Cardiac Surgery during Pregnancy

Cardiovascular adaptations during pregnancy are normally well tolerated in healthy women. However, 2% to 4% of women of childbearing age have some degree of concomitant heart disease, and these changes may compromise cardiac function. Of these, a few who do not respond to medical treatment may require surgical correction. In this setting, maternal mortality rate has improved to levels similar to those in non-pregnant counterparts. However, the fetal mortality rate remains high (up to 33%). Factors contributing to high fetal mortality rates include the timing of the operation, the urgency of the operation, and the fetal/fetoplacental response to cardiopulmonary bypass. Modulation of the fetoplacental response to cardiopulmonary bypass may prevent placental dysfunction and sustained uterine contractions, which underlie fetal hypoxia and acidosis.

In this article, we review cardiovascular adaptations to pregnancy and the pathophysiologic effects of cardiopulmonary bypass on the mother, fetus, and fetoplacental unit, and we talk about whether manipulation of these responses can help in improving fetal outcome. Finally, approaches regarding perfusion management and off-pump cardiac surgical techniques in pregnancy are discussed. (Tex Heart Inst J 2008;35(3):307-12)

Approximately 2% to 4% of women of childbearing age have concomitant heart disease. In the Western world, congenital heart disease (CHD) accounts for most of the structural heart disease that affects women of childbearing age. Acquired cardiac disease seen during pregnancy is mainly valvular in nature, usually a consequence of rheumatic fever. Even though rheumatic fever is decreasing in developed countries, it continues to be a serious problem in the developing world. Immigrants also form a high-risk population, especially those who are unaware of the inherent risks of heart disease during pregnancy or are even unaware of the presence of any cardiac disease. Mitral stenosis is the most common lesion encountered, although its incidence is on the decline. Aortic valve disease is less common: aortic incompetence is usually a consequence of endocarditis (1 in 8,000 pregnancies) or aortic dissection, in which case there may be an underlying connective tissue disorder such as Marfan syndrome. Significant aortic stenosis is uncommon in this age group. Ischemic events during pregnancy are rare. The incidence of myocardial infarction is approximately 1 in 10,000 pregnancies. Infarction is usually secondary to underlying coronary artery disease, although spontaneous coronary artery dissection seems to be more common during pregnancy and accounts for 30% of all myocardial infarctions seen in pregnancy.

Predictors of Maternal and Fetal Outcome

In the United Kingdom, cardiac disease in the mother is the major cause of maternal death during pregnancy. Of these patients, 25% have CHD. In a large, prospective multicenter study of pregnancy outcomes among women with heart disease, adverse maternal cardiovascular events were seen in 13% of patients. Independent predictors of maternal cardiac complications included prior cardiac events, New York Heart Association functional class III/IV or cyanosis, left-heart obstruction, and left ventricular systolic dysfunction (Table I). Neonatal complications were seen in 20% and were associated with poor functional class or cyanosis, left-heart obstruction, or smoking.

A recent prospective observational study in pregnant patients with CHD found that both cardiac complication and neonatal complication rates were considerable in these women. In mothers, right subpulmonary ventricular systolic dysfunction and severe pulmonary regurgitation were predictors of an adverse fetal outcome. In a recently published literature review that described the outcomes of 2,491 pregnancies among women with structural CHD, substantial cardiac complications were seen in 11% of the pregnancies. Obstetric complications did not appear to be more prevalent,
except for hypertensive disorders and thromboembolic events. In patients with complex CHD, premature delivery rates ranged from 22% to 65%, and the neonates were smaller than normal for gestational age.11

Maternal Cardiovascular Changes during Pregnancy
In the presence of maternal heart disease, the circulatory changes of pregnancy can result in decompensation and in death of the mother or fetus.9,10 Pregnancy produces changes in the cardiovascular system that have profound implications for cardiac surgery. Cardiac output increases markedly by the end of the 1st trimester, and this is followed by a more gradual increase to 30% to 40% above baseline by the 3rd trimester,12,13 partly due to an increase in stroke volume and heart rate. In most patients, this hyperdynamic situation results in a soft midsystolic murmur. Diastolic murmurs may be normal, but they warrant further investigation.

In late pregnancy, compression of the gravid uterus on the inferior vena cava in the supine decubitus position decreases venous return and reduces cardiac output. Relief of vena caval compression is easily achieved by positioning the patient in the left lateral decubitus position.

Systemic and pulmonary vascular resistances fall due to the effects of circulating prostaglandins and other hormones and to the low resistance of the placental circulation. This reduces blood pressure during the 1st half of pregnancy, but the pressure tends to increase in the 2nd half.14

Blood volume increases, with a concomitant rise in plasma volume and red-blood-cell volume. Plasma volume expands by approximately 40% at full term, when red-cell mass increases by about 20%. Consequently, there is a fall in hematocrit and viscosity.15,16 The oxygen-carrying capacity of hemoglobin is increased by a right shift in the oxygen dissociation curve. Pregnancy induces a pro-coagulant state with a 2-fold rise in fibrinogen level and an increase in factors V, VII, VIII, IX, and X, which has teleologic advantage insofar as it aids hemostasis and reduces blood loss during delivery.17 In addition, this state provides optimal oxygen and nutrient delivery for both mother and fetus.

Maternal Response to Cardiopulmonary Bypass
Because the circulation of pregnant women already has undergone significant alterations, the additional effect of cardiopulmonary bypass (CPB) induces a nonphysiologic hemodynamic state that can adversely affect the mother during cardiac surgery.18 This effect is amplified by simultaneous alterations in the cellular and protein components of the blood. Hemodilution and changes in coagulation, complement activation, release of vasoactive substances by leukocytes, particulate and air embolism, and hypotension during CPB further add to the deleterious effect.3 However, these effects are relatively well tolerated by the mother, to the extent that the maternal mortality rate associated with CPB in pregnant women is similar to that in nonpregnant women who undergo similar cardiac procedures on CPB.18

Uterine Response to Maternal Cardiopulmonary Bypass
Sustained uterine contractions during cardiac surgery and CPB are accepted as the most important cause of fetal death.19 Sustained uterine contractions reduce uterine blood flow and intervillous perfusion, which results in fetoplacental insufficiency and subsequent fetal hypoxia. Cardiopulmonary bypass has other potentially deleterious effects on the uterus in pregnancy. Both the cooling and the rewarming phases are associated with increased sustained uterine contractions.20 This obser-

### Table I. Risk of Maternal Morbidity and Death Resulting from Certain Cardiac Lesions in Pregnancy*

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Moderate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most commonly repaired lesions</td>
<td>Single ventricle</td>
<td>NYHA functional class &gt; III</td>
</tr>
<tr>
<td>Uncomplicated left-to-right shunt</td>
<td>Systemic right ventricle</td>
<td>History of peripartum cardiomyopathy</td>
</tr>
<tr>
<td>Pulmonary stenosis</td>
<td>Uncorrected coarctation</td>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td>Pulmonary regurgitation</td>
<td>Unrepaired cyanotic lesions</td>
<td>Marfan syndrome with aortic size &gt; 4 cm</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>Use of anticoagulants</td>
<td>Severe left ventricular dysfunction</td>
</tr>
<tr>
<td>Mitral regurgitation, mitral valve prolapse</td>
<td>Mitral stenosis</td>
<td></td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>Left ventricular dysfunction</td>
<td></td>
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</tbody>
</table>

NYHA = New York Heart Association

*Adapted from a table in Dob and Yentis.8
vation is supported by the fact that there is a notably higher fetal mortality rate with hypothermic than with normothermic CPB.¹⁸

The excitability of uterine muscle is probably enhanced by hormonal dilution, mainly by the dilution of progesterone. The postoperative administration of progesterone has successfully eliminated premature labor.²¹ The use of tocolytic therapy with ritodrine has been reported to prevent early labor with good effect, resulting in a favorable fetal outcome.¹⁹,²² However, more recent evidence suggests that there is no benefit in tocolytic therapy,²³,²⁴ especially β-agonists—which have the theoretical disadvantage of increasing myocardial oxygen demand and myocardial work in a circulation that already is physiologically compromised by the burden of pregnancy and by the initiation of CPB.

Fetoplacental Response to Cardiopulmonary Bypass

Experimental studies of fetal CPB have provided much insight into the fetoplacental response, which could shape future management of CPB in pregnant women. Studies in sheep have repeatedly shown that standard nonpulsatile flow perfusion rapidly triggers severe placental dysfunction dominated by a strong vasoconstrictive reaction.²⁵ Vasodilators have been used with some success to overcome this rise in placental vascular resistance, yielding improvement in both placental blood flow and acidosis.₂⁶,₂⁷

Pulsatile flow prevents the drop in placental perfusion and limits the rise in placental vascular resistance that is observed with nonpulsatile flow.²⁵ Pulsatile flow preserves endothelial nitric oxide synthesis and decreases the activation of the fetal renin-angiotensin pathway, resulting in improved blood flow to the fetoplacental unit.₂⁵,₂⁸ Reddy and colleagues compared the vasoactive effects of acetylcholine (endothelium-dependent) and nitroprusside (endothelium-independent) before and after CPB to evaluate the ability of the endothelium to produce nitric oxide in a sheep model. These investigators showed that nonpulsatile perfusion generated selective impairment of endothelium-dependent vasodilation. Also, levels of the vasoconstrictor endothelin-1 were measured in both pulsatile- and nonpulsatile-CPB-flow groups and were found to be elevated after 60 minutes of CPB in both groups, but significantly more so in the CPB group with nonpulsatile flow.

A study of the human placenta under physiologic conditions reveals that an active fetal renin-angiotensin system may modulate placental perfusion in vivo.²⁹ Whether endothelial dysfunction is a cause or an effect of excessive renin-angiotensin activity is yet to be resolved.³⁰ Lactate levels during pulsatile-flow CPB have been shown to remain stable, whereas a continuous increase is observed with nonpulsatile CPB.²⁵ Manipulation of the fetal lamb during CPB has been shown to produce significant lactic acidosis; this was considered to be a result of metabolic debt from fetal stress,³¹ and of anesthesia.³² Because lactate release into the maternal circulation was similar between the initiation and the end of CPB, the rise in fetal lactate most likely originated from within the fetus. The placenta plays an important role in regulating circulating lactate levels under hypoxic conditions, thus enabling the fetus to maintain stable lactate levels.³³ However, a reduction in the placental perfusion impedes lactate clearance in the fetal circulation.³³

Fetal Response to Cardiopulmonary Bypass

The fetal mortality rate during maternal cardiac surgery with CPB ranges from 16% to 33%.²⁰,³⁴,³⁵ Increased gestational age and increased hypothermia are factors known to increase fetal morbidity during CPB.³⁶ Unfortunately, little experimental evidence is available on the fetal response to maternal CPB. Fetal heart monitoring usually shows that the response to the initiation of CPB is bradycardia, which in most cases reverts to sinus rhythm immediately after cessation of CPB.³⁷ Alternatively, an initial tachycardia can occur, accompanied by an increase in blood pressure.³⁸ Fetal bradycardia observed after the initiation of CPB is corrected by increasing the blood flow,³⁷,³⁹ and upon restoration of maternal circulation on discontinuation of CPB.³⁸ The mechanism of this bradyresponse is unknown, but various causes have been postulated, including fetoplacental dysfunction, fetal hypoxia and acidosis, maternal hypothermia, and drugs that cross the placental barrier, such as β-adrenergic blockers. Fetal hypoxia during CPB may be a consequence of hemodilution, because hemodilution reduces the oxygen content in the maternal blood. Other causes of fetal hypoxia include reduced uterine perfusion pressure and increased uterine vascular resistance.⁴⁰,⁴¹

Because placental blood vessels are maximally dilated during pregnancy, the uterine blood flow is not autoregulated but depends directly upon the maternal mean arterial pressure and the uterine vascular resistance.⁴⁰,⁴¹ A decrease in maternal blood pressure can result in fetal bradycardia just before the initiation of CPB. Maternal hypotension shortly after the commencement of CPB is caused by a decrease in the systemic vascular resistance, decreased flow rate, hemodilution, and release of vasoactive substances, which can result in significant reduction in placental perfusion.³⁸,⁴¹ The observed fetal heart decelerations during CPB are likely to be caused by reduced blood flow to the intervillous spaces and the resulting fetal hypoxia. Factors such as nonpulsatile flow, uterine arteriovenous shunting, and the obstruction of venous drainage by inferior vena caval cannulation, by particulate and gaseous emboli, and by uterine artery spasm can all reduce placental circulation and lead to fetal hypoxia.³⁸,⁴² When CPB is prolonged, there
is a significant risk of the fetus’s developing a sustained and prolonged bradycardic response.¹⁸

Maternal core temperature affects the fetal response during CPB. The deeper the hypothermia, the greater the risk of fetal death.¹⁸,³⁶ Hypothermia can alter the acid-base balance, affect coagulation pathways, cause predisposition to arrhythmias, and precipitate uterine contractions, thereby reducing placental oxygen exchange. Transplacental flow and subsequent perfusion and oxygen delivery to fetal organs is impaired under these conditions.¹³,⁴⁴ Although mild hypothermia can be tolerated because the fetal heart is able to autoregulate rate, more profound hypothermia induces a decline in fetal and placental function, and therefore increases the risk of fetal arrhythmias and cardiac arrest.⁴⁵ However, fetal arrhythmias during normothermic CPB have also been reported.²¹ There is the occasional exception to the rule: deep hypothermic circulatory arrest was used in a woman at 21 weeks’ gestation when a ruptured aortic aneurysm required an emergency aortic root replacement; the patient delivered a normal infant at term by caesarean section.⁴⁶

Alterations in fetal heart rate may be observed even when maternal circulation, acid-base balance, and perfusion pressure are stable. It has therefore been postulated that these alterations are related to the narcotic effect of drugs used during anesthesia. Vasoconstrictors may reduce utero-placental flow (direct evidence of this is lacking) and should be avoided, although phenylephrine and ephedrine are still considered to be safe during pregnancy.⁴⁴

External monitoring of the fetal heart rate and the uterus is only an indirect measure of fetoplacental physiology, but it assists in the early recognition of the potentially deleterious effects of CPB, thus enabling timely intervention to minimize fetal mortality.¹³,²⁰,²⁷ Continual and frequent monitoring of the fetus postoperatively is also recommended, because there is a risk of preterm labor in this period.⁴⁸

**Management Approach for Cardiac Surgery in Pregnant Patients**

The principles for the management of pregnant patients who are undergoing cardiac surgery with CPB are similar to those for pregnant women who are undergoing surgical intervention. These include attention to maternal well-being, avoidance of teratogenic drugs, avoidance of intrauterine hypoxia, and the prevention of premature labor. In addition, strong consideration should be given to the administration of maternal corticosteroids⁴⁰ to initiate endothelial membrane stability and maturation of the fetal lungs, which can substantially improve fetal outcome, should delivery occur after CPB.

In summary, the chief concerns in the optimal management of pregnant patients who are undergoing CPB are the control of temperature, perfusion pressure, and the nature of the bypass flow. Current evidence favors maintaining normothermic CPB, avoiding the use of vasoconstrictors (which may have a profound effect on the placental unit), and maintaining both high hematocrit and high flow rates. Fetal hypoperfusion and hypoxia may also be ameliorated by the use of pulsatile perfusion. Other adjuncts, such as the use of arterial line filters or of leukocyte-depleting filtration, have not been evaluated in the specific context of pregnant patients.

**Cardiac Surgery without Cardiopulmonary Bypass in Pregnant Patients**

Aggarwal and co-authors⁵⁰ reported that closed mitral valvotomy offers excellent results, comparable to those of nonsurgical treatments; it is still the procedure of choice in certain parts of the world.

Off-pump coronary artery bypass grafting (OPCAB) is a safe and accepted technique for coronary revascularization; however, its role in pregnancy needs further evaluation. The current medical literature contains only 1 documented case of OPCAB in pregnancy—that of a 32-year-old woman in the 22nd week of gestation who experienced a spontaneous dissection of the left anterior descending artery and subsequently gave birth to a healthy baby at term. Hemodynamic instability during OPCAB—invoking a drop in mean systemic arterial pressure and a rise in mean pulmonary pressure during construction of the distal anastomosis and manipulation of the heart to gain access to the lateral and posterior branches—may not be tolerated well by pregnant patients and could cause significant placental malperfusion. However, if only an anterior target (such as the left anterior descending coronary artery territory) is grafted, this can usually be undertaken with minimal hemodynamic compromise and avoidance of all the inherent risks of CPB, such as hemodilution, the systemic inflammatory response to CPB, and the increased risk of bleeding.⁵²

To further our understanding of placental and fetoplacental response to OPCAB, it is helpful to look at the way that other vascular beds, such as the splanchic circulations, behave during coronary artery bypass grafting (CABG) with CPB or OPCAB. If we hypothesize that the splanchic and the fetoplacental circulations will respond in a manner similar to hemodynamic insults during CABG with CPB or OPCAB, much can be learned from looking at splanchic and gastrointestinal physiology during cardiac operations. L-Lactate concentration has been shown to be significantly higher in the gut mucosa of patients who undergo CABG with CPB than with OPCAB.⁵³ This supports the view that OPCAB produces less dysfunction in these vascular beds than does CPB. When Fiore and colleagues⁴¹ looked at superior mesenteric blood flow during OPCAB, they found that cardiac manipulation to gain access to inferior and
lateral walls caused hemodynamic changes that resulted in significant mesenteric hypoperfusion. Such information may help us plan the approach to revascularization that we wish to undertake in pregnant patients who develop spontaneous coronary artery dissection. Single- or 2-vessel spontaneous dissections, particularly in the left anterior descending or the right coronary artery territory, are probable the best candidates for off-pump surgery: use of OPCAB in these instances avoids manipulation of the heart to reach the posterior and inferior surfaces, thus averting hemodynamic instability and its effects on the fetoplacental circulation.

More observational data should be gathered in the setting of OPCAB in pregnancy, with special attention to the fetal and maternal cardiovascular responses, before OPCAB can safely be recommended as the optimal therapy for this challenging group of patients.

References