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Valvular Heart Disease in Pregnancy

M. Panja, S. Basu, D. Kumar

Introduction

Valvular heart disease in young women is most commonly due to rheumatic heart disease, congenital abnormalities, or previous endocarditis and may increase the maternal and fetal risks associated with pregnancy. The likelihood of an adverse outcome is related to the type and severity of maternal valvular disease and the resulting abnormalities of functional capacity, left ventricular function, and pulmonary pressure. Clinical recommendations concerning valvular heart disease and pregnancy are based on limited data from case reports and observational studies or on inferences from data for other groups of patients.

Normal hemodynamic changes

To understand the consequences of valvular heart disease during pregnancy, it is important to review the hemodynamic changes that occur in all pregnant women. First, blood volume increases, starting at the sixth week and rising rapidly until mid pregnancy. Thereafter, the rise continues but at a much slower rate. The increase in blood volume ranges from about 20% to 100%, with an average of 50%. Proportionately, plasma volume increases much more than erythrocyte mass, which can lead to physiologic anemia. An estrogen-mediated stimulation of the renin-angiotensin system that results in sodium and water retention appears to be the mechanism underlying the blood volume increase. Similarly, cardiac output increases steadily during pregnancy up to about 34 weeks of gestation, when it begins to fall. The average increase in cardiac output is about 45% by 24 weeks of gestation. The increase is due to both the expansion in blood volume and the augmentation of stroke volume and heart rate. Thus, early in pregnancy, an increase in stroke volume (20% to 30%) is responsible for the increase in cardiac output. Later in pregnancy, the rise is related to an acceleration of heart rate (25%), since stroke volume decreases as a result of vena caval compression. In addition, cardiac output rises still higher and heart rate increases during labor and delivery. After delivery, when vena caval compression is relieved, there is a surge of venous return that augments cardiac output and places additional burden on the heart.

Other hemodynamic changes associated with pregnancy are a 21% decrease in systemic vascular resistance and a 34% decrease in pulmonary vascular resistance; there is no change in left ventricular contractility. Pregnant women tend to maintain normal left ventricular filling pressures because of left ventricular dilatation with an increase in left ventricular mass, as measured by echocardiography[1]

Symptoms of normal pregnancy can mimic those of valvular heart disease. Specifically, women with normal pregnancies may have exertional dyspnea, orthopnea, fatigue, lower extremity edema, and presyncope. Physical examination can also be confusing in a woman whose pregnancy is progressing normally. For example, a and v waves are prominent on jugular venous pressure studies, pulse pressure is increased, and the maximal apical impulse is laterally displaced. The first heart sound is accentuated, and the pulmonary component of the second heart sound is also increased. The third heart sound is heard in about 80% of pregnant women, whereas the fourth heart sound is rarely heard. The universal early ejection flow systolic murmur of less than grade 3/6 along the left sternal border is heard in 90% of pregnant women and may be enhanced by anemia.

The presence of certain physical signs in pregnant women should raise suspicion of cardiac abnormalities. These include a loud fourth heart sound, a diastolic murmur, a grade 3/6 or greater systolic murmur, a fixed split of the second heart sound, and an opening snap. The presence of one or more of these signs should signal the need for echocardiographic evaluation.

Consequences of valvular heart disease during pregnancy

Although the prevalence of clinically significant maternal heart disease during pregnancy is low (probably less than 1 per cent)[2] its presence increases the risk of adverse maternal, fetal, and neonatal outcomes[3].

The American Heart Association and the American College of Cardiology have classified maternal and fetal risk during pregnancy on the basis of the type of valvular abnormality and the New York Heart Association (NYHA) functional class (Table1).[4]

The absolute risk conferred on a given woman by pregnancy also depends on additional clinical factors. Recent analyses of the outcomes of pregnancy in Canada[2] identified predictors of adverse maternal and fetal outcomes in a heterogeneous group of women with congenital or acquired heart disease (546 women and 599 pregnancies). Approximately40 per cent of the women had a primary valve disorder. Adverse maternal cardiac events (pulmonary edema, sustained bradyarrhythmia or tachyarrhythmia requiring therapy, stroke, cardiac arrest, or death) occurred in 13 per cent of completed pregnancies and were significantly more likely among women with reduced left ventricular systolic function (an ejection fraction below 40 per cent), left heart obstruction (aortic **stenosis with a valve** area of less than 1.5 cm^2 or mitral stenosis with a valve area of less than 2.0 cm^2) previous cardiovascular events (heart failure, transient ischemic attack, or stroke), or disease of NYHA class II or higher[3].These outcomes occurred in 4 per cent of the women with none of these risk factors, 27 per cent of those with one risk factor, and 62 per cent of those with two or more risk factors. The three women who died all had two or more risk factors. Abnormal functional capacity (NYHA class II or higher) and left heart obstruction were also predictors of neonatal complications, including premature birth, intrauterine growth retardation, respiratory distress syndrome, intraventricular hemorrhage, and death. Other predictors of adverse fetal outcomes included the use of anticoagulant drugs throughout pregnancy, smoking during pregnancy, and multiple gestation. Fetal mortality was 4 per cent among pregnancies in women with one or more of these risk factors, as compared with 2 per cent among those with none of these risk factors. The risks of adverse fetal outcomes were also substantially greater among women older than 35 years of age or younger than 20 years of age than among women between these ages with similar risk factors. Indexes of risk derived from and validated in this population may be used in the counseling of women before conception.

In another cohort including 64 women with valvular heart disease,[5] most adverse maternal outcomes, including heart failure and arrhythmias, occurred in patients with clinically significant mitral or aortic stenosis (valve area, < 1.5 cm). Premature birth, intrauterine growth retardation, and low birth weight were also more common

Table I : Classification of Valvular Heart Lesions According to Maternal, Fetal and Neonatal Risk.*

Low Maternal and Fetal Risk	High Maternal and Fetal Risk	High Maternal Risk	High Neonatal Risk
Asymptomatic aortic stenosis with a low mean outflow gradient (< 50 mm Hg) in the presence of normal left ventricular systolic function	Severe aortic stenosis with or without symptoms	Reduced left ventricular systolic function (left ventricular ejection fraction < 40%)	Maternal age < 20 yr or > 35 yr
Aortic regurgitation of NYHA Class I or II with normal left ventricular systolic function	Aortic regurgitation with NYHA class III or IV symptom	Previous heart failure	Use of anticoagulant therapy throughout pregnancy
Mitral regurgitation of NYHA class I or II with normal left ventricular systolic function	Mitral stenosis with NYHA class II, III or IV symptoms	Previous stroke or transient ischemic attack	Smoking during pregnancy
Mitral-valve prolapsed with no mitral regurgitation or with mild-to-moderate mitral regurgitation and with normal left ventricular systolic function	Mitral regurgitation with NYHA class III or IV symptoms		Multiple gestations
Mild-to-moderate mitral stenosis (mitral-valve area > 1.5 cm^2, gradient < 5 mm Hg) without severe pulmonary hypertension	Aortic-valve disease, mitral-valve disease, or both, resulting in severe pulmonary hypertension (pulmonary pressure > 75% of systemic pressures)		
Mild-moderate pulmonary-valve stenosis	Aortic-valve disease, or both, with left ventricular systolic dysfunction (ejection fraction < 0.40)		
	Maternal cyanosis		
	Reduced functional status (NYHA class III or IV)		

*Derived from ACC/AHA Guidelines[6] and Siu et al.[4,5] NYHA denotes New York Heart Association.

among the offspring of the women in this subgroup. The fetus is at increased risk for congenital heart disease, if the underlying maternal valvular disease is congenital[6]. Although these studies included few patients, with pulmonary hypertension, primary pulmonary hypertension is associated with high maternal mortality (33 to 40 per cent), as well as with an increased rate of adverse neonatal events[7]. Secondary pulmonary hypertension due to valvular disease is associated with an increased rate of adverse maternal events, but the absolute risk of such events is unclear.

A systolic pulmonary-artery pressure that is more than 75 per cent as high as the systemic pressure places the woman at high risk.

Mitral stenosis

Mitral stenosis is the most common chronic rheumatic valvular lesion in pregnancy. Since the natural history of rheumatic mitral stenosis typically includes a 20- to 25-year asymptomatic period, symptoms often first appear during pregnancy. Congenital fusion of the commissures, or "parachute mitral valve," and left atrial myxoma are other causes of mitral stenosis during pregnancy.

Symptoms related to mitral stenosis reflect an increased pressure gradient across the mitral valve. This pressure gradient is a function of both the cross-sectional area of the valve and the flow through the valve. The rise in cardiac output during pregnancy increases the pressure gradient.

Hemodynamic abnormalities in a pregnant woman with mitral stenosis depend on the severity of the disease but normally include increased left atrial pressure associated with elevation of both pulmonary venous and arterial pressures. This results in pulmonary edema, pulmonary hypertension, and right ventricular failure. In addition, an increase in heart rate caused by exercise, fever, or emotional

stress decreases diastolic left ventricular filling time and further elevates left atrial pressure and reduces cardiac output. This increase in pressure also predisposes pregnant women to development of atrial arrhythmias. Furthermore, loss of atrial contractility associated with a rapid ventricular response has devastating effects and can lead to pulmonary edema.

Clinical presentation

Pregnant women with mitral stenosis present clinically with symptoms of both left-sided heart failure and right ventricular failure, depending on the severity and duration of the valvular disease. Symptoms of left-sided heart failure are more common and include orthopnea, paroxysmal nocturnal dyspnea, and dyspnea on exertion. Unless the patient has long-standing valve disease, symptoms of right ventricular failure are less common and include peripheral edema and ascites, which in pregnancy are difficult to recognize as being related to valvular heart disease.

Careful examination should include a search for an opening snap and a diastolic rumbling murmur with presystolic accentuation, which are classic auscultatory findings in mitral stenosis. The presence of elevated jugular venous pressure, hepatomegaly, a loud pulmonary component of the second heart sound, and right ventricular heave on examination also supports a diagnosis of mitral stenosis.

Diagnostic assessment

Echocardiography is the diagnostic study of choice for evaluation of mitral stenosis in pregnant women and both confirms the diagnosis and helps determine the severity of the stenosis. In addition, the echocardiogram allows assessment of pulmonary pressures, right ventricular function, mitral regurgitation, and the configuration of the subvalvular apparatus, which is important in determining the success of percutaneous mitral balloon valvuloplasty (PMBV). Invasive diagnostic testing is rarely indicated in pregnant women with mitral stenosis.

Medical management

For women with mild or moderate symptoms during pregnancy, medical therapy is directed at the treatment of volume overload and includes diuretic therapy, the avoidance of excessive salt, and the reduction of physical activity. Beta-blockers attenuate the increases in heart rate and prolong the diastolic filling period, which provides symptomatic benefit. Development of atrial fibrillation requires prompt treatment, including cardioversion. Beta-blockers and digoxin are used for rate control. If suppressive antiarrhythmic therapy is needed, procainamide and quinidine are the drugs with which we have the most extensive experience. Because of the increased risk of systemic embolism in patients with mitral stenosis and atrial fibrillation, anticoagulant therapy is indicated. Patients with severe symptoms (NYHA class III or IV) who undergo balloon mitral valvuloplasty or valve surgery before conceiving appear to tolerate pregnancy with fewer complications than similar women who are treated medically or tighten mitral stenosis (a valve area of less than 1.0 cm^2)

Most pregnant women with mitral stenosis can be managed medically. Since an increased preload contributes to the exacerbation of heart failure, it is prudent to restrict salt and fluid intake. Diuretics should be used judiciously to avoid hypotension and increased heart rate. Use of beta-blocking drugs to slow the heart rate can dramatically improve symptoms. Digoxin (Lanoxin) is not very effective because the adrenergically driven increased heart rate overrides its effect.

Balloon valvuloplasty

PMBV is an invasive procedure that is being used more often because of its proven safety. However, PMBV is contraindicated in women who have moderate to severe mitral regurgitation, calcified mitral valve, or clot in the left atrium. In addition, even though PMBV is considered a fairly safe procedure, it should be used cautiously to avoid radiation exposure during the first trimester. 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. Risks to the fetus associated with exposure to radiation may be reduced by avoiding exposure to radiation during the first half of pregnancy.

Pregnant women who are to be exposed to radiation should have the uterus shielded and should be informed about the possible risks. Mitral valvuloplasty has also been performed under transesophageal echocardiographic guidance, eliminating these risks. Open cardiac surgery has been performed during pregnancy for severe mitral stenosis. Maternal outcomes are approximately the same as those among nonpregnant patients, but there is fetal loss in 10 to 30 per cent of cases.

Surgical intervention

In early investigations, open commissurotomy and valve replacements carried a maternal mortality rate of about 5% and a fetal mortality rate of 20% to 30%. Many factors (e.g., anesthetic agents used, hypothermia during surgery) can adversely affect the outcome. Improved cardiopulmonary bypass techniques have resulted in improved outcomes. A recent study of 168 pregnant women who underwent open commissurotomy showed no maternal mortality and a fetal mortality of 1.8%[8] Prosthetic mitral valve replacement is now a feasible option in patients who are not candidates for either PMBV or open commissurotomy.

Labor and delivery

In view of the increase in cardiac output during labor and after delivery, it is important to plan management carefully. Vaginal delivery is possible in most patients with mitral stenosis. However, optimal management may require invasive haemodynamic studies in patients with moderate to severe stenosis. Oxygen should be given to reduce pulmonary pressures, and fluid restriction and use of diuretics and epidural anesthesia are recommended as well. Vigoros manual uterine massage and oxytocin infusion can reduce the risk of excessive blood loss.

Mitral regurgitation

This condition is usually well tolerated in pregnancy, presumably because of left ventricular unloading secondary to the physiologic fall in systemic vascular resistance. The cause of mitral regurgitation during pregnancy has changed over the years. In the past, it was usually a consequence of rheumatic fever, but today it is more often related to mitral valve prolapse complicated by ruptured chordae tendinae. Other possible causes are Libman-Sacks endocarditis, infective endocarditis, Marfan syndrome and pseudoxanthoma elasticum, Ehlers-Danlos syndrome, and dilated cardiomyopathy.

Mitral regurgitation leads to a progressive increase in the volume of blood going to the left ventricle, which results in enlargement of both the left ventricle and the left atrium. Moreover, left ventricular cavity dilatation is associated with mitral valve annular dilatation and asynergic contraction of the papillary muscle, which exacerbate mitral regurgitation.

Increased left ventricular volume and left atrial enlargement are associated with an elevation of pulmonary venous and arterial pressures, leading to pulmonary hypertension and right-sided heart failure. Because of the decrease in left ventricular afterload associated with mitral regurgitation, systolic wall stress is also lowered. These changes are more pronounced in pregnancy because of a reduction in systemic vascular resistance.

Symptoms and physical examination

Mitral regurgitation during pregnancy is usually well tolerated. Symptoms may include dyspnea on exertion, orthopnea, and paroxysmal nocturnal dyspnea. The apical impulse of the left ventricle is shifted outward, and a holosystolic murmur is heard at the apex on auscultation. The murmur radiates toward the axilla and increases during expiration. Some pregnant women with mitral regurgitation present with atrial fibrillation associated with heart failure and cardiomegaly.

If tricuspid regurgitation is associated with mitral regurgitation, peripheral edema might be present, a right ventricular heave may be noted on palpation, and a systolic murmur may be heard along the left lower sternal border on auscultation. Unlike the murmur of mitral regurgitation, the tricuspid regurgitation murmur increases with inspiration.

Assessment and diagnosis

Doppler echocardiography is useful in diagnosis of chronic mitral regurgitation. The following information can be obtained from these studies:

Evaluation of the structure of the mitral valve. Mitral valve prolapse can cause "hammocking" of the mitral valve in M mode, which is evidence of vegetative growths on the valve. Assessment of left ventricular size and function, left atrial size, and left atrial appendage thrombosis Evaluation of structure and function of subvalvular apparatus (papillary muscle, chordae tendinae) Assessment of severity of mitral regurgitation

Management

In symptomatic pregnant patients with mitral regurgitation, hydralazine hydrochloride, diuretics, and digoxin can be used when systolic function is impaired. If severe symptomatic mitral regurgitation due to mitral valve prolapse is found, surgical mitral valve repair may be a good option because it avoids the need for anticoagulant therapy. Mitral valve replacement can be done as a last resort. In most cases, maternal and neonatal outcomes are good. However, women with pulmonary arterial pressure greater than 50 mm Hg are at increased risk for complications.

Aortic stenosis

Symptomatic aortic valve disease is less common than mitral valve disease in pregnant women. In the United States, congenital aortic stenosis secondary to membrane on the bicuspid aortic valve appears to be the predominant cause. In contrast, rheumatic heart disease is the most common cause in developing countries. During pregnancy, women with bicuspid aortic valves are at risk for aortic dissection related to the effects of hormones on connective tissue.

The pressure gradient across the aortic valve is responsible for the hemodynamic changes in aortic stenosis. The increase in left ventricular systolic pressure needed to maintain sufficient pressure in arterial circulation leads to increased stress on the ventricular wall. To compensate for this, left ventricular hypertrophy develops, which can result in diastolic dysfunction, fibrosis, diminished coronary flow reserve, and late systolic failure.

An increase in stroke volume and a fall in peripheral resistance are largely responsible for the increase in the gradient across the aortic valve. The clinical consequences of the increased aortic gradient depend on the degree of preexisting left ventricular hypertrophy and left ventricular systolic function. When compensatory changes in the left ventricle are inadequate to meet the demands imposed by the need for increased cardiac output late in pregnancy, symptoms develop. This usually occurs with moderate to severe aortic stenosis.

Clinical findings

Clinical presentation and symptoms depend on the degree of aortic stenosis. Women with aortic valve areas more than 1.0 cm^2 tolerate pregnancy well and are asymptomatic. However, women with more severe aortic stenosis may have symptoms of left-sided heart failure (dyspnea on exertion). Syncope or presyncope is rare, and pulmonary edema is even more unusual. However, arrhythmias are sometimes present. Because symptoms of aortic stenosis are similar to those of normal pregnancy, diagnosis of this condition is challenging. Physical findings vary with the severity of the disease. The left ventricular impulse is sustained and displaced laterally. A systolic ejection murmur is heard along the right sternal border and radiates toward the carotid arteries, and a systolic ejection click is heard. A fourth heart sound may be present, suggesting abnormal diastolic function. The presence of

pulsus parvus et tardus suggests hemodynamically significant aortic stenosis.

Assessment and diagnosis

Diagnosis can be confirmed with echocardiography. The aortic gradient and valve area can be calculated by Doppler flow studies. In addition, echocardiography can detect left ventricular hypertrophy. Estimation of ejection fraction and left ventricular dimensions may be useful to predict outcome during pregnancy, labor, and delivery. Women with an ejection fraction less than 55% are at high risk for development of heart failure during pregnancy. Cardiac catheterization is indicated if the clinical picture is consistent with severe aortic stenosis, if noninvasive data are inconclusive, and if percutaneous balloon valvuloplasty is needed. Fetal echocardiography is indicated if the mother has congenital aortic stenosis, since the risk that the fetus has similar anomalies is 15%.

Management

Patients who are symptomatic or who have a peak outflow gradient of more than 50 mm Hg are advised to delay conception until after surgical correction.

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.

The severity of the condition and its symptoms largely determines management of aortic stenosis. Most asymptomatic patients and those who have mild to moderate stenosis can be managed with medical therapy and close monitoring. It is important to maximize cardiac output and fetal blood flow by avoiding intense exercise, potent vasodilators, and diuretics. In patients with low ejection fractions, digoxin can be used, provided drug levels are monitored regularly.

Percutaneous balloon valvuloplasty and aortic valve replacement are options for management. Balloon valvuloplasty can be used as a bridge to valve replacement in women who are too ill to undergo surgery. The risk of death in nonpregnant patients managed in centers experienced in this technique is about 5%. In pregnancy, balloon valvuloplasty carries added risk because circulation to the fetus is stopped for a short time during the procedure. However, several studies of balloon valvuloplasty for severe aortic stenosis during pregnancy suggest favorable outcomes for both mother and fetus [9]

Balloon valvuloplasty is not the preferred treatment in patients with calcified aortic valves or in the presence of significant aortic regurgitation. In those circumstances, valve replacement is indicated. The choice of a bioprosthetic versus a mechanical valve should be individualized. Bioprosthetic valves avoid the need for long-term anticoagulant therapy.

Labor and delivery

Vaginal delivery is preferred unless there is an obstetric indication for cesarean section. Avoidance of severe vasodilatation and maintenance of an adequate fluid balance are paramount so that cardiac output is not compromised. Low epidural anesthesia may be used to minimize vasodilatory effects, and antibiotic prophylaxis should be given to patients with previous endocarditis. In general, outcomes for both the mother and the fetus are favorable. However, some evidence suggests that as many as 20% of women who have severe aortic stenosis choose to have therapeutic abortion.

Aortic insufficiency

Aortic insufficiency in pregnancy can be either acute or chronic. The acute form is caused by aortic dissection, bacterial endocarditis, or malfunction of a prosthetic valve. Because the left ventricle has no time to adapt to volume overload, pulmonary edema and cardiogenic shock often occur. Acute aortic insufficiency should be considered a surgical emergency, and valve replacement is urgent, even in pregnancy.

Another condition that requires emergency surgery is proximal aortic dissection with aortic insufficiency. Marfan syndrome, bicuspid aortic valve, and hypertension add to deleterious hormonal effects and are predisposing conditions for aortic dissection.

In pregnant women, chronic aortic insufficiency is often associated with a bicuspid aortic valve or rheumatic heart disease. The gradual increase in left ventricular volume overload allows the left ventricle to adapt by increasing left ventricular end-diastolic diameter. This adaptation appears to maintain the forward flow unless systolic dysfunction sets in. Therefore, as with mitral insufficiency, chronic aortic insufficiency is well tolerated during pregnancy.

Clinical presentation

Patients with chronic aortic insufficiency usually present with dyspnea, decreased exercise tolerance, and chest pain. Some patients have syncope due to arrhythmias and left ventricular dysfunction. Pregnant women tolerate aortic regurgitation well because of the normal peripheral vasodilatation during pregnancy, which improves hemodynamic parameters in aortic insufficiency.

On the other hand, women with aortic insufficiency and either New York Heart Association functional class I or II symptoms or systolic ventricular dysfunction do not tolerate pregnancy well. Findings on physical examination are typical of hyperdynamic circulation. Such findings may complicate diagnosis, since a hyperdynamic state also can be associated with normal pregnancy. Physical findings include a wide pulse pressure, brisk carotid pulse, and mildly displaced apical impulse. An early diastolic murmur on the left sternal border and soft second heart sounds are clear clues to aortic insufficiency.

Assessment

Transthoracic echocardiography and Doppler flow studies are helpful in making a diagnosis and assessing the severity of aortic insufficiency. Transesophageal echocardiography can be used to detect vegetation in bacterial endocarditis and aortic dissection. Cardiac catheterization is usually not indicated, but magnetic resonance imaging can be helpful in diagnosis of aortic dissection. Fetal echocardiography is indicated in women with congenital abnormalities of the aortic valve or Marfan syndrome.

Management

In patients with chronic aortic regurgitation, management depends on the severity of the disease and symptoms. In asymptomatic patients, close monitoring is all that is needed. Symptomatic patients can be treated with vasodilators, including hydralazine, nitrates, and diuretics. Digoxin may be beneficial in patients who have systolic dysfunction. Use of angiotensin-converting enzyme inhibitors is contraindicated during pregnancy.

Special concerns with valvular heart disease

Pregnant women with valvular heart disease are no more likely to have bacterial endocarditis than non-pregnant women with such heart disease. However, prophylactic therapy does seem warranted when valvular heart disease is present (see box below)[10,11] Similarly, women who require anticoagulant therapy during pregnancy need special care. Recommended antibiotic prophylaxis for high-risk women undergoing genitourinary or gastrointestinal procedures

Category	Drug and dosage
High-risk patient	Ampicillin, 2 g IM or IV, plus gentamicin sulfate 1.5 mg/kg IV 30 min before procedure; ampicillin, 1 g IV, or amoxicillin 1 g PO 6 hr after procedure
High-risk patient who has penicillin allergy	Vancomycin HCl, 1 g IV over 2 hr, Plus gentamicin sulfate, 1.5 mg/kg IV 30 min before procedure

Most pregnant women with valvular heart disease can be managed medically. However, severe symptomatic disease may pose a threat to the survival of both mother and fetus. In this situation,

Table 2 : Fetal Effects of, Maternal Indications for, and Risks Associated with Drugs Used in the Treatment of Maternal Valvular Heart Disease.*

Drug	Fetal Effects	Indications in Pregnant Patients with Valve Disease	Risk Category
Diuretics			
Furosemide	Increased Urinary sodium and potassium levels	To decrease Congestion Associated with valvular heart disease	C_m
Antihypertensive agents			
Beta-blockers	Possible decreased heart rate, possible lower birth weight	Hypertension, supraventricular arrhythmias, to control heart rate in women with clinically significant mitral stenosis	D_m
Methyldopa	No major adverse effects	Hypertension	C
Vasodilator agents			
Angiotensin-converting-enzyme inhibitors	Urogenital defects, death, intrauterine growth retardation	Not indicated during pregnancy and should be discountinued	D_m
Hydralazine	No major adverse effects	For vasodilation in cases of aortic regurgitation and ventricular dysfunction	C_m
Nitrates	Possible bradycardia	Rarely used to decrease venous congestion	B-C_m
Anticoagulant and antithrombotic agents			
Warfarin	Hemorrhage, developmental abnormalities when used between wk 6 and 12 of gestation	For anticoagulation of mechanical heart valves, valvular heart disease with associated atrial fibrillation during wk 12-36 of pregnancy	D_m
Unfractionated heparin	Hemorrhage, no congenital defects	For anticoagulation of mechanical heart, valves, valvular heart disease with associated atrial fibrillation during wk 6-12 and after wk 36 of pregnancy	C_m
Low-molecular-weight heparin	Hemorrhage	Not currently indicated during pregnancy	D_m
Aspirin	Hemorrhage, prolongation of labor, low birth weight (When taken in high doses)	Low-dose aspirin (81 mg/day) occasionally used as an adjunct in patients with previous embolic events or prosthetic-valve thrombosis	C
Antiarrhythmic agents			
Digoxin	No major adverse effects	For suppression of supraventricular arrhythmias	C
Adenosine	No major adverse effects	For immediate conversion of supraventricular arrhythmias	C_m
Quinidine	High doses may be oxytocic	Occasionally used for suppression of atrial or ventricular arrhythmias	C_m
Procainamide	No major adverse effects	Occasionally used for suppression of atrial ventricular arrhythmias	C_m
Amiodarone	Hypothyroidism, intrauterine growth retardation, premature birth	Rarely used during pregnancy because of side effect; may be used to suppress atrial or ventricular arrhythmias in high-risk patients	C_m

Table 3 : Recommendations for the Evaluation and Care of Women of Childbearing Age with Mechanical Valve Prostheses Who are taking Anticoagulants.*

Before Conception
• Clinical evaluation of cardiac functional status and previous cardiac events
• Echocardiographic assessment of ventricular and valvular function and pulmonary pressure
• Discussion of risks associated with pregnancy
• Discussion of risk and benefits associated with anticoagulant therapy
• Family or pregnancy planning
Conception
• Change to therapeutic, adjusted-dose unfractionated heparin (titrated to a mid-interval therapeutic activated partial-thromboplastin time or anti-factor Xa level) from time of confirmed pregnancy through wk 12
Completion of first trimester
• Warfarin therapy, wk 12-36
Week 36 †
• Discontinue warfarin
• Change to unfractionated heparin titrated to a therapeutic activated partial-thromboplastin time or anti-factor Xa level
Delivery
• Restart heparin therapy 4 to 6 hr after delivery if no contraindications
• Resume warfarin therapy the night after delivery if no bleeding complications

*Information is from ACC/AHA Guidelines, [6] Gohlke-Barwolf et al., [43] and Ginsberg et al. [42]

† If labor begins while the woman is receiving warfarin, anticoagulation should be reversed and cesarean delivery should be performed.

valve replacement may be the only option. When needed, valve replacement is best performed during the second trimester. It is important to point out that this procedure involves cardiopulmonary bypass and its associated complications. Hypothermia during bypass can increase the chance of fetal bradycardia and death, and anesthetic agents used during surgery may have teratogenic effects, according to anecdotal reports. Blood pressure during cardiopulmonary bypass should be carefully maintained to ensure adequate placental perfusion. Fetal heart monitoring is an excellent way to assess placental perfusion.

Pregnancy in women who have prosthetic valves carries a high risk of morbidity and mortality for both mother and fetus. The hypercoagulable state increases the likelihood of thrombosis and thromboembolic complications associated with artificial heart valves. Pregnancy outcome has been good when patients were managed with heparin for the first 12 weeks, followed by warfarin sodium anticoagulation. The fetal outcome has been better with bioprosthetic valves, compared with mechanical prostheses, in both aortic and mitral positions.

Outcome of pregnancy in women with mechanical or biological prostheses [12]

Study	No. of pregnancies	Live births (%)	Thromboembolic complications	
			Valve thrombosis (%)	Emboli (%)
Mechanical valves				
Hanania	95	53	11	9
Sbarouni	151	73	9	5
Born	35	63	8	3
Bioprosthetic valves				
Hanania	60	80	0	0
Sbarouni	63	83	0	0
Born	25	100	0	5

Adapted from Baughman

Conclusion

Pregnant women who have valvular disease represent a major challenge for physicians involved in their care. Careful history taking and physical examination, along with a judicious use of diagnostic tools (mainly echocardiography), can lead to better management and ultimately to excellent outcomes for both mother and baby.

If the patient has abnormal functional capacity, left ventricular dysfunction, valve obstruction, or a history of heart failure or embolic events, she should be counseled regarding the risk of adverse cardiac outcomes. In patients with more than one such risk factor, pregnancy may not be advisable. A patient who becomes pregnant should be seen by a cardiologist once each trimester and more often if complications ensue. Serial echocardiography during pregnancy generally is not warranted. Patients with prosthetic valves must be counseled regarding the risks and benefits associated with anticoagulant therapy. Although definitive data are lacking, we would recommend the use of warfarin to achieve a target INR of 2.0 to 3.0 throughout most of the pregnancy. The only exceptions are the periods between 6 and 12 weeks of pregnancy and after 36 weeks of pregnancy,when we would opt for the closely monitored use of unfractionated heparin (Table 3)

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