to 50	30 (14–50)	20–66	75–95
	27		56 (35–76)		86–91
Eisenmenger syndrome	70	14	33	—	63
	53	35	5.7 (5.3–5.9)	—	84
Cyanotic lesions without Eisenmenger reaction	96	49	1.0	29	87
Mechanical heart valve	240	78	2.9 (2.0–4.2)	13 ^c	83
Biologic heart valve	60	9	0	3.3	94
Acute myocardial infarction	68 ^b	3	37	—	72

^aOnly deliveries. ^bIndicates “review of case reports.” ^cMainly thromboembolic complications. Abbreviation: TGA, transposition of great arteries. Source: From Ref. 7.

Table 5 Indications for Pregnancy Termination

Pulmonary arterial hypertension of any cause
Severe ventricular systolic dysfunction
NYHA III–IV symptom class or LVEF <30%
Previous peripartum cardiomyopathy with any residual impairment of left ventricular function
Severe left heart obstruction defined as mitral stenosis: mitral valve area <1.0 cm² Aortic stenosis: aortic valve area <1.0 cm² or (nonpregnant) mean gradient >50 mmHg
Marfan syndrome with aorta dilated >40 mm

Abbreviations: LVEF, left ventricular ejection fraction; NYHA, New York Heart Association. Source: From Ref. 17,18.

etiologies are rheumatic (almost always seen in association with mitral stenosis) and as a component of Barlow’s syndrome (click–murmur or mitral valve prolapse syndrome).

The characteristic finding on examination is a holosystolic murmur at the apex, which radiates to the axilla. Echocardiography provides a comprehensive assessment of the etiology and the severity of the MR. In general, pregnancy is very well tolerated. Mitral valve surgery, preferably repair for

symptomatic MR, may be indicated before conception (35). However, any associated left ventricular dysfunction is unlikely to improve after surgery (36) and will increase maternal risk during pregnancy (37). Severe MR may lead to HF during pregnancy or labor. The management of HF is discussed separately.

Aortic Insufficiency

Aortic insufficiency is seen infrequently in women of child-bearing age, and the usual etiology is rheumatic, bicuspid aortic valve, previous endocarditis, and Marfan syndrome.

Physical findings include widened pulse pressure, and a diastolic murmur (blow) heard at the upper sternal border and the diagnosis is confirmed by echo. Aortic insufficiency without HF is generally well tolerated during pregnancy, and these patients remain essentially asymptomatic. Patients with NYHA class III–IV are at increased risk.

Tricuspid and Pulmonary Valve Lesions

Tricuspid regurgitation is an extremely common finding in normal pregnancy (38) and is rarely clinically important. The

Table 6 Initial Evaluation for Known or Suspected Cardiac Disease During Pregnancy**History**

- Previous surgeries
- Previous pregnancies (symptoms, admissions, outcomes)
- Previous admissions (centers, physicians' names, medical records, evaluations)
- History of rheumatic fever or of monthly prophylactic antibiotic injections
- Drug and alcohol abuse
- Functional class assessment

Physical examination

- General appearance including specific facies and cyanosis
- Funduscopic examination
- Heart examination: rhythm, rate, precordial thrill, S1 and S2 characteristics, presence of S3 or S4, presence of murmurs and characteristics
- Evaluation of pulses in all extremities
- Presence and grading of edema

Cardiac diagnostics

- 12-lead electrocardiogram
- Holter evaluation
- Chest radiograph
- Echocardiogram

Source: From Ref. 2.

exception is tricuspid regurgitation seen in association with Ebstein's anomaly, which increases the morbidity of pregnancy. Tricuspid stenosis and pulmonary insufficiency are uncommon findings in pregnancy, and there are few published data on the outcome of pregnancy in these patients.

Pulmonary stenosis (PS) represents a common congenital cardiac defect and is seen both alone and as part of the syndrome of tetralogy of Fallot. Isolated PS is usually detected in childhood; both surgical and nonsurgical (with balloon valvuloplasty) repairs are often curative. Patients with all but the severest forms of PS often tolerate pregnancy well (31,39,40). The incidence of inherited cardiac defects in the offspring of these patients appears to be high (41). Balloon valvuloplasty is recommended before conception if the gradient across the right ventricular outflow track is >50 mmHg at rest (42) or if the patient is symptomatic. The procedure is rarely indicated during pregnancy in patients who are either asymptomatic or mildly symptomatic before pregnancy. Vaginal delivery is tolerated well and can be permitted in the great majority of patients with PS.

Mitral Valve Prolapse

Mitral valve prolapse (MVP) is a common cardiac condition, seen in up to 2.4 % of the general population (43).

Figure 1 Anatomic locations of left-to-right shunts.

Although the majority of patients with mitral valve prolapse are asymptomatic, some patients may experience palpitations, fatigue, and chest pain. On physical examination, mid-systolic ejection click and a murmur of MR may be heard. Management of MVP is similar to patients with MR. Infective endocarditis prophylaxis is no longer recommended (44) (see section on antibiotic prophylaxis below).

SPECIFIC CARDIOVASCULAR ABNORMALITIES OF MODERATE RISK TO THE PREGNANT PATIENT (FIG. 2) Mitral Stenosis

A common etiology for mitral stenosis in a woman of childbearing years is rheumatic heart disease, and mitral stenosis represents the most common rheumatic valvular lesion. Physiologic changes in pregnancy and atrial fibrillation can result in pulmonary edema.

These patients may have symptoms of fatigue and dyspnea. Physical examination may reveal evidence of pulmonary congestion and a diastolic murmur at the apex associated with an opening snap. Echo can assess the severity, suggest etiology, and guide in the management of mitral stenosis.

It is not uncommon for women with occult mitral stenosis to become symptomatic during pregnancy, usually by mid-pregnancy, when the pregnancy-induced hemodynamic changes are at the maximum. The risk of pulmonary edema exists from this period until several days after delivery.

Predictors of adverse maternal outcomes in these patients include a reduced mitral valve area (less than 1.5 cm^2) and the NYHA functional class before pregnancy (45). Mortality among pregnant women with minimal symptoms is less than 1% (15). Severe mitral stenosis with NYHA class III–IV symptoms has a 4% to 5% maternal mortality and 30% fetal mortality (46). The mortality is even higher if atrial fibrillation is present (47). Improved diagnostic techniques,

better prenatal management, and effective cardiac drugs have improved the outcome of these patients. Development of atrial fibrillation requires prompt treatment, including cardioversion. Beta blockers and digoxin can be safely used for rate control. Antiarrhythmic drugs preferred are beta blockers (sotalol, atenolol) or flecainide. Procainamide is another safe alternative, while mexiletine and amiodarone have also been used with success in small numbers of patients in the acute setting with success (48). Anticoagulant therapy is indicated in patients with mitral stenosis and atrial fibrillation to decrease the risk of systemic embolism (49,50). Anticoagulation in pregnancy is discussed separately. In patients who present with severe symptoms during pregnancy, successful percutaneous balloon mitral valvuloplasty, performed during the second trimester, has been associated with normal subsequent deliveries and excellent fetal outcomes (51). The maternal and perinatal benefits of the procedure probably outweigh the small risk of fetal exposure to the radiation. Open cardiac surgery has been performed during pregnancy for severe mitral stenosis. Maternal outcomes are approximately the same as those among nonpregnant, but there is fetal loss in 10% to 30% of cases (52). See also Figure 3.

Aortic Stenosis

Aortic stenosis is not a commonly seen valvular abnormality in pregnancy, because it is usually prevalent in an older population. However, patients with aortic stenosis who have a bicuspid aortic valve may become symptomatic in their twenties and thirties. Patients may present with symptoms of angina, syncope, and HF. The physical examination reveals a crescendo-decrescendo systolic murmur at the upper sternal border, and in severe cases, a single or absent second heart

Black arrows indicate abnormal direction of flow

Figure 2 Normal and diseased aortic and mitral valve states.

sound may be present. EKG may show left ventricular hypertrophy. Echo assesses the severity of stenosis and left ventricular (LV) systolic function.

Pregnancy can usually be successfully carried to term in all but the most severe cases of aortic stenosis; reported maternal mortality in severe aortic stenosis is 17% (53). A more recent review of 12 studies demonstrated an average maternal mortality of 6.6% and an average perinatal mortality of 4% (54). The fetal risks of congenital heart diseases range from 17% to 26% (12,55). Complications arise when the already low forward output is compromised further by reduced preload from either hypovolemia or peripheral vasodilatation.

Patients who are symptomatic or who have a peak outflow gradient of more than 50mmHg are advised to delay conception until after surgical correction (56). Termination of pregnancy should be strongly considered if the patient is symptomatic before the end of the first trimester. Aortic valve replacement and palliative aortic balloon valvuloplasty have been performed during pregnancy with some associated maternal and fetal risk (52,57–59).

Coarctation of the Aorta, Uncomplicated

Coarctation of the aorta is a stenosis of the aorta, usually located just distal to the left subclavian artery at the ligamentum arteriosum (fetal ductus arteriosus). The lesion may be associated PDA, congenital bicuspid aortic valve, and aneurysms of the circle of Willis.

The hallmark of coarctation is an asymmetry of upper and lower limb blood pressures with a markedly decreased pressure in the lower extremities. Patients who have had coarctation of the aorta corrected prior to pregnancy and no other associated anomalies usually tolerate the pregnancy well. These patients, however, are still at a higher risk for cardiovascular compromise compared with nonpregnant patients.

Complications associated with uncorrected coarctation of the aorta include hypertension, HF, and aortic dissection. The mainstay of therapy is control of hypertension and avoidance of hypovolemia during the peripartum period. In cases of

aortic dissection or severe HF unresponsive to medical therapy, surgical repair has been successfully attempted during pregnancy (60,61). Fetal morbidity and mortality are high because of decreased placental blood flow from hypertension or reduced cardiac output and increased incidence of fetal cardiac anomalies (34).

Marfan Syndrome, Normal Aortic Root

Marfan syndrome is an autosomal dominant condition with defective collagen synthesis affecting the ocular, skeletal, and cardiovascular abnormalities with variable severity. The cardiovascular manifestations include mitral valve prolapse with MR and aneurysmal dilatation of the proximal aorta; the latter may be occasionally associated with aortic regurgitation and dissection.

Pregnancy seems to increase the risk of aortic rupture in patients with Marfan syndrome. The maternal morbidity and mortality depends on whether there are aortic root dilatation or valvular abnormalities (62,63). Maternal mortality from aortic rupture or dissection may be up to 50% when the aortic root diameter is greater than 40mm (63). On the other hand, pregnancy in patients who have aortic root diameter less than 40mm and no valvular involvements can be successfully carried to term with minimal maternal mortality or morbidity. Patients should be advised of the risk and should be closely followed for signs and symptoms of aortic dissection. Serial echocardiograms during pregnancy are recommended to assess the size of the aortic root and the presence of valvular regurgitation. In selected patients, beta beta blockers may lower the risk of progressive aortic dilatation (64,65).

Prior History of Myocardial Infarction

Coronary artery disease is rare in women of childbearing years, and there are only a few reports of pregnancies in women who have sustained myocardial infarctions prior to pregnancy. The pregnancy outcome of these patients is related to left ventricular function. Myocardial infarction during pregnancy poses a much higher risk (see section below).

SPECIFIC CARDIOVASCULAR ABNORMALITIES OF HIGH RISK TO THE PREGNANT PATIENT

Considering the high morbidity and mortality of pregnancy in patients with lesions in this category, counseling should be directed toward the avoidance of pregnancy. If pregnancy occurs, elective termination during the first trimester may be offered. If the pregnancy has to be continued, it is imperative that the patient is followed up closely in a tertiary care center with a multidisciplinary team including obstetrician, cardiologist, anesthesiologist, and neonatologist with experience in high-risk pregnancies (66–68). Frequent visits are recommended, and hospitalization during the third trimester may facilitate management. Detailed plans including timing and mode of delivery should be discussed with the patient in advance (66). Maternal safety needs to be weighed against the risk of premature delivery, intrauterine growth retardation, and the need for neonatal care, when decisions about timing and type of delivery are made.

These conditions are associated with a very high maternal mortality (23–50%), which may occur during the pregnancy or the postpartum period (33,69). The patient should be

Figure 3 Relation between severity of multiple sclerosis (MS) and frequency of adverse maternal cardiac, fetal, or neonatal events. Any event refers to cardiac, fetal, or neonatal events. White bars indicate pregnancies in women who have mild MS; gray bars indicate pregnancies in women who have moderate MS, and black bars indicate pregnancies in women who have severe MS. Source: From Ref. 138.

informed about the risk and offered the option of termination of pregnancy.

If the patient continues the pregnancy, careful monitoring of arterial oxygen saturation, cardiac rhythm, and blood pressure is recommended in the peripartum period. The management also includes oxygen supplementation to prevent fetal hypoxemia, invasive hemodynamic monitoring in select cases, and shortening of the second stage of labor with low or outlet forceps delivery. Hospitalization is necessary. Since the incidence of intrauterine growth retardation and fetal death is high (69), close fetal monitoring with serial ultrasound examinations and nonstress tests and/or biophysical profiles is recommended.

Eisenmenger's Syndrome

In patients with left-to-right shunts (e.g., PDA, VSD, ASD), worsening pulmonary hypertension, approaching systemic levels, results in a reversal of shunting (Eisenmenger physiology) and causes hypoxemia and death. These patients may present with peripheral cyanosis, HF, and hemoptysis.

General principles of management are discussed above. Other measures include maintaining maternal PaO₂ above 70% to ensure adequate fetal oxygenation (70). There is no standard thromboprophylaxis for pregnant women with Eisenmenger (71). However, anticoagulation is needed if patient has documented pulmonary artery thrombosis.

The peripartum period is a precarious time, owing to a rapid shift in blood volume and chance of hemorrhage. Measures should be taken to avoid a reduction in preload such as hypotension or hemorrhage, since severe hypoxemia and death may ensue from decreased cardiac output. The patients should be closely monitored in the hospital setting for at least several days after delivery, since the significantly increased risk of maternal mortality still persists during this period.

Idiopathic Pulmonary Artery Hypertension

Idiopathic pulmonary artery hypertension (IPAH) is a disease of unknown etiology, primarily seen in young women and results in a progressive increase in pulmonary artery pressures. Presenting symptoms include dyspnea, fatigue, palpitations, and occasional syncope.

Right ventricular failure (elevation of jugular venous pressure, hepatomegaly, and peripheral edema) may be present.

Echocardiography remains the key diagnostic test in pulmonary hypertension, and a right heart catheterization may be needed to confirm the diagnosis of pulmonary arterial hypertension and, if needed, for the assessment of response to therapy. Right heart catheterization can be done without exposure to any radiation.

Pregnancy is poorly tolerated in patients with IPAH, with maternal mortality in excess of 40% (72). This excess mortality appears to be present even in patients who were asymptomatic or only mildly symptomatic prior to becoming pregnant. In addition, there appears to be a high incidence of fetal and neonatal death associated with maternal IPAH. Patients with IPAH often come to clinical attention during the second trimester, when the hemodynamic changes of pregnancy are maximum and the presenting symptoms are often those of right ventricular failure.

General principles of management are discussed above. Over the past decade, advanced therapies (prostacyclin analogs, phosphodiesterase inhibitors, and endothelin-receptor antagonists) have revolutionized PAH management considered before patients decompensate or thrombotic complications ensue. The effect of advanced therapies in pregnancy with PAH is unknown.

Bosentan may have teratogenic effects (73) and is, thus, contraindicated during pregnancy; limited data on sildenafil suggest no deleterious effects on the mother or offspring (74). Calcium channel blockers are safe during pregnancy (75) and may prevent preterm labor (76), a common complication in patients with PAH. However, calcium channel blockers may be beneficial only in responders to vasoreactivity tests, and only 6.8% are reported to have a long-term benefit (77).

Inhaled nitric oxide (NO) has been shown to decrease the pulmonary vascular resistance in IPAH, in Eisenmenger syndrome, and in chronic pulmonary thromboembolic disease. The effect of NO during pregnancy or labor on outcomes remains uncertain (78).

Low-dose subcutaneous heparin prophylaxis is generally recommended in pregnant women with PAH, but some patients may require higher levels of anticoagulation (e.g., patients with a history of thromboembolic events or atrial fibrillation) (68).

The optimal mode of delivery (vaginal vs. caesarean section) in patients with PAH remains a matter of debate (29). Invasive pulmonary arterial pressure monitoring remains controversial and the lack of evidence that it improves outcomes in these patients (79).

Complex Cyanotic Congenital Heart Disease

Many children with complex cyanotic congenital heart disease die during infancy and childhood, and do not reach child-bearing age, but with greatly improved surgical techniques, a larger number of these patients are surviving into adulthood. Specific congenital lesions of interest include (i) tetralogy of Fallot (PS, VSD, overriding aorta, and right ventricular hypertrophy); (ii) Ebstein's anomaly (displacement of the tricuspid valve into the right ventricular cavity, resulting in a small right ventricle and poor forward output, often associated with right-to-left shunting through an ASD); (iii) truncus arteriosus (single outflow tract and outflow valve distal to both ventricles, often associated with a VSD); (iv) transposition of the great vessels (separate pulmonary and systemic circulations operating in parallel with communication via a VSD; and (v) tricuspid atresia (absent tricuspid orifice, small non-functional right ventricle, and a connection between the pulmonary and systemic circulations). These lesions represent many of the important cyanotic congenital heart lesions, and individual lesions may be variable in severity.

In general, patients with uncorrected cyanotic congenital heart defects do not survive long enough to become pregnant; those who do survive should be counseled against pregnancy. Despite the high morbidity and mortality of pregnancy in these patients, there are case reports of successful completion of pregnancy in patients with these congenital lesions (72). If the cardiac abnormality has been surgically corrected, maternal morbidity and mortality during pregnancy appears to be related to residual cardiac defects, with a marked improvement

in prognosis for those who have undergone successful complete correction. Infective endocarditis prophylaxis is discussed below.

Marfan Syndrome Associated with an Abnormal Aortic Root

Marfan syndrome, discussed earlier in this chapter, markedly increases maternal and fetal mortality if there is evidence of a dilated aortic root, valvular regurgitation, or dissection. Transesophageal echocardiography is superior to transthoracic echocardiography in diagnosing aortic root dilatation and aortic dissection. Preventive replacement of the ascending aorta with a graft has been recommended in patients with the aortic root diameter of at least 60mm prior to pregnancy (80). Patients who contemplate pregnancy may consider preventive replacement of the ascending aorta when the aortic root dilatation is progressive and approaching 55mm in diameter (64). If pregnancy occurs in patients with significant aortic root dilatation, therapeutic termination during the first trimester may be offered. If the patient chooses to continue the pregnancy, careful assessment of the patient throughout pregnancy should include evaluation for aortic dissection and use of beta blockers during pregnancy to reduce the incidence of dissection. The patient should be encouraged to avoid strenuous physical activity. Urgent delivery and vascular repair should be undertaken if clinical evidence of dissection occurs, regardless of the viability of the fetus.

Myocardial Infarction During Pregnancy

The epidemiology of coronary artery disease is such that myocardial infarction is extremely rare in women of childbearing years, estimated to occur in 1 in 10,000 pregnancies (81). Risk factors for coronary heart disease in pregnant women are the same as those for the general population and include cigarette smoking, hyperlipidemia, diabetes mellitus, and hypertension. The causes of occlusion or stenosis of the coronary arteries include thrombus and atherosclerosis; uncommon etiology includes dissection and vasospasm (82–86).

In ST elevation myocardial infarction (STEMI) in the general population, primary PCI (percutaneous coronary intervention) is the recommended therapy, if the infarct-related artery can be opened within 90 minutes of presentation (commonly referred to as door to balloon time). Treatment with thrombolytics is relatively contraindicated in pregnancy (87).

In selected group of pregnant patients with myocardial infarction, including patient with STEMI and high-risk non-ST elevation myocardial infarction (NSTEMI), PCI may be the therapy of choice during pregnancy. However, before completion of major organogenesis (before 15 weeks after menses), radiation exposure must, whenever possible, be avoided.

Cardiac catheterization offers the advantage of diagnosing and treating, in addition to thromboembolic disease, other causes such as coronary artery dissection.

All reported stenting during the acute phase of MI during pregnancy were performed with bare metal stents. The safety of drug-eluting stents in pregnant woman is therefore still unknown. Because drug-eluting stents require prolonged antiplatelet therapy with aspirin and thienopyridine, and the incidence of cesarean section deliveries in patients with heart

disease is relatively high, the use of drug-eluting stent during pregnancy should be avoided if possible. Although animal experiments do not demonstrate teratogenic effect, there are no studies in pregnant women and should be used in pregnancy only if clearly needed.

Successful vaginal deliveries without further myocardial injury have been reported (82,84–86). Therefore, myocardial infarction is not a contraindication for a vaginal delivery.

HEART FAILURE (HF) SYNDROMES

Peripartum Cardiomyopathy

This entity involves the development of HF during the last month of pregnancy or in the first five postpartum months, without obvious etiology. In the United States, the incidences vary from 1 in 4000 deliveries to 1 in 1500 deliveries, peak during the second postpartum month and increase among older, multiparous black females. The overall maternal mortality ranges from 25% to 50% (88,89).

Although the etiology of peripartum cardiomyopathy is not known, various factors have been suggested to play a role in its development, including hypertension (90), viral illness (91), an immunologic reaction (92), and vitamin deficiency (93).

Presenting clinical symptoms include those of left-sided HF (orthopnea, dyspnea, weakness) as well as peripheral edema, palpitations, and occasionally hemoptysis. On physical examination, these patients may have pulmonary rales, cardiomegaly, a gallop rhythm, distended neck veins, and peripheral edema. Cardiomegaly and pulmonary venous congestion are typical chest X-ray findings.

The diagnosis of PPCM has been based upon four clinical criteria (94–96):

- Development of cardiac failure in the last month of pregnancy or within 5 months of delivery.
- Absence of an identifiable cause for the cardiac failures (see “Causes of dilated cardiomyopathy”).
- Absence of recognizable heart disease prior to the last month of pregnancy.
- LV systolic dysfunction (e.g., LVEF<45% or a reduced shortening fraction).

Echocardiography is helpful in ruling out a valvular or pericardial etiology for the clinical presentation, assessing cardiac chamber size and overall left ventricular function.

Treatment is directed toward managing HF, which is discussed below. These patients are at risk for thromboembolic disease, so prophylactic anticoagulation with heparin should be considered. If HF is refractory to medical management, early delivery should be considered.

The prognosis appears to be related to the course following pregnancy. Patients who have persistent cardiomegaly have a poor prognosis (97), whereas a return to normal heart size within 6–12 months postpartum predicts a more favorable outcome (94). Women with persistent LV dysfunction should be advised to avoid pregnancy due to the risk of HF progression and death (98). Successful subsequent pregnancies have been reported in patients who have a return to normal heart size (99,100). For patients who have a refractory downhill course following the diagnosis of peripartum cardiomyopathy, cardiac transplantation should be considered. Case reports of successful completion of pregnancy following

cardiac transplantation have been published (101–105). Patients in whom left ventricular dysfunction develops as a result of peripartum cardiomyopathy require echocardiographic follow-up of ventricular function. Improvement in systolic function beyond that assessed at 6 months after delivery is uncommon.

Heart Failure

The etiology of the HF could be ischemic or non-ischemic. Ischemia is an uncommon etiology in this population. Non-ischemic causes include peripartum cardiomyopathy, viral illness, and valvular heart disease among the many. Presenting symptoms include fatigue, dyspnea, orthopnea, and pedal edema. Prognosis depends on the etiology for congestive HF (Table 7).

In patients with stable HF, initial evaluation includes careful history and physical examination, assessment of NYHA functional class, and echocardiogram. In addition, medication adjustments and serial echocardiography during each trimester is recommended. The goals of therapy include relief of symptoms and continuation of the chronic therapy if possible, and treat precipitating causes such as anemia, arrhythmia, and thyroid disorders.

Angiotensin-converting enzyme inhibitors (ACEI), and angiotensin receptor blockers (ARB), and aldosterone antagonists like spironolactone are contraindicated throughout pregnancy. Due to the risks of embryopathy associated with ACE inhibitor use in the first trimester, ACEI should be discontinued when the woman with chronic stable HF is attempting conception. Beta blockers are generally safe and effective during pregnancy, although some adverse effects have been reported (106).

In patients with moderate symptoms of HF, in addition to sodium restriction, diuretics such as furosemide and afterload-reducing agents like hydralazine should be considered. Digitalis is safe during pregnancy and may be used to maximize contractility and control heart rate, but improved survival rates have not been shown.

In decompensated HF, positive inotropes like dobutamine and dopamine and, in select patients, intravenous nitroglycerin may be needed.

Table 7 New York Heart Association Classification of Heart Failure	
NYHA class	Symptoms
I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea (shortness of breath)
II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea
III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea
IV	Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy has an autosomal dominant inheritance pattern with a widely variable penetrance, but sporadic cases occur as well.

The clinical presentation is characterized by dyspnea, chest pain, angina, dizziness, and syncope, although many patients may remain asymptomatic. Occasionally, sudden death is the presenting symptom. In patients with outflow obstruction, a loud systolic murmur and thrill can be detected along the left sternal border. Maneuvers that increase venous return or chamber size (handgrip, squatting) decrease the intensity of the murmur and Valsalva maneuver increases the intensity of the murmur.

The echocardiogram provides comprehensive assessment of the thickness of the left ventricular wall, dynamic outflow tract obstruction with different maneuvers, and valvular regurgitation.

In a study of 82 pregnancies, Kumar and Elkayam (107) concluded that the outcome of pregnancy is generally favorable, although worsening of symptoms may occur.

In asymptomatic patients, management involves avoiding situations that increase the outflow tract obstruction such as hypovolemia, vasodilatation, and medications like digoxin, inotropes, and diuretics (Table 8). For symptomatic pregnant patients, treatment should be aimed at alleviating symptoms with beta blockers or non-dihydropyridine calcium channel blockers. Arrhythmias, both atrial and ventricular, occur frequently in patients with hypertrophic cardiomyopathy. General measures during labor and delivery in these patients include laboring in the left lateral decubitus position to maximize venous return to the heart, avoidance of hypovolemia, and a shortened second stage of labor. Prostaglandins, such as PGE₂ (because of their vasodilatory effect), and beta-adrenergic stimulants should be avoided in these patients.

OTHER CONDITIONS WITH VARIABLE RISKS:

ARRHYTHMIAS

Tachyarrhythmias

Cardiac arrhythmias may be classified as supraventricular or ventricular and may occur during pregnancy either spontaneously or related to preexisting heart disease. Sinus tachycardia is a frequent occurrence during pregnancy, as are premature atrial and ventricular contractions. The hormonal and hemodynamic changes of pregnancy may predispose women, even those with normal cardiovascular systems, to frequent ectopic beats. Although the essentials of treatment of the arrhythmias in pregnant women are similar to those for nonpregnant women, the treatment has to be individualized depending on the stage of pregnancy and the risk–benefit ratio of exposing the fetus to the drugs. The principle is to avoid maternal hypotension and fetal hypoperfusion.

Atrial fibrillation in pregnancy is usually seen in the setting of rheumatic mitral stenosis. Two important considerations in pregnancy are the following: (i) If the ventricular rate is rapid, the diastolic filling time shortens, resulting in a fall in both stroke volume and forward output. This can cause decreased placental perfusion and fetal compromise. For this reason, women who are at risk for developing atrial fibrillation during pregnancy should be maintained on prophylactic digoxin or a beta blocker to prevent the rapid ventricular response, should atrial fibrillation develop. (ii) Atrial fibrillation in mitral

Table 8 Cardiovascular Drugs in Pregnancy

Drug	Use in pregnancy	Potential side effects	Breast feeding	Risk factors
Adenosine	Maternal and fetal arrhythmias	No side effects reported; data on use during first trimester are limited	Data NA	C
Amiodarone	Maternal arrhythmias	IUGR, prematurity, congenital goiter, hypothyroidism and hyperthyroidism, transient bradycardia, and prolonged QT in the newborn	Not recommended	C
Angiotensin-converting enzyme inhibitors	Hypertension	Oligohydramnios, IUGR, prematurity, neonatal hypotension, renal failure, anemia, death, skull ossification defect, limb contractures, patent ductus arteriosus	Compatible	First trimester: C Second and third trimester: D
Aldomet	Hypertension			C
Beta blockers	Hypertension, maternal arrhythmias, myocardial ischemia, mitral stenosis, hypertrophic cardiomyopathy, hyperthyroidism, Marfan syndrome	Fetal bradycardia, low placental weight, possible IUGR, hypoglycemia, no information on carvedilol	Compatible, monitoring of infant's heart rate recommended	Acebutolol: B Labetalol: C Metoprolol: C Propranolol: C Atenolol: D
Digoxin	Maternal and fetal arrhythmias, heart failure	No evidence for unfavorable effects on the fetus	Compatible	C
Diltiazem	Myocardial ischemia, tocolysis	Limited data; increased incidence of major birth defects	Compatible	C
Disopyramide	Maternal arrhythmias	Limited data; may induce uterine contraction and premature delivery	Compatible	C
Diuretics	Hypertension, congestive heart failure	Hypovolemia leads to reduced uteroplacental perfusion, fetal hypoglycemia, thrombocytopenia, hyponatremia, hypokalemia; thiazide diuretics can inhibit labor and suppress lactation	Compatible	C
Flecainide	Maternal and fetal arrhythmias	Limited data; two cases of fetal death after successful treatment of fetal SVT reported, but relation to flecainide uncertain	Compatible	C

(Continued)

Table 8 (Continued) Cardiovascular Drugs in Pregnancy

Drug	Use in pregnancy	Potential side effects	Breast feeding	Risk factors
Heparin	Anticoagulation	None reported	Compatible	C
Hydralazine	Hypertension, hypertensive emergencies	None reported	Compatible	C
Lidocaine	Local anesthesia, maternal arrhythmias	No evidence for unfavorable fetal effects; high serum levels may cause central nervous depression at birth	Compatible	C
Mexiletine	Maternal arrhythmias	Limited data	Not recommended	C
Nifedipine	Hypertension, tocolysis	Fetal distress related to maternal hypotension reported	Compatible	C
Nitrates	Myocardial infarction and ischemia, hypertension, pulmonary edema, tocolysis	Limited data; use is generally safe, few cases of fetal heart rate deceleration and bradycardia have been reported	Data NA	C
Procainamide	Maternal and fetal arrhythmias	Limited data; no fetal side effects reported	Compatible	C
Propafenone	Fetal arrhythmias	Limited data; fetal death reported after direct intrauterine administration in fetuses with fetal hydrops	Data NA	C
Quinidine	Maternal and fetal arrhythmias	Minimal oxytocic effect, high doses may cause premature labor or abortion; transient neonatal thrombocytopenia and damage to eighth nerve reported	Compatible	C
Sodium nitroprusside	Hypertension, aortic dissection, hypertensive emergencies	Limited data; potential thiocyanate fetal toxicity, fetal mortality reported in animals	Data NA	C
Sotalol	Maternal arrhythmias, hypertension, fetal tachycardia	Limited data; two cases of fetal death and two cases of significant neurologic morbidity in newborns reported, as well as bradycardia in newborns	Compatible, monitoring of infant's heart rate recommended	B
Verapamil	Maternal and fetal arrhythmias, hypertension, tocolysis	Limited data; other than a single case of fetal death of uncertain cause, no adverse fetal or newborn effects have been reported	Compatible	C

(Continued)

Warfarin	Anticoagulation	Crosses placental barrier; fetal hemorrhage in utero, embryopathy, central nervous system abnormalities	Compatible	X
Aspirin	Antiplatelet	Increased maternal and fetal hemorrhage, increased perinatal mortality, intrauterine growth retardation, and premature closure of the ductus arteriosus. Chronic high-dose use not recommended. Low-dose use (<150 mg/day) safe	Cautious use of aspirin during lactation	High dose in third trimester: D
Thienopyridine derivatives		Very limited data	Not recommended	B
Glycoprotein IIb/IIIa inhibitors		Data NA, cesarean section should be considered as the method of delivery to avoid the risk of fetal intracranial hemorrhage	Data NA	(Risk category B: eptifibatide, tirofiban; risk category C: abciximab)
HMG-CoA reductase inhibitors (statins)		Skeletal abnormalities maternal, fetal, and neonatal mortality in animal studies. Post marketing surveillance—no adverse outcome	Not recommended	X
<p>FDA classification: Category B: Either animal reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women, or animal reproduction studies have shown an adverse effect that was not confirmed in controlled studies in women. Category C: Either studies in animals have revealed adverse effects on the fetus and there are no controlled studies in women or studies in women and animals are not available. Drugs should be given only if potential benefits justify the potential risk to the fetus. Category D: There is positive evidence of human fetal risk, but the benefits from use in pregnant woman may be acceptable despite the risk. Category X: Studies in animals or human beings have demonstrated fetal abnormalities. The risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant. <i>Abbreviations:</i> NA, not available; SVT, supraventricular tachycardia; IUGR, intrauterine growth retardation. <i>Source:</i> From Refs. 9,87.</p>				

stenosis carries a higher risk of systemic embolization. Anticoagulation in pregnancy is described below.

Supraventricular tachycardias can be terminated by vagal maneuvers such as carotid sinus massage, splashing the face with cold water, or a Valsalva maneuver. If these vagal maneuvers are unsuccessful, intravenous adenosine or verapamil should be tried. Electrical cardioversion has been used successfully during pregnancy for reversion to sinus rhythm (108).

Ventricular tachycardia is rare during pregnancy and often accompanies structural heart disease. If the ventricular tachycardia is slow (<100–120 beats/min) or non-sustained (self-terminating within 30 seconds), and there is no apparent structural heart disease, the prognosis is excellent and further therapy with antiarrhythmic drugs is usually not necessary. Patients with ventricular tachycardia who have structural heart disease or those with symptomatic episodes of ventricular tachycardia warrant treatment. The urgency of treatment depends on the presenting symptoms. Rapid ventricular tachycardia in the pregnant patient who is demonstrating significant hemodynamic compromise should be treated urgently with electrical cardioversion, to maintain the fetal blood supply. Patients who are hemodynamically stable can be treated with intravenous procainamide or lidocaine, both of which have been shown to be safe for the fetus. Once sinus rhythm has been reestablished, a thorough evaluation should be undertaken to determine the cause of the ventricular tachycardia before long-term therapy is initiated.

Bradyarrhythmias, Conduction Blocks

Despite the fact that sinus bradycardia and Wenckebach atrioventricular (AV) block (type I second-degree AV block) have been observed during pregnancy, labor, and delivery (109), conduction blocks are not a normal finding in pregnancy. Type II second-degree AV block and third-degree AV block are associated with an increased incidence of sudden death, and permanent pacemaker should be considered. The exception to this is congenital complete heart block, which is generally well tolerated and, because it carries a good prognosis, usually does not need to be treated with a pacemaker, unless it is symptomatic.

MANAGEMENT DURING LABOR AND DELIVERY

As discussed elsewhere in this chapter, a number of profound cardiovascular changes take place during labor and delivery, and these changes are affected by numerous variables including type of delivery (vaginal vs. cesarean), level of pain, and anesthesia.

Labor and Delivery

Timing of Delivery

The main factors considered in deciding the time for delivery are as follows:

- The current NYHA functional status (hemodynamic compensation)
- The presence or absence of fetal compromise (intrauterine growth restriction, oligohydramnios, or nonreassuring fetal testing)
- The functional status trend over time

- The possibility of improving or relieving the current functional status through optimization of treatment (e.g., evaluation of compliance, adjustment of medication doses or additional medications, additional rest)

Women in functional classes NYHA I and II and without fetal indications for delivery are allowed to go into labor spontaneously. Women in functional classes III and IV or in high risk are electively delivered. If the maternal and fetal conditions allow, the induction of labor is scheduled between 38 and 39 weeks of gestation (110). Patients in functional class III or IV are best managed in an obstetric intensive care unit, if available, or in an alternative intensive care unit.

Route of Delivery

Considering the hemodynamic changes of an uncomplicated vaginal delivery in comparison with an abdominal delivery, the vast majority of these women better tolerate a vaginal delivery (12,64,110,111). Cesarean delivery increases the risk of hemorrhage, postpartum infection, pulmonary morbidity, and the fluid shifts and metabolic demands of these women during the period of recovery (13).

The indications for cesarean delivery are the same for women with cardiac disease and the general population (112). There are a few exceptions to this principle. Some women with heart disease may benefit from proceeding directly to cesarean delivery including women with endocarditis needing an emergency valve replacement at or near term; women with severe intrauterine growth restriction and Eisenmenger's reaction and unripe cervical conditions; and women with severe aortic stenosis, aortic dilatation, or dissection (2). Similarly, acute severe cardiovascular decompensation during labor might prompt the performance of a cesarean delivery (2).

Induction and Augmentation

General guidelines for the management of pregnant cardiac patients include induction of labor at term with favorable cervix and laboring in the lateral position. Women in higher functional classes may need cervical ripening procedures before induction. Mechanical methods (e.g., Foley catheter) have the advantage of avoiding hemodynamic effects and are associated with lower rates of uterine hyperstimulation and fetal bradycardia. They are the method of choice in higher functional classes and patients with cyanotic lesions. Prostaglandin-based ripening can be used in patients with lower functional classes without tachycardia or a history of asthma.

Maternal and Fetal Monitoring Considerations

Continuous EKG and pulse oximetry monitoring is recommended to monitor for hypotension, hypoxemia, myocardial ischemia, and arrhythmias. The role of pulmonary artery catheter is controversial and should be decided on a case-by-case basis. Women in functional class IV and selected cases in functional class III, pulmonary hypertension, may benefit from a pulmonary artery catheter insertion before the process of labor and delivery is started (8). In some conditions, such as mitral stenosis, controlling the heart rate with a beta blocker infusion may be indicated to avoid tachycardia and decrease in cardiac output (113).

Continuous fetal heart rate monitoring is indicated throughout labor. The fetus is an excellent parameter of maternal perfusion. If cervical conditions allow, internal monitoring is preferable. In the presence of nonreassuring fetal patterns (e.g., nonreactive fetal strip, fetal tachycardia, repetitive late decelerations), prompt evaluation of the maternal hemodynamic parameters and oxygenation is indicated.

Analgesic and Anesthetic Considerations

Anaesthesia can alleviate anxiety and pain, which are associated with tachycardia, increased oxygen consumption and increase in cardiac workload. Cardiovascular hemodynamics is also affected by the type and amount of anesthesia.

An anesthesiologist with experience in managing these patients is pivotal to a successful maternal and fetal outcome. The combination of intrathecal and epidural analgesia (combined spinal–epidural technique or coaxial anesthesia) provides excellent analgesic control, minimizing the patient's anxiety and tachycardia. Epidural anesthesia should be used with caution in patients with hypertrophic cardiomyopathy, in other conditions with low or fixed cardiac outputs such as aortic stenosis, and in potential or actual right-to-left shunts (114). Epidural anesthesia may be contraindicated in patients with Eisenmenger's physiology because it can increase the right-to-left shunt (115). Alternatively, parenteral administration of meperidine or morphine can be used to achieve patient comfort, with the combined use of a pudendal block for analgesic relief of the second stage (114). For vaginal delivery, the second stage of labor is routinely shortened with outlet forceps or vacuum extractor (2).

Postpartum Considerations

It is important to remember that the majority of deaths in this group of patients occur during the puerperium (110). Specifically, the risks of pulmonary edema persist 24 to 72 hours postpartum (2).

Some studies have reported a significantly higher incidence of postpartum hemorrhage among patients with Marfan syndrome, higher functional classes (NYHA III or IV), or cyanosis (2). Postpartum hemorrhage should be managed promptly. Patients who have Eisenmenger syndrome may sustain an increase in the right-to-left shunt during the immediate postpartum period secondary to a decrease in systemic vascular resistance due to blood loss or relief of aortic compression by the fetus (13). In this subset of patients, vasopressors like norepinephrine may be started at the time of delivery to prevent the increase in right-to-left shunting (16).

Early assisted ambulation, use of elastic support stockings, and prophylactic anticoagulation, if needed, will minimize the risk of thromboembolism and are encouraged. If the patient has a need for prolonged anticoagulation, warfarin can be started the day after delivery with an overlap with heparin for 1 or 2 more days after reaching goal INR (116).

Prolonged postpartum admissions are recommended for patients with Eisenmenger syndrome and those with IPAH because most deaths occur during the first month after delivery (68).

Breastfeeding

No specific contraindications for breastfeeding exist provided that an adequate state of hydration is maintained. It is important to consider the fetal risks from the drugs that may be excreted in the breast milk.

Follow-Up

Cardiovascular responses do not completely normalize until 7 months after delivery. These patients should be closely followed by the cardiologists, in addition to the obstetrician.

SPECIAL CONSIDERATION

Cardiac Surgery

Cardiac Surgery During Pregnancy

Certain patients with heart disease may develop refractory symptoms during pregnancy that necessitate cardiac surgical procedures. In some cases, surgery may be lifesaving for the mother, albeit resulting in increased fetal mortality. The outcome of cardiovascular surgery performed during pregnancy is affected by numerous variables, such as the indication, maternal condition, the timing of the surgery relative to the duration of the pregnancy, the interval between admission and surgery, and the use of duration of cardiopulmonary bypass. These factors should be reviewed with the patient on an individual basis.

With the advances in knowledge and technology, the maternal and fetal outcome has improved significantly. Numerous pregnant patients with mitral stenosis have undergone valve replacement for both aortic and mitral valve diseases (92,117,118). Although this procedure has been shown to be relatively safe and effective, it carries a high fetal mortality and should be reserved for patients refractory to medical management. In selected patients, closed mitral valvotomy offers excellent results, comparable with those of nonsurgical treatments (119). Other successful intracardiac procedures during pregnancy include pulmonary valvuloplasty, ASD and VSD repair, excision of left atrial myxomas, and, as an emergency, repair of an aortic dissection. In addition, there have been several successful coronary artery bypass graft procedures carried out during pregnancy (92,117). The chief concerns in the optimal management of pregnant patients who are undergoing cardiopulmonary bypass (CPB) are the control of temperature, perfusion pressure, and the nature of the bypass flow. Current evidence favors maintaining normothermic CPB instead of the hypothermic CPB. The role of off pump coronary artery bypass grafting is a safe and accepted technique for coronary revascularization; however, its role in pregnancy needs further evaluation.

Pregnancy Following Cardiac Surgery

The outcome of pregnancy in women with corrected congenital heart disease depends on many factors including the success of the surgical repair, the extent of residual cardiac lesions, and the need for cardiovascular medications such as Coumadin. In addition, some maternal cardiac defects are associated with an increased incidence of congenital fetal cardiac and noncardiac defects that may affect fetal prognosis. Pregnancies following a heart transplant are usually not complicated (101,102,104,105). Peripartum cardiomyopathy may not recur after the heart transplant (102).

Patients with successfully corrected cardiac lesions without sequelae have a good prognosis during pregnancy and can

often be managed in the same way as a noncardiac patient. Patients with residual stenosis, or residual pulmonary hypertension, are at an increased risk.

Women who have had valve replacement with a mechanical prosthesis pose a special problem, owing to the need for anticoagulation. Anticoagulation in pregnancy is discussed below. Management of the pregnant patient with a bioprosthetic valve is not markedly different from that of patients with native valves, because the valve does not require anticoagulation.

Devices

With the expanding indications for implantable cardioverter defibrillators (ICDs), there are increasing number of pregnant patients with ICD. The mere presence of an ICD should not deter women from becoming pregnant and that pregnancy does not increase the risk of major ICD-related complications or result in high number of ICD discharges (120). For those pregnant women with ongoing malignant arrhythmias despite pharmacologic treatment, an ICD may be a safe alternative (48). It is recommended that ICD should remain activated during labor and should be switched off during cesarean section due to the interference with electrocautery and promptly reprogrammed after the surgery.

Medications
Anticoagulation

Certain medical conditions such as venous thrombosis of the proximal venous system, or certain types of prosthetic valves, necessitate anticoagulation during pregnancy. As with other therapy during pregnancy, the risks arising from the untreated condition must be weighed against the risks and side effects of the treatment. For conditions such as mechanical prosthetic valve, anticoagulation is a necessity.

Warfarin

Warfarin, a vitamin K antagonist, crosses the placenta and has been associated with increased risk of spontaneous abortion and “warfarin embryopathy.” This condition is characterized by hypoplasia of the nasal bone and a wide variety of central nervous system abnormalities including optic atrophy, mental retardation, deafness, and microcephaly (121–123). The risk is higher in the second half of first trimester. In addition, warfarin predisposes both the mother and her fetus to hemorrhagic complications including fetal intracranial hemorrhage (124–127).

Heparin

Unfractionated heparin (UFH) is a large molecule that does not cross the placenta and has little effect on the fetus. Heparin can be administered by continuous intravenous infusion or by intermittent subcutaneous doses (every 8–12 hours).

Low–Molecular Weight Heparins

Low–molecular weight heparins (LMWHs) have potential advantages over UFH during pregnancy. They do not cross the placenta and are safe for the fetus (128). Plasma anti-Xa levels 4 to 6 hours after the morning dose may be used to guide therapy with LMWH. Dosage of LMWH is adjusted to achieve an anti-Xa level of approximately 0.7 to 1.2 units/LmL (129).

Although LMWHs have been used successfully to treat deep venous thrombosis in pregnant patients, there are no data to guide their use in the management of patients with mechanical heart valves (130). Reports of LMWH use in pregnant women with prosthetic heart valves are becoming more frequent, and many physicians now prescribe these agents during pregnancy in women with mechanical valves, but treatment failures have been reported.

The 2008 ACCP Guidelines for antithrombotic therapy recommended one of three approaches for anticoagulation during pregnancy: (131)

- Adjusted-dose bid LMWH throughout pregnancy. Dosing to be adjusted to achieve the manufacturer’s peak anti-Xa LMWH 4 hours after subcutaneous injection.
- Adjusted-dose UFH throughout pregnancy administered subcutaneously q12 hours in doses adjusted to keep the mid-interval activated partial thromboplastin time at least twice control or attain an anti-Xa heparin level of 0.35 to 0.70 U/mL.
- UFH or LMWH (as above) until the 13th week with warfarin substitution until close to delivery when UFH or LMWH is resumed.

Antibiotic Prophylaxis

Per most recently updated American Heart Association guidelines (44), prophylactic antibiotics solely to prevent endocarditis are not recommended for patients who undergo gastrointestinal (GI) or genitourinary (GU) tract procedures. In general, the incidence of infective endocarditis is relatively low during uncomplicated vaginal delivery and antibiotic prophylaxis is not recommended.

Patients with infections of the GI or GU tract may have intermittent or sustained enterococcal bacteremia. For patients with the conditions listed in Table 9, with an established GI or GU tract infection, or for those who receive antibiotic therapy to prevent wound infection or sepsis associated with a GI or GU tract procedure, it may be

Table 9 Conditions Requiring Infective Endocarditis (IE) Prophylaxis

Prosthetic cardiac valve or prosthetic material used for cardiac valve repair
Previous IE
Congenital heart disease (CHD) ^a
Unrepaired cyanotic CHD, including palliative shunts and conduits
Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure ^b
Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)
Cardiac transplantation recipients who develop cardiac valvulopathy

^aExcept for the conditions listed above, antibiotic prophylaxis is no longer recommended for any other form of CHD. ^bProphylaxis is reasonable because endothelialization of prosthetic material occurs within 6 months after the procedure. Prevention of infective endocarditis: guidelines from the American Heart Association (44).

reasonable that the antibiotic regimen includes an agent active against enterococci, such as penicillin, ampicillin, piperacillin, or vancomycin (44).

Cardiac Diagnostic Testing During Pregnancy

Tests Not Involving Ionizing Radiation

Electrocardiogram

The EKG can be enormously helpful in diagnosing a wide variety of abnormalities, including arrhythmias, and poses no risk to either the mother or the fetus. Premature atrial and ventricular complexes are usually benign and seen frequently, and a wide variety of brady- and tachyarrhythmias have been documented during labor (132).

Echocardiography

Echocardiography has been widely used and poses no risk to either the mother or the fetus. An echocardiographic evaluation would be appropriate in instances of systolic murmurs in the presence of symptoms, systolic murmurs with associated thrill, pansystolic murmurs, diastolic murmurs, or murmurs accompanied by arrhythmias or gallop.

Transesophageal echocardiography has been reported to be well tolerated during pregnancy and is helpful to further elucidate structural and functional changes not well defined on transthoracic echocardiography, such as endocarditis vegetations, prosthetic valves, and the severity of valvular disease (16,64,133).

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) has been studied in detail and no apparent long-term adverse effects have been demonstrated on the fetuses of pregnant mice. The safety of fetal MRI has not been fully evaluated. Fetal MRI using 1.5-T magnets may be performed in any trimester (134). However, because of limited data, MRI in the first trimester is currently avoided whenever feasible.

Cardiac Diagnostic Tests Involving Ionizing Radiation

Ionizing radiation, depending on the dose and the gestational age, may pose risks to the fetus. During the first few weeks after conception, a maternal dose of 0.1 Gy results in a 0.1% increase in abortions over the naturally occurring spontaneous abortion rate of 25% to 50%. The period of organogenesis (2–8 weeks) is critically important. A dose of 0.1 Gy is estimated to produce a 1% increase in the frequency of congenital fetal abnormalities (135). After 8 weeks of gestation, the primary effect of radiation exposure is an increased incidence of childhood leukemia. A dose of 0.01 Gy may increase the frequency of malignant disease by up to 11 cases per 1,000,000 live births (135).

Fetal exposure of 0.1 Gy or greater may increase the rise of childhood leukemia and fetal abnormalities such as microcephaly (136). Some limit the safe fetal dose to 5 mGy. Occasionally, the need arises during pregnancy for cardiac diagnostic testing that involves ionizing radiation. If the information obtained is crucial for the management of the patient, the test should be performed in such a way as to minimize exposure to the fetus.

Chest Radiograph

A chest X-ray delivers approximately 0–0.05 mGy to the fetus, which is considered a negligible amount. In addition, the abdomen of the pregnant patient can often be shielded during

the test to minimize exposure by scattered radiation. An inadvertent chest X-ray during early pregnancy poses little, if any, risk to the fetus, but should be performed only if the benefits outweigh the very small risk.

Myocardial Perfusion Imaging and Radionuclide

Ventriculogram

Radionuclide imaging using ^{99m}Tc -labeled sestamibi or ^{201}Tl is expected to yield <1 rad of radiation to the conceptus (87). These tests are rarely needed in pregnancy and can be substituted by echocardiography if indicated.

Cardiac Catheterization

There are cardiac events during pregnancy that require cardiac catheterization and obligate exposure to ionizing radiation. The classic example would be acute myocardial infarction, where the risk of fetal exposure to ionizing radiation may be less than the benefits of immediate revascularization and prevention of complications.

The amount of fetal exposure to radiation during chest radiography in PCI results in a mean exposure of 0.02 mSv and a maximum of 0.1 mSv in difficult PCI procedures (National Council of Radiation Protection and Measurements 1998). Radiation that scattered from the directly irradiated area reaches the fetus. Shielding the abdomen and pelvis will not intercept the scattered irradiation. Catheterization through the radial artery will keep fetal radiation exposure to a minimum.

As with other tests, catheterization should be avoided unless the critical information cannot be obtained in other ways. Before completion of major organogenesis (before 15 weeks after menses), radiation exposure must, whenever possible, be avoided. Doses in excess of 50 to 100 mSv increase the incidence of fetal malformation and may warrant termination of pregnancy (137).

Pregnancy in cardiac patients poses multitude of challenges to the multidisciplinary team taking care of these patients. With meticulous planning, education, counseling, and advances in technology, the maternal and fetal outcome continues to improve.

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