Cardiac Surgery in the Parturient

Shobana Chandrasekhar, MD

Christopher R. Cook, DO

Charles D. Collard, MD

Heart disease is the primary cause of nonobstetric mortality in pregnancy, occurring in 1%–3% of pregnancies and accounting for 10%–15% of maternal deaths. Congenital heart disease has become more prevalent in women of childbearing age, representing an increasing percentage (up to 75%) of heart disease in pregnancy. Untreated maternal heart disease also places the fetus at risk. Independent predictors of neonatal complications include a maternal New York Heart Association heart failure classification >2, anticoagulation use during pregnancy, smoking, multiple gestation, and left heart obstruction. Because cardiac surgical morbidity and mortality in the parturient is higher than nonpregnant patients, most parturients with cardiac disease are first managed medically, with cardiac surgery being reserved when medical management fails. Risk factors for maternal mortality during cardiac surgery include the use of vasoactive drugs, age, type of surgery, reoperation, and maternal functional class. Risk factors for fetal mortality include maternal age >35 yr, functional class, reoperation, emergency surgery, type of myocardial protection, and anoxic time. Nonetheless, acceptable maternal and fetal perioperative mortality rates may be achieved through such measures as early preoperative detection of maternal cardiovascular decompensation, use of fetal monitoring, delivery of a viable fetus before the operation and scheduling surgery on an elective basis during the second trimester. Additionally, fetal morbidity may be reduced during cardiopulmonary bypass by optimizing maternal oxygen-carrying capacity and uterine blood flow. Current maternal bypass recommendations include: 1) maintaining the pump flow rate >2.5 $L \cdot min^{-1} \cdot m^{-2}$ and perfusion pressure >70 mm Hg; 2) maintaining the hematocrit > 28%; 3) using normothermic perfusion when feasible; 4) using pulsatile flow; and 5) using α-stat pH management.

(Anesth Analg 2009;108:777–85)

Heart disease is the primary cause of nonobstetric mortality in pregnancy occurring in 1%–3% of pregnancies and accounting for 10%–15% of maternal mortality.[1,2] Congenital heart disease (CHD) has become more prevalent in women of childbearing age representing an increasing percentage (up to 75%) of heart disease in pregnancy.[2] Although maternal cardiac disease results in only 15% of obstetric intensive care unit admissions, affected patients account for nearly 50% of maternal intensive care unit deaths.[3]

Untreated maternal heart disease also places the fetus at risk. A prospective study on pregnancy outcomes in women with heart disease identified several independent predictors of neonatal complications, including a maternal New York Heart Association (NYHA) heart failure classification >2, anticoagulation use during pregnancy, smoking, multiple gestation, and left-heart obstruction.[4,5] In this study, premature delivery and/or small for gestational age infants occurred in 20% of the patients.[4] Additionally, the rates of neonatal miscarriage and complications, such as intraventricular hemorrhage and death, occur more commonly in pregnant patients than those without cardiac disease.[5]

Because cardiac surgical morbidity and mortality in the parturient (Table 1) is higher than nonpregnant patients, most parturients with cardiac disease are first managed medically, with cardiac surgery being reserved when medical management fails. Risks to the fetus during maternal cardiac surgery are high, with reports of fetal morbidity and mortality as high as 9% and 30%, respectively.[6] The practicing anesthesiologist must have a firm understanding of the perioperative management of these complex, high risk patients. We review common conditions that occur in women with cardiac disease during pregnancy and provide recommendations for perioperative management of the parturient undergoing cardiac surgery.

CARDIOVASCULAR CHANGES OF PREGNANCY

Several fundamental alterations occur in the cardiovascular and pulmonary systems during pregnancy that improve oxygen and nutrient flow to the fetus *in utero*. In a parturient with preexisting heart disease,

From the Division of Cardiovascular Anesthesiology, Department of Anesthesiology, Baylor College of Medicine, Texas Heart® Institute, St. Luke's Episcopal Hospital, Houston, TX.

Accepted for publication September 12, 2008.

Address correspondence and reprint requests to Charles D. Collard, MD, Baylor College of Medicine Division of Cardiovascular Anesthesiology at the TX Heart Institute, St. Luke's Episcopal Hospital, 6720 Bertner Ave., Room 0520, Houston, TX 77030. Address e-mail to ccollard@bcm.tmc.edu.

DOI: 10.1213/ane.0b013e31819367aa

Table 1. Cardiac Surgical Procedures and Maternal Outcomes[6]

Surgical indication	Maternal morbidity (%)	Maternal mortality (%)
Valvular disease	19	9
Aortic dissection	34	22
Aortic aneurysm	41	0
Prosthetic valve dysfunction	23	9
Congenital anomaly	17	0
Pulmonary thromboembolism	44	22
Cardiac tumor	43	0
Coronary artery disease	75	0

these physiological adaptations to pregnancy can eventually lead to cardiopulmonary collapse. Such maternal changes include increased intravascular volume, cardiac output (CO), and heart rate, along with decreased systemic vascular resistance (SVR). Furthermore, these changes may be aggravated by the physiologic anemia of pregnancy (disproportionate increase in plasma volume compared to red cell mass) and by aortocaval compression that occurs after 24 wk gestation. Moreover, during labor each uterine contraction results in an autotransfusion of blood that, coupled with pain and anxiety, can increase the CO as much as 40% above that seen in late pregnancy. Immediately after delivery, CO significantly increases further because of mobilized extracellular fluid and of increased venous return because of relief of venocaval compression by the enlarged uterus. Thus, it is not surprising that the majority of obstetric patients who die with cardiac disease do so after delivery because of the increased demands upon the cardiovascular system. Lastly, the hypercoagulable state associated with pregnancy can increase the risk of thrombosis in diseased or prosthetic valves, and in dilated, poorly contracting hearts.

INDICATIONS AND CONSIDERATIONS FOR SURGICAL INTERVENTION

Cardiovascular maternal morbidity and mortality during pregnancy correlate strongly with maternal functional status.[7–9] Four major risk factors predict adverse maternal outcomes: 1) a history of transient ischemic attack, stroke, or arrhythmia; 2) a NYHA heart failure classification of three or four before onset of pregnancy; 3) left-heart obstruction (e.g., mitral valve area <2 cm^2, aortic valve area <1.5 cm^2, peak left outflow gradient $>$ 30 mm Hg); and 4) a left ventricular (LV) ejection fraction $<40\%$.[1] Indeed, in patients with a NYHA heart failure classification of three or four before pregnancy, maternal morbidity, and mortality may be as high as 50%, and 15%–55% of patients will have a deterioration in functional status during pregnancy.[7] Furthermore, the risk of maternal complications increases proportionately with the number of risk factors identified.[10] When more than one risk factor is present, the incidence of maternal complications increases to nearly 75%.[10] Common complications include pulmonary edema, arrhythmias, myocardial infarction, cardiac failure, stroke, and death. Thus, not only is there a need to counsel women with known preexisting cardiac disease, attention must also be paid to screening women before pregnancy for evidence of cardiac risk factors, and for cardiac disease that develops *de novo* during pregnancy.[8]

Valvular Heart Disease

Mitral valve disease remains the most common valvular disorder requiring surgery during pregnancy. Women who have chronic mitral or aortic regurgitation will commonly experience an improvement in symptoms as the pregnancy-associated decreases in SVR and increased heart rate reduce the regurgitant fraction.[11] Surgical therapy for regurgitant lesions is only required in the most severe cases.

In contrast, women with severe stenotic lesions require close monitoring by both their obstetricians and their cardiologists, especially during the third trimester, labor and delivery, and the early postpartum period.[11] The consequences of mitral stenosis worsen during pregnancy because of the tachycardia, increased CO, and increased blood volume causing increased transmitral flow and decreased diastolic filling time. In severe cases, cardiac decompensation and pulmonary edema may result. Medical therapy with β-blockers, diuretics, and digoxin to control the ventricular response is the first line of management. When the valve area is <1.5 cm^2, the severity of mitral stenosis might require a percutaneous balloon valvotomy which, when done in experienced centers, has a low complication rate (albeit this may be a temporizing measure). This is preferred over closed mitral commissurotomy, which has a maternal and fetal mortality rate of 2.5% and 7%, respectively.[12] If the valve is calcified and nonpliable, balloon mitral valvotomy cannot be performed, and mitral valve replacement with cardiopulmonary bypass (CPB) may be necessary. Whenever possible the baby should be delivered before valve replacement surgery because of the high fetal mortality during cardiac surgery. Cardiac surgery should be reserved for patients with mitral valve disease and severe pulmonary arterial (PA) hypertension, especially if there is multivalvular disease.[11]

Aortic stenosis in pregnant patients is usually due to bicuspid aortic valve. The hemodynamic changes of pregnancy increase the risk of myocardial decompensation, particularly if the valve area is <1 cm^2. Development of dyspnea, syncope, angina, and arrhythmias indicate critical LV outflow obstruction and surgical intervention, such as balloon valvuloplasty or valve replacement, must be considered.

Peripartum Cardiomyopathy

Peripartum cardiomyopathy (PPCMP) is the fifth leading cause of maternal death, with a mortality rate of 20%–50%. A report from the United Kingdom documented that PPCMP is the most common maternal cause

of cardiac death, followed by myocardial infarction and aortic dissection.[13] New onset LV systolic dysfunction in the last month of pregnancy, or within 5-mo postpartum, with no determinable cause and the absence of prior heart disease is indicative of PPCMP. Furthermore, the risk of recurrent PPCMP is increased in subsequent pregnancies if cardiomegaly persists.[14]

Afterload reduction with hydralazine or amlodipine before delivery is useful for PPCMP management. However, angiotensin converting enzyme (ACE) inhibitors and amiodarone should be avoided during pregnancy as they may adversely affect fetal renal function, although they may be useful after delivery if the patient is not breast feeding.[15] Fluid reduction, inotropes, bed rest, and anticoagulation before delivery should be considered. Phosphodiesterase inhibitors have been used with some success.[16] Recently, it was reported that some postpartum cardiomyopathy patients benefited from bromocriptine-induced inhibition of prolactin release.[17] Although not yet proven, there are also anecdotal reports of patients with active myocarditis benefiting from immunosuppressive therapy with pooled polyclonal human antibodies.[18]

Delivery of the fetus often relieves the stress on the maternal hemodynamics. Vaginal delivery by elective induction at term, with close invasive hemodynamic monitoring and administration of inotropes and vasodilators as needed is recommended, and requires close communication between the obstetrician, anesthesiologist, and intensivist.[19] Cardiac transplant should be considered if medical therapy and delivery are ineffective. Five-year maternal survival rates are 60%–88%, with a higher incidence of early rejection and infection as compared to idiopathic dilated cardiomyopathy.[20,21] Intraaortic balloon pumps and ventricular assist devices have been successfully used as a bridge-to-transplant.[22,23]

Ischemic Heart Disease

Ischemic heart disease occurs in 1 in 10,000 pregnancies.[8] Risk factors for myocardial infarction in pregnancy include older age, smoking, diabetes, hypertension, IV ergometrine use, cocaine abuse, and severe hemorrhage. Early diagnosis and therapy are important to reducing maternal morbidity and mortality. As the maternal mortality rate in the setting of an acute myocardial infarction is as high as 50%, it has been suggested that delivery should be avoided for 2 wk postinfarction. [24] Interventions like coronary stenting and angioplasty have been successful, with coronary artery bypass graft surgery being reserved for pregnant patients who are otherwise not good candidates. Tissue plasminogen activator may be administered for thrombolysis, as it has a short half-life (5 min) and does not cross the placenta.[8] Hemodynamic monitoring, oxygen supplementation, β-blockade, and pain control are all effective strategies to optimize myocardial oxygen consumption during surgery.[8]

Arrhythmias

The effects of common antiarrhythmics in pregnancy are shown in Table 2. Electrical cardioversion is generally safe during pregnancy.[25–27] Firm application of paddles, adequate sedation, and aspiration prophylaxis are important considerations. The energy needed for defibrillation is unchanged in pregnancy, and there is no evidence that maternal defibrillation adversely affects the fetal heart.[25–27] In paroxysmal supraventricular tachycardia, adenosine is the drug of choice if vagal maneuvers are unsuccessful.[27] Cardioselective β-blockers may also be useful, although esmolol has been associated with fetal bradycardia.[28] Amiodarone use is controversial as it may adversely affect fetal renal function.[15]

The compromise in venous return by the gravid uterus after 20 wk can precipitate maternal cardiac arrest in a patient with severe heart disease.[29,30] A 15° uterine tilt, manually or by mechanical means, should be done immediately. A higher hand position for chest compression may be needed to adjust for the elevated diaphragm and abdominal contents. Ventricular arrhythmias can be treated with IV lidocaine, procainamide, or cardioversion. The most recent guidelines for cardiopulmonary resuscitation in pregnancy suggest early cesarean delivery of a fetus >24 wk gestation. Advanced Cardiac Life Support drugs should use standard doses during pregnancy.[26,27]

Congenital Heart Disease

A recent review of 2500 pregnant women with CHD revealed that 11% had cardiac complications, 15% had spontaneous abortions, and 5% electively terminated their pregnancies.[7] Moreover, fetal outcomes were significantly worsened, with high premature mortality rates.[7]

Aortic Coarctation

Uncomplicated, uncorrected aortic coarctation carries a low-maternal mortality risk (3%) but can be higher with coexisting hypertension or other cardiac anomalies.[5] The most severe complication is aortic dissection and rupture, particularly in the third trimester.[5] Other complications include congestive heart failure and bacterial endocarditis. Coarctation is also associated with a frequent incidence of bicuspid aortic valve, aneurysms of the Circle of Willis, ventricular septal defect, and Turner syndrome. Anesthetic management should be focused on maintaining the SVR, heart rate, and intravascular volume.[8] Placement of invasive hemodynamic monitoring in a postductal location may provide a better estimate of intravascular volume status, arterial blood pressure, and uterine perfusion.[8]

Septal Defects

Pregnancy in patients with left-to-right shunts is generally well tolerated in patients with good ventricular function, no pulmonary hypertension, and small

Table 2. Effect of Antiarrhythmics in Pregnancy[35]

Class	Maternal effect	Fetoplacental effect	Safety profile	Indication
Class Ia				
Quinidine	Oxytocin-like effects, depresses pseudocholinesterase activity (60%), potentiates the effect of ester local anesthetics	Thrombocytopenia; 8th nerve toxicity	C	SVT
Procainamide	Lupus-like syndrome	Good safety profile	C	SVT/VT
Disopyramide	Oxytocin-like effects, promotes uterine contractions	No adverse effects in fetus	C	SVT
Class Ib				
Lidocaine	Neurological and cardiovascular toxicity in large doses	Ion trapping in the fetus	B	VT
Mexiletine	Nausea, vomiting, dizziness, tremor	Fetal bradycardia, neonatal hypoglycemia, small for gestational age, low Apgar scores	C	VT
Tocainide	Nausea, vomiting, tremor, paresthesias, confusion, frank psychosis, increased liver enzymes, lupus like syndrome, agranulocytosis		C	VT
Class Ic				
Flecainide	Mild side effects	No adverse effects	C	SVT
Class II				
β-Blockers	Increased uterine tone	Fetal bradycardia, IUGR, Neonatal hypoglycemia, apnea	C	SVT/VT
Class III				
Amiodarone	Hypothyroidism	Fetal hypothyroidism small for gestation, prematurity, neurodevelopmental problems	D	
Sotalol	Bradycardia	Relatively better safety profile	B	SVT/VT
Class IV				
Ca^{2+}-channel blockers	Hypotension, uterine atony, enhances effect of magnesium, cardiac depression	No adverse effects reported	C	SVT
Miscellaneous				
Digoxin	Close maternal monitoring to prevent toxicity	Safe extensive experience; low birth weight reported.	C	SVT
Adenosine	Chest pressure, dizziness, headache	Limited data; lack of teratogenic or adverse side effects; occasional fetal bradycardia reported	C	SVT

Food and Drug Administration Drug Risk Classification: A, Controlled studies show no risk; B, No evidence of risk, either animal studies show risk, but humans do not, or animal studies do not show risk and no adequate human studies; C, Studies in pregnant women are lacking and animal studies are positive or lacking; D, Positive evidence for risk.

SVT = supraventricular tachycardia; VT = ventricular tachycardia; IUGR = Intrauterine Growth Retardation.

shunt fractions. However, larger shunts can lead to progressive LV dysfunction, pulmonary hypertension, shunt reversal, and paradoxical emboli. In Eisenmenger syndrome, pregnancy is associated with 40% maternal mortality, with 80% of deaths occurring postpartum.[6] If surgical closure of the septal defect is necessary, these patients should receive endocarditis prophylaxis, air filters should be placed on all IV lines to avoid paradoxical emboli and, in the case of severe right-to-left shunting, maternal SVR and oxygenation maintained throughout the procedure.[31] Pulmonary vasodilation using inhaled nitric oxide has had minimal impact on maternal survival.[32]

Tetralogy of Fallot

Tetralogy of Fallot is the most common form of cyanotic CHD. Patients who have had a previous tetralogy correction usually tolerate pregnancy well. In contrast, women with uncorrected tetralogy or those with major residual defects have a high rate of

Table 3. Maternal and Fetal Cardiovascular Side Effects of Commonly Used Tocolytic Drugs

Tocolytic agent	Maternal side effects	Fetal side effects
Magnesium	Hypotension and Cardiovascular collapse (narrow therapeutic index) Pulmonary edema, increased sensitivity to nondepolarizing relaxants	Loss of beat-to-beat variability
Beta-adrenergic drugs	Tachycardia, decreased systemic vascular resistance, hypokalemia, pulmonary edema	Fetal tachycardia
Nitroglycerin	Decreased preload with hypotension, pulmonary edema (?)	
Prostaglandin inhibitors	Prolonged bleeding time	Premature closure of ductus arteriosus

Uterine atony can occur with all these drugs, with increased risk of bleeding after cesarean section.

spontaneous abortion and prematurity, and the infants are often small for gestational age and have an increased frequency of CHD.[8] The increased physiological demands of pregnancy and effort of labor can increase right-to-left shunting, resulting in maternal cyanosis, and fetal hypoxemia. In such situations, delivery by cesarean delivery using general anesthesia is preferred, making sure the mother is adequately hydrated, avoiding systemic vasodilation and pulmonary vasoconstriction, adequately replacing blood loss and maintaining adequate right ventricular filling pressures.[8]

Aortic Disease

Patients with Marfan syndrome or a bicuspid aortic valve may develop aortic root dilation and dissection secondary to the hyperdynamic and hypervolemic state associated with pregnancy. The incidence of acute Type A dissection in Marfan patients is increased when the aortic root dilation is >4 cm or there is a rapid increase in aortic size.[8] Delivery of a viable fetus (>24 wk gestation) is preferable before undergoing emergency aortic dissection repair. In situations in which the fetus is not viable, the mother's condition takes priority and emergency dissection repair should be performed with the parents' informed consent that the fetus will likely poorly tolerate CPB and deep hypothermic circulatory arrest.

PERIOPERATIVE EVALUATION AND MONITORING

Fetal and Uterine Monitoring

Fetal monitoring during and after cardiac surgery is an individualized decision that requires consultation between the anesthesiologist, obstetrician, neonatologist, and cardiovascular surgeon. Fetal heart rate (FHR) monitoring should be considered after 18 wk gestation, but technical difficulties because of fetal size, position, and maternal obesity may prevent consistent and accurate monitoring.[30] After 22 wk gestation, intraoperative fetal monitoring is generally indicated when feasible, with some authors advocating external tococardiographic FHR monitoring as the standard of care.[33] FHR monitoring requires a qualified individual to interpret the tracing, and a preoperative agreed upon plan of action with regard to how a nonreassuring tracing will be managed.[33] Potential causes of fetal bradycardia during surgery include hypotension, hypoxia, uterine contractions, decreased uterine blood flow, maternal malpositioning, medications, and hypothermia. Persistent fetal bradycardia should be treated aggressively by optimizing maternal oxygen saturation, increasing CPB blood flow, correcting any acid-base abnormalities, minimizing anesthetic depth, replenishing fetal glycogen stores (i.e., avoiding maternal hypoglycemia) and, in the situation of a viable fetus, surgical delivery by an obstetrician.

Monitoring of uterine contractions can also be performed. If uterine contractions are detected, maternal intravascular volume can be increased and tocolytic treatment instituted after consulting with the obstetrician and cardiac surgeon. Table 3 lists potential maternal and fetal cardiovascular side effects of commonly used tocolytic drugs.

Invasive Hemodynamic Monitoring

Invasive hemodynamic monitoring may be altered in the parturient. For example, unlike the healthy, nonpregnant patient for which the central venous pressure and pulmonary capillary wedge pressure are roughly equivalent, there may be poor correlation between these central pressures because of the physiological changes of pregnancy, especially in patients with pregnancy-induced hypertension.[34] If assessment of LV preload is necessary, transesophageal echocardiography and/or insertion of a PA catheter may be useful. Common indications for a PA catheter in the parturient undergoing cardiac surgery include severe mitral or aortic valvular stenosis, NYHA Class 3 or 4 heart disease, intraoperative or intrapartum cardiac failure, refractory pulmonary edema, adult respiratory distress syndrome, and preeclampsia with refractory oliguria or pulmonary edema.[3] Very little data are available on the PA catheter complication rate in pregnant women. If PA catheters are deemed useful for cardiac surgery, the parturient should be treated no differently than the nonpregnant patient, with PA catheter use being individualized per patient and physician.[3]

Echocardiography

Transthoracic or transesophageal echocardiography can provide invaluable information about the type and severity of cardiac lesions in pregnancy. Cardiac chamber enlargement, annular dilation, functional multivalvular regurgitation, particularly in the

Table 4. Impact of Pregnancy on Drug Pharmacokinetics and Pharmacodynamics[35]

Physiological changes of pregnancy	Effect on drug pharmacokinetics and pharmacodynamics
↑ CO ↑ Blood volume	↑ Volume of distribution
↑ Plasma volume ↓ Albumin ↑ α_1-acid glycoprotein	Altered protein binding
↓ GI motility	Prolonged GI transit time
↑ CO ↑ GFR ↑ Hepatic and renal blood flow ↑ Hepatic enzyme activity	↑ Clearance

CO = cardiac output; GFR = glomerular filtration rate; GI = gastrointestinal.

right-sided valves, are all considered normal in the late stages of pregnancy and should be borne in mind when interpreting echocardiographic findings.[8] One study showed that echocardiography significantly over-estimated PA pressures compared with catheterization in pregnant patients with suspected pulmonary hypertension.[34] Indeed, 32% of pregnant patients with normal PA pressures may be misclassified as having PA hypertension when measured by echocardiography alone.[34] Nonetheless, echocardiography may be extremely valuable for evaluating the completeness of surgical repair or ventricular function post-CPB, especially when the findings are correlated with a PA catheter.

ANESTHETIC MANAGEMENT

Impact of Pregnancy on Drug Pharmacokinetics and Pharmacodynamics

The physiologic changes of pregnancy alter cardiovascular, gastrointestinal, hematologic, hepatic, and renal function, resulting in altered maternal drug pharmacokinetics and pharmacodynamics (Table 4).[35] The net effect is increased variability of unbound drug concentrations during a dosing interval, with increased risk of drug toxicity at the beginning, and potential loss of therapeutic effect at the end. In general, drug transfer across the placenta obeys Fick Law of diffusion.[35] Therefore, the drug concentration gradient from the maternal-to-fetal circulation, and the placental surface area and membrane thickness, significantly influence the amount of drug that reaches the fetus. Additionally, medication properties, including molecular weight, lipid solubility, maternal-fetal pH difference, and degree of ionization influence drug diffusion to the fetal circulation.[35] Thus, drugs often require more frequent dosing, without a change in the total daily maternal dosage.

Anticoagulation in Pregnancy

The effects of many drugs commonly used during the perioperative period on pregnancy are shown in Table 5. Potential indications for anticoagulation during pregnancy include deep venous thromboembolism, mechanical heart valves, new onset atrial fibrillation, dilated cardiomyopathy, and during CPB. Oral anticoagulation with warfarin has the lowest incidence of maternal mortality and thromboembolism, with the caveat that warfarin use in the first trimester can cause fetal growth retardation, spontaneous abortion, and embryopathy.[36] Additionally, warfarin has been reported to be associated with premature birth and fetal and placental hemorrhage in the third trimester.[36] Unfractionated heparin and low molecular weight heparin (e.g., enoxaparin) do not cross the placenta and have no teratogenic effects on the fetus but are not as effective as warfarin in preventing thrombosis.[37] A widely accepted method is to use heparin in the first trimester of pregnancy, and then switch to warfarin for the remainder of pregnancy until 36 wk when heparin can be reinstated until delivery.[38] For the purposes of CPB, heparin may be safely used in the usual doses for anticoagulation without risk to the fetus.[29,30]

CPB Management

CPB may have deleterious effects on uteroplacental blood flow (UBF) and the fetus that may be exacerbated by activation of inflammatory processes, nonpulsatile flow, hypotension, and hypothermia.[39,40] If the fetus is viable, uterine tone and FHR should be monitored, and a dedicated perinatologist or obstetrician on standby, if emergency delivery is required.[41] Fetal bradycardia, sinusoidal patterns, and late decelerations are all indicators of fetal asphyxia and may occur during CPB initiation or emergence.[41] Potential reasons for fetal asphyxia include reduced SVR, low UBF, hemodilution, hypothermia, particulate or air embolism, obstruction of venous drainage during inferior vena caval cannulation, prolonged CPB, or maternal narcotic administration.[41]

Fetal protection strategies during CPB are listed in Table 6.[39,40] During CPB, a high pump flow rate (>2.5 $L \cdot min^{-1} \cdot m^{-2}$) and perfusion pressure (>70 mm Hg) are recommended to maintain UBF.[42] Additionally, it is recommended that the maternal hematocrit be maintained >28% to optimize oxygen-carrying capacity.[39,40] In one series, fetal mortality was 24% vs 0% when hypothermic versus normothermic CPB was compared, respectively.[43] Thus, normothermic perfusion during CPB is recommended when feasible.[43] Although controversial, pulsatile flow may also better preserve UBF.[9] Finally, changes in CO_2 tension can also affect UBF. Specifically, hypocapnia causes uteroplacental vasoconstriction and hypercapnia increases UBF. Therefore, α-stat pH management may be advantageous for maintenance of CO_2 homeostasis and UBF.[19,40,43]

Anesthetics

All inhaled anesthetics and most IV anesthetics are highly lipid soluble and freely cross the placenta.

Table 5. Common Perioperative Drugs and Their Effects in Early Pregnancy

Medication	Effects on early gestational fetus	Safety profile
Diazepam	Oral clefts with prolonged usage	D
Midazolam	Not known	C
Propofol	Not known	B
Thiopental	Not known	B
Etomidate	Embryocidal in large doses in animal studies	C
Ketamine	Unknown, recommended not to be used in first trimester	D
Fentanyl, morphine	Not known	B
Neuromuscular blockers (succinylcholine, vecuronium, pancuronium, rocuronium, cisatracurium)	Safe for clinical use as they do not cross the placental barrier in significant amounts	C
Epinephrine/dopamine[a]	Not known	C
Vasopressin	Not known	C
Ephedrine[b]	Not known	C
Phenylephrine[b]	Minor defects reported	C
Atropine	Minor malformation possible	C
Anticoagulants		
Warfarin[c]	Congenital malformations	D
Heparin[d]	None reported	B

Food and Drug Administration Drug Risk Classification: A, Controlled studies show no risk; B, No evidence of risk, either animal studies show risk, but humans do not, or animal studies do not show risk and no adequate human studies; C, Studies in pregnant women are lacking and animal studies are positive or lacking; D, Positive evidence for risk.

[a] Epinephrine and dopamine have been used safely in pregnant patients.

[b] Vasopressors of choice for pregnant patients with hypotension.

[c] Warfarin is contraindicated in the first trimester.

[d] Heparin does not cross the placental barrier and does not affect the fetus.

Table 6. Fetal Protection Strategies During Cardiopulmonary Bypass[39–44]

Monitor uterine tone and FHR (especially if fetus [>24 wk gestation])
Maintenance of a 15° left lateral tilt using a wedge under the right hip or a left lateral tilt of the table to prevent aortocaval compression
Maintenance of maternal hematocrit >28%
Maintenance of maternal oxygen saturation
Normothermia
High flow rate (>2.5 $L \cdot min^{-1} \cdot m^{-2}$)
Increased perfusion pressure (>70 mm Hg)
Minimize CPB time
Consider pulsatile perfusion
α-Stat pH management
Tocolytic therapy (e.g., magnesium sulfate, ritodrine, or terbutaline) versus dedicated perinatologist and obstetrician on standby if emergency delivery

CPB = cardiopulmonary bypass; FHR = fetal heart rate.

Volatile anesthetics are also potent uterine relaxants and decrease UBF. In contrast, nitrous oxide has minimal impact on UBF or tone.[44] However, because of its effect on DNA synthesis in animal studies, nitrous oxide use is best avoided during the first trimester.[44] Moreover, nitrous oxide use is generally not recommended during cardiac surgery.

The effect of etomidate is not well described but likely has minimal impact on the fetus or UBF.[29,30] Therefore, in addition to providing hemodynamic stability, etomidate is an excellent choice for IV induction in the parturient with cardiac disease. Ketamine in doses <1.5 mg/kg minimally alters UBF.[29,30] However, uterine hypertonus may occur with doses >2 mg/kg. Thiopental and propofol, although acceptable choices, may decrease UBF secondary to decreased maternal arterial blood pressure.

All opioids may cause fetal respiratory depression, bradycardia and loss of beat-to-beat variability as they readily cross the placental barrier.

Muscle Relaxants and Reversal Drugs

Neuromuscular blocking drugs are quaternary ammonium salts which are highly ionized and do not readily cross the placental barrier. Therefore, these drugs generally do not affect neonatal muscle tone. However, large doses of succinylcholine when given repeatedly, or when the fetus has pseudocholinesterase deficiency, can cause neonatal muscle blockade.

Antihypertensives

Antihypertensives such as labetalol, hydralazine, nicardipine, and nifedipine may be used in pregnant patients with acute aortic dissection, severe hypertensive emergencies, and myocardial ischemia.[45] Hydralazine, a direct acting arterial vasodilator, is popular because of its long track record of safety.[46] However, labetalol, nicardipine, and nifedipine have also been used in preeclamptic patients without any major adverse effects on the mother or fetus. Nitroglycerin, when administered to gravid ewes, relaxed the uteroplacental vasculature, and produced no changes in UBF, arterial blood pressure or heart rate.[47] However, nitroglycerin can cause decreased preload and uterine atony. Use of sodium nitroprusside during pregnancy is controversial, with some data suggesting that there may be an increased rate of stillbirths, tachyphylaxis, and maternal and fetal cyanide toxicity.[14,48] The

α_2-agonist dexmedetomidine readily crosses the placenta.[29] Data from pregnant animal models on dexmedetomidine are lacking, and it has not been approved for use in pregnancy.[29] Finally, ACE inhibitors and ACE receptor antagonists are contraindicated in pregnancy.[15] Fetal ACE inhibitor risks include intrauterine growth retardation, oligohydramnios, preterm labor, bony abnormalities, severe pulmonary and cardiac disease, and stillbirth.

CESAREAN DELIVERY: INDICATIONS AND MANAGEMENT IN PATIENTS WHO REQUIRE SUBSEQUENT CARDIAC SURGERY

In situations in which the fetus is not viable, the mother's condition takes priority and, if necessary, cardiac surgery should be performed with the parents' informed consent that the fetus may poorly tolerate CPB and/or deep hypothermic circulatory arrest. In contrast, in situations in which the baby is viable, it may be in the best interest of the mother and baby for the obstetrician to perform a cesarean delivery before the cardiac operation, with a neonatologist available for resuscitation, because of the high fetal mortality associated with cardiac surgery. In such situations, delivery by cesarean delivery using general anesthesia is preferred, making sure the mother is adequately hydrated, avoiding systemic vasodilation and pulmonary vasoconstriction, adequately replacing blood loss and maintaining adequate ventricular filling pressures.[8] However, it is also important to recognize that a cesarean delivery may impact the subsequent cardiac surgery. For example, uterine atony because of the smooth muscle relaxation by inhaled anesthetics can be a major cause of bleeding after heparinization for CPB. Thus, it may be useful to avoid volatile anesthetics during cesarean delivery and, instead, use total IV anesthesia (e.g., etomidate and opioids) if the patient is to be subsequently heparinized for CPB.[29,30] Positive pressure ventilation can reduce venous return, and hyperventilation should be avoided as hypocapnia can cause uteroplacental vasoconstriction and decrease UBF. The $Paco_2$ should be maintained within the physiologic range of pregnancy (i.e., 28–32 mm Hg).[29,30]

Average blood loss for a cesarean delivery is between 500 and 1000 mL and may need to be replaced before subsequent cardiac surgery. Oxytocin for uterine atony can cause systemic hypotension particularly when given rapidly which can exacerbate the hypovolemia caused by blood loss and should always be given as an infusion and not a bolus. If uterine atony persists despite uterine massage and oxytocin, methylergonovine maleate (methergine; 0.2 mg) may be given IM, keeping in mind the risk of hypertension. In general, methylergonovine maleate should not be given IV unless used as a life-saving measure. Carboprost tromethamine (15-methylprostaglandin $F_{2\alpha}$) is another ecbolic drug but may cause bronchospasm and hypertension. Even though uterine bleeding may appear to be clinically controlled, recurrence of bleeding may occur after heparinization for CPB, and the uterus should be frequently checked for adequate hemostasis.

SUMMARY

Heart disease is the primary cause of nonobstetric mortality in pregnancy. Close monitoring by both obstetricians and cardiologists is thus needed for women with complex heart disease, and pregnancy should still be considered contraindicated in certain types of CHD. Women at increased risk for morbidity in pregnancy include those with a prior stroke or arrhythmia, NYHA heart failure classification >2, anticoagulation use during pregnancy, smoking, multiple gestation, and left heart obstruction.[4,5]

Because cardiac surgical morbidity and mortality in the parturient is higher than nonpregnant patients, most parturients with cardiac disease are first managed medically, with cardiac surgery being reserved when medical management fails. Risk factors for maternal mortality during cardiac surgery include the use of vasoactive drugs, age, type of surgery, reoperation, and maternal functional class.[9] Risk factors for fetal mortality include maternal age >35 yr, functional class, reoperation, emergency surgery, type of myocardial protection, and anoxic time.[9] Nonetheless, acceptable maternal and fetal mortality rates may be achieved through such measures as early preoperative detection of maternal cardiovascular decompensation, use of perioperative fetal monitoring, optimization of CPB, delivery of a viable fetus because of the operation and scheduling surgery on an elective basis during the second trimester.[6]

REFERENCES

1. Klein LL, Galan HL. Cardiac disease in pregnancy. Obstet Gynecol Clin North Am 2004;31:429–59, viii
2. Davies GA, Herbert WN. Congenital heart disease in pregnancy. J Obstet Gynaecol Can 2007;29:409–14
3. Martin SR, Foley MR. Intensive care in obstetrics: an evidence-based review. Am J Obstet Gynecol 2006;195:673–89
4. Siu SC, Sermer M, Colman JM, Alvarez AN, Mercier LA, Morton BC, Kells CM, Bergin ML, Kiess MC, Marcotte F, Taylor DA, Gordon EP, Spears JC, Tam JW, Amankwah KS, Smallhorn JF, Farine D, Sorensen S. Prospective multicenter study of pregnancy outcomes in women with heart disease. Circulation 2001;104:515–21
5. Siu SC, Colman JM, Sorensen S, Smallhorn JF, Farine D, Amankwah KS, Spears JC, Sermer M. Adverse neonatal and cardiac outcomes are more common in pregnant women with cardiac disease. Circulation 2002;105:2179–84
6. Weiss BM, von Segesser LK, Alon E, Seifert B, Turina MI. Outcome of cardiovascular surgery and pregnancy: a systematic review of the period 1984–1996. Am J Obstet Gynecol 1998;179:1643–53
7. Drenthen W, Pieper PG, Roos-Hesselink JW, van Lottum WA, Voors AA, Mulder BJ, van Dijk AP, Vliegen HW, Yap SC, Moons P, Ebels T, Van Veldhuisen DJ. Outcome of pregnancy in women with congenital heart disease: a literature review. J Am Coll Cardiol 2007;49:2303–11
8. Tsen LC. Anesthetic management of the parturient with cardiac and diabetic diseases. Clin Obstet Gynecol 2003;46:700–10

9. Arnoni RT, Arnoni AS, Bonini RC, de Almeida AF, Neto CA, Dinkhuysen JJ, Issa M, Chaccur P, Paulista PP. Risk factors associated with cardiac surgery during pregnancy. Ann Thorac Surg 2003;76:1605–8
10. Khairy P, Ouyang DW, Fernandes SM, Lee-Parritz A, Economy KE, Landzberg MJ. Pregnancy outcomes in women with congenital heart disease. Circulation 2006;113:517–24
11. Davies GA, Herbert WN. Acquired heart disease in pregnancy. J Obstet Gynaecol Can 2007;29:507–9
12. De Souza JA, Martinez EE Jr, Ambrose JA, Alves CM, Born D, Buffolo E, Carvalho AC. Percutaneous balloon mitral valvuloplasty in comparison with open mitral valve commissurotomy for mitral stenosis during pregnancy. J Am Coll Cardiol 2001;37:900–3
13. de Swiet M. Maternal mortality: confidential enquiries into maternal deaths in the United Kingdom. Am J Obstet Gynecol 2000;182:760–6
14. Demakis JG, Rahimtoola SH, Sutton GC, Meadows WR, Szanto PB, Tobin JR, Gunnar RM. Natural course of peripartum cardiomyopathy. Circulation 1971;44:1053–61
15. George LM, Gatt SP, Lowe S. Peripartum cardiomyopathy: four case histories and a commentary on anaesthetic management. Anaesth Intensive Care 1997;25:292–6
16. Robin NM, Wenstone R. The use of enoximone in peripartum cardiomyopathy. Intensive Care Med 1998;24:988–9
17. Hilfiker-Kleiner D, Meyer GP, Schieffer E, Goldmann B, Podewski E, Struman I, Fischer P, Drexler H. Recovery from postpartum cardiomyopathy in 2 patients by blocking prolactin release with bromocriptine. J Am Coll Cardiol 2007;50:2354–5
18. Bozkurt B, Villaneuva FS, Holubkov R, Tokarczyk T, Alvarez RJ Jr, MacGowan GA, Murali S, Rosenblum WD, Feldman AM, McNamara DM. Intravenous immune globulin in the therapy of peripartum cardiomyopathy. J Am Coll Cardiol 1999;34:177–80
19. Lee W. Clinical management of gravid women with peripartum cardiomyopathy. Obstet Gynecol Clin North Am 1991;18:257–71
20. Keogh A, Macdonald P, Spratt P, Marshman D, Larbalestier R, Kaan A. Outcome in peripartum cardiomyopathy after heart transplantation. J Heart Lung Transplant 1994;13:202–7
21. Rickenbacher PR, Rizeq MN, Hunt SA, Billingham ME, Fowler MB. Long-term outcome after heart transplantation for peripartum cardiomyopathy. Am Heart J. 1994;127:1318–23
22. Monta O, Matsumiya G, Fukushima N, Miyamoto Y, Sawa Y, Koseki M, Nakamichi I, Matsuda H. Mechanical ventricular assist system required for sustained severe cardiac dysfunction secondary to peripartum cardiomyopathy. Circ J 2005;69:362–4
23. Lewis R, Mabie WC, Burlew B, Sibai BM. Biventricular assist device as a bridge to cardiac transplantation in the treatment of peripartum cardiomyopathy. South Med J. 1997;90:955–8
24. Hankins GD, Wendel GD Jr, Leveno KJ, Stoneham J. Myocardial infarction during pregnancy: a review. Obstet Gynecol 1985;65:139–46
25. Nanson J, Elcock D, Williams M, Deakin CD. Do physiological changes in pregnancy change defibrillation energy requirements? Br J Anaesth 2001;87:237–9
26. Soar J, Deakin CD, Nolan JP, Abbas G, Alfonzo A, Handley AJ, Lockey D, Perkins GD, Thies K. European Resuscitation Council guidelines for resuscitation 2005. Section 7. Cardiac arrest in special circumstances. Resuscitation 2005;67(suppl 1):S135–S170
27. Blomstrom-Lundqvist C, Scheinman MM, Aliot EM, Alpert JS, Calkins H, Camm AJ, Campbell WB, Haines DE, Kuck KH, Lerman BB, Miller DD, Shaeffer CW, Stevenson WG, Tomaselli GF, Antman EM, Smith SC Jr, Alpert JS, Faxon DP, Fuster V, Gibbons RJ, Gregoratos G, Hiratzka LF, Hunt SA, Jacobs AK, Russell RO Jr, Priori SG, Blanc JJ, Budaj A, Burgos EF, Cowie M, Deckers JW, Garcia MA, Klein WW, Lekakis J, Lindahl B, Mazzotta G, Morais JC, Oto A, Smiseth O, Trappe HJ. ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias—executive summary. a report of the American college of cardiology/American heart association task force on practice guidelines and the European society of cardiology committee for practice guidelines (writing committee to develop guidelines for the management of patients with supraventricular arrhythmias) developed in collaboration with NASPE-Heart Rhythm Society. J Am Coll Cardiol 2003;42:1493–531
28. Ducey JP, Knape KG. Maternal esmolol administration resulting in fetal distress and cesarean section in a term pregnancy. Anesthesiology 1992;77:829–32
29. Van d, V, De Buck F. Anesthesia for non-obstetric surgery in the pregnant patient. Minerva Anestesiol 2007;73:235–40
30. Ni MR, O'Gorman DA. Anesthesia in pregnant patients for nonobstetric surgery. J Clin Anesth 2006;18:60–6
31. Naulty JS, Ostheimer GW, Datta S, Knapp R, Weiss JB. Incidence of venous air embolism during epidural catheter insertion. Anesthesiology 1982;57:410–2
32. Goodwin TM, Gherman RB, Hameed A, Elkayam U. Favorable response of Eisenmenger syndrome to inhaled nitric oxide during pregnancy. Am J Obstet Gynecol 1999;180:64–7
33. Goodman S. Anesthesia for nonobstetric surgery in the pregnant patient. Semin Perinatol 2002;26:136–45
34. Penning S, Robinson KD, Major CA, Garite TJ. A comparison of echocardiography and pulmonary artery catheterization for evaluation of pulmonary artery pressures in pregnant patients with suspected pulmonary hypertension. Am J Obstet Gynecol 2001;184:1568–70
35. Qasqas SA, McPherson C, Frishman WH, Elkayam U. Cardiovascular pharmacotherapeutic considerations during pregnancy and lactation. Cardiol Rev 2004;12:240–61
36. Chan WS, Anand S, Ginsberg JS. Anticoagulation of pregnant women with mechanical heart valves: a systematic review of the literature. Arch Intern Med 2000;160:191–6
37. ACOG committee opinion. Anticoagulation with low-molecular-weight heparin during pregnancy. Number 211, November 1998. Committee on Obstetric Practice. American College of Obstetricians and Gynecologists. Int J Gynaecol Obstet 1999;65:89–90
38. Bonow RO, Carabello BA, Kanu C, de LA Jr, Faxon DP, Freed MD, Gaasch WH, Lytle BW, Nishimura RA, O'Gara PT, O'Rourke RA, Otto CM, Shah PM, Shanewise JS, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Page RL, Riegel B. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 Guidelines for the Management of Patients with Valvular Heart Disease): developed in collaboration with the Society of Cardiovascular Anesthesiologists: endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. Circulation 2006;114:e84–e231
39. Kole SD, Jain SM, Walia A, Sharma M. Cardiopulmonary bypass in pregnancy. Ann Thorac Surg 1997;63:915–6
40. Parry AJ, Westaby S. Cardiopulmonary bypass during pregnancy. Ann Thorac Surg 1996;61:1865–9
41. Karahan N, Ozturk T, Yetkin U, Yilik L, Baloglu A, Gurbuz A. Managing severe heart failure in a pregnant patient undergoing cardiopulmonary bypass: case report and review of the literature. J Cardiothorac Vasc Anesth 2004;18:339–43
42. Iscan ZH, Mavioglu L, Vural KM, Kucuker S, Birincioglu L. Cardiac surgery during pregnancy. J Heart Valve Dis 2006; 15:686–90
43. Pomini F, Mercogliano D, Cavalletti C, Caruso A, Pomini P. Cardiopulmonary bypass in pregnancy. Ann Thorac Surg 1996;61:259–68
44. Fujinaga M. Teratogenicity of nitrous oxide. Baillière's Best Pract Res Clin Anaesthesiol 2003;15:363–75
45. Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Data base of Syst Rev 1999;CD001449. DOI: 10.1002/14651858. CD001449.pub2(2)
46. Mabie WC. Management of acute severe hypertension and encephalopathy. Clin Obstet Gynecol 1999;42:519–31
47. Bootstaylor BS, Roman C, Parer JT, Heymann MA. Fetal and maternal hemodynamic and metabolic effects of maternal nitroglycerin infusions in sheep. Am J Obstet Gynecol 1997; 176:644–50
48. Hoyert DL: Maternal mortality and related concepts. Vital Health Stat 2007;3:1–13

