

HEART DISEASE IN PREGNANCY 5

Prosthetic Heart Valves and Arrhythmias in Pregnancy

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Abstract

The majority of women with bioprosthetic valves do not require anticoagulation during pregnancy. In women with mechanical valves, a detailed discussion of the advantages and disadvantages of the three anticoagulant options (warfarin, unfractionated heparin and low molecular weight heparin) is indicated. The majority of women with arrhythmias during pregnancy have a benign increased rate of atrial or ventricular premature beats. Those women who are hemodynamically stable can be reassured and do not usually require treatment. Women with more ominous arrhythmias should be managed in collaboration with a cardiologist, usually using the same agents that would be chosen in the non-pregnant patient, including electrical cardioversion when necessary.

This is the fifth and final article in a series reviewing in detail the assessment and management of specific cardiac disorders in pregnancy.

Résumé

La plupart des femmes portant des bioprothèses cardiaques ne nécessitent pas une anticoagulation au cours de la grossesse. Chez les femmes portant des valvules mécaniques, une analyse détaillée des avantages et des désavantages des trois options disponibles en matière d'anticoagulants (warfarine, héparine non fractionnée et héparine de faible poids moléculaire) s'avère indiquée. La plupart des femmes qui connaissent des arythmies au cours de la grossesse présentent un taux accru bénin de battements auriculaires ou ventriculaires prématurés. Les femmes qui sont stables sur le plan hémodynamique peuvent être rassurées et ne nécessitent pas habituellement de traitement. Les femmes qui connaissent des arythmies plus inquiétantes devraient être prises en charge, conjointement avec un cardiologue, en ayant habituellement recours aux mêmes agents que ceux que l'on choisirait pour une patiente n'étant pas enceinte (y compris la cardioversion électrique, au besoin).

Il s'agit du cinquième et dernier article d'une série analysant en détail l'évaluation et la prise en charge de troubles cardiaques particuliers au cours de la grossesse.

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Prosthetic Cardiac Valves in Pregnancy

Patients with biologic prosthetic valves do not routinely require anticoagulation in pregnancy.¹⁻⁵ However, it has been recommended that women who have coexisting dilated atria or atrial fibrillation receive anticoagulation.⁶⁻⁸ Badduke et al. described 17 women with bioprosthetic valves who were followed through 37 pregnancies.¹ Two of these patients, with atrial fibrillation, received anticoagulant therapy. Six pregnancies (16.2%) resulted in spontaneous abortion, and a further five ended with therapeutic termination. Excluding the therapeutic abortions, the live birth rate was 71.9%. The preterm delivery rate was 18.8% and included two stillbirths. There were no neonatal deaths or congenital anomalies. Twelve pregnant patients (70.6%) experienced a valve-related complication, whereas the complication rate in a group of 70 non-pregnant controls with bioprosthetic valves was 30%. Ten pregnant patients (59%) subsequently required replacement of their damaged valves. The corresponding replacement rate for the non-pregnant controls was 18.6%. These findings of successful pregnancy at the expense of a significant reoperation rate for biologic prostheses are supported by others.^{5,9}

Conversely, Sbarouni and Oakley reported a series of 182 patients with prosthetic cardiac valves who had 214 pregnancies and found better maternal and fetal outcomes for patients with bioprosthetic valves than for those with mechanical valves.⁴ The live birth rate was 91% for bioprosthetic valves and 84% for mechanical valves, but this difference was not statistically significant. The incidence of prematurity was significantly higher in the mechanical valve group (25%) than in the bioprosthetic group (7%). Although 17 (35%) of bioprosthetic valves deteriorated and two required replacement during pregnancy, there were no maternal deaths in the bioprostheses group. However, there were six maternal deaths (4.5%) in

the mechanical valve group. Including four of the patients who died, 13 patients had mechanical valve thrombosis, and five of the 13 required valve replacement. Eight other patients with a mechanical valve suffered embolic events, and two of these patients died. Seven patients with mechanical valves had episodes of bleeding that were severe enough to require transfusion of more than two units of blood. Two of these patients required hysterectomy for postpartum bleeding.

The need for anticoagulation with mechanical valve replacement is widely acknowledged, although the optimal agent for anticoagulation is unclear. Use of warfarin in pregnancy is controversial. Although some experts advise using warfarin or its derivatives throughout pregnancy, the great majority recommend avoiding this anticoagulant if possible, especially during the first trimester.^{3,5-7,9-15}

Warfarin and its derivatives are vitamin K antagonists and readily cross the placenta.¹¹ Reported abnormalities in infants exposed in the first trimester, often collectively called warfarin embryopathy, include midface and nasal hypoplasia, optic atrophy, hypoplasia of the digits, stippled epiphyses, mental impairment, seizures, scoliosis, deafness and hearing loss, and congenital heart disease.^{11,16} There is also an increased risk of central nervous system defects in those exposed in the second or third trimester. Risks of first-trimester spontaneous abortion, stillbirth or neonatal death, and fetal hemorrhage are increased.¹⁶

The frequency with which these anomalies are associated with warfarin varies. Sbarouni and Oakley reported no WE in 46 patients with first trimester exposure.⁴ In contrast, Iturbe-Alessio et al. described 72 patients with artificial cardiac valves who were divided into three groups.¹⁵ Group I (n = 23) received the warfarin derivative acenocoumarol until the sixth week of gestation. This was then replaced with heparin 5000 units subcutaneously every 12 hours until the twelfth week of gestation, when the acenocoumarol was restarted. Group II (n = 12) received heparin substitution as well but not until after the seventh week of gestation. The acenocoumarol was restarted after the twelfth week of gestation, as in group I. In group III (n = 37) the acenocoumarol was continued throughout pregnancy. There were no cases of WE in group I; however, the incidence of WE in groups II and III was 25% and 29.6% respectively. It was also observed in this study that three women, one of whom died, had massive thrombosis of

their mechanical valve during treatment with low-dose heparin therapy, and another woman had a pulmonary embolus. The authors concluded that a fixed dose of 5000 units of subcutaneous heparin every 12 hours did not provide adequate protection against thromboembolic complications in pregnant women with artificial heart valves.

Whereas warfarin and its derivatives are more widely accepted for use during pregnancy in Europe, heparin is the drug of choice in North America. In the pregnant woman with a mechanical valve, a joint guideline of the American College of Chest Physicians and the American Heart Association recommends full anticoagulation with sodium heparin to achieve a midinterval activated partial thromboplastin time of two to three times the control value. This is usually accomplished using a split dose of sodium heparin (17 500 to 20 000 units subcutaneously every 12 hours).¹⁷ However, thromboembolic events have been described in patients with mechanical heart valves who were receiving heparin doses large enough to keep the partial thromboplastin time greater than two times normal.¹⁸

The use of low molecular weight heparin has not resolved the controversy over the choice of anticoagulant in the pregnant population.¹⁹ Low molecular weight heparins appear to be associated with a very low rate of thrombotic complications in the non-pregnant population. In an evidence-based comparative review, Seshadri et al. reported only a single thromboembolic event in 391 non-pregnant women with mechanical valves.¹⁹ However, a recent randomized trial comparing use of low molecular weight heparin (enoxaparin), unfractionated heparin, and warfarin in a group of pregnant women with mechanical valves was prematurely stopped after the recruitment of only 12 subjects because two of the women receiving low molecular weight heparin died from heart valve thrombosis.¹⁹ Both of these women had blood drawn for assay of anti-factor Xa levels as part of the study protocol. Despite receiving standard doses of low molecular weight heparin, these two women had anti-factor Xa levels that were sub-therapeutic. This finding raises the following questions: were these thrombotic complications associated with the use of low molecular weight heparin or the dosage, and should anti-factor Xa levels be used during pregnancy to adjust dosing in this high risk population?¹⁹ Currently, there are no firm guidelines to direct clinicians in the best choice of anticoagulant in the pregnant woman with a mechanical valve.

ABBREVIATIONS

SVT	supraventricular tachycardia
WE	warfarin embryopathy
WPW	Wolff-Parkinson-White

Cardiac Arrhythmias in Pregnancy

Serious cardiac arrhythmias are uncommon in pregnancy but may be associated with congenital or acquired cardiac lesions. Few antiarrhythmic agents have been investigated well enough to understand their safety for use in pregnancy.

Most antiarrhythmic agents are FDA category C, which states these agents should be given only if the potential benefit justifies the potential risk to the fetus. An in-depth review of this subject has been carried out by Cox and Gardner.²⁰

The prevalence of maternal cardiac arrhythmias is unknown. Symptoms of palpitations are not uncommon in pregnancy; however, these are usually of a benign nature, secondary to ectopic beats or non-sustained paroxysmal atrial tachycardia. After appropriate evaluation and reassurance, most patients do not require treatment, and symptoms are transient.²¹ However, if symptoms are severe or associated with hemodynamic instability, then treatment is indicated.^{20,21} Underlying modifiable causes of symptoms include hyperthyroidism, use of caffeine, alcohol, tobacco, cocaine or other illicit drugs, over-the-counter sympathomimetic compounds such as nasal decongestants, and sympathomimetic tocolytic agents such as terbutaline.

Premature Atrial Beats

Premature atrial beats occur in most adults, and their incidence has been reported to be increased in pregnancy.²² In the reproductive age group these are not usually associated with organic heart disease. Precipitating factors, as listed above, should be sought during history taking and eliminated or reduced if possible. Patients should be reassured and treatment limited to those with severe symptoms. Administration of β -blockers is usually effective. In patients with underlying organic heart disease, premature atrial beats may be associated with congestive heart failure and may require treatment with digitalis and diuretic agents.²¹

Supraventricular Tachycardia

For unknown reasons, the incidence of paroxysmal supraventricular tachycardia is increased in pregnancy; in patients with a history of paroxysmal SVT the number of episodes and their severity are often increased.^{23, 24} This is especially true in the third trimester.²⁵ Medical treatment is similar to that used in the non-pregnant patient and includes Valsalva manoeuvres and verapamil.^{21,26,27} Case reports of the use of adenosine in pregnancy detail the successful control of SVT without fetal effect.²⁸⁻³⁰ Adenosine is usually given as an initial 6 mg intravenous bolus followed by a saline flush. This can be followed by a further 12 mg intravenous bolus if the rate has not been controlled after two minutes, and repeated once more if necessary. Because adenosine has a rapid onset of action, low complication rate, and short half-life, several authors suggest that it may be the drug of choice for SVT in pregnancy.^{28,29} If medical therapy is unsuccessful, or if patients are hemodynamically unstable, then electrical cardioversion using 10 to 100 joules should be attempted.^{21,27}

Once patients have been cardioverted, prophylaxis is not necessary unless attacks are frequent or are poorly tolerated. If prophylaxis is indicated, then digitalis 0.125 to 0.5 mg daily usually provides adequate treatment. Other options include verapamil 80 to 120 mg every six to eight hours, propranolol 10 to 40 mg every six hours, or quinidine 200 to 400 mg every six hours.^{21,27}

Atrial Fibrillation and Flutter

Atrial fibrillation and flutter in the reproductive age group are usually associated with underlying cardiac disease. Atrial fibrillation may be associated with rheumatic mitral valve disease, hypertensive heart disease, cardiomyopathy, ostium secundum atrial septal defect, Ebstein's anomaly, thyrotoxicosis, chronic lung disease, and pulmonary embolism.²¹

For patients with acute atrial fibrillation, cardiac compromise, and hemodynamic instability, electrical cardioversion is indicated, using 50 to 100 joules. In patients who are hemodynamically stable, medical cardioversion can be accomplished using digitalis with or without a β -blocker, verapamil, or diltiazem to slow the ventricular rate, followed by quinidine to stimulate conversion. Quinidine has been successfully used in pregnant women for 60 years without evidence of teratogenesis or adverse fetal outcome, although there is some suggestion that chronic maternal ingestion may increase the risk of sudden cardiac death.²⁰ If fibrillation has persisted for more than a few days, then anticoagulation with heparin is indicated.

Atrial flutter is usually seen in patients with chronic heart disease and enlarged atria.³⁰ Like patients with atrial fibrillation, those with flutter who are hemodynamically unstable usually respond to electrical cardioversion of low energy (10 to 50 joules).^{30,31} In the stable patient the ventricular rate can be slowed using digitalis and propranolol, and quinidine may be used for conversion to sinus rhythm. Once conversion has occurred, a maintenance dose of digitalis, quinidine, verapamil, or propranolol should be given.^{21,27}

Ventricular Premature Beats

Like premature atrial beats, ventricular premature beats seem to be more common during pregnancy.²² They are usually benign and do not require treatment. Inciting factors such as alcohol, caffeine, fatigue, and anxiety may play a role and should be reduced if possible.

Ventricular Tachycardia and Fibrillation

The treatment of the pregnant patient with ventricular tachycardia or fibrillation does not differ from the treatment of the non-pregnant patient. The mainstay of hemodynamically stable ventricular tachycardia is lidocaine. The successful use of other antiarrhythmics to control

ventricular arrhythmias in pregnancy has been reported, but in numbers too small to comment on the true risks to the fetus.²⁰ Other antiarrhythmics that have been used include mexiletine, moricizine, flecainide, and propafenone. Amiodarone has also been successfully used in pregnancy but concerns exist about its potential relationship with fetal hypothyroidism because it contains iodine in significant amounts. Until further information is available, its use should be restricted to women with life-threatening arrhythmias that are refractory to the effects of other agents.²⁰ As a class, β -blocking agents have been more widely studied in pregnancy. There is no evidence of teratogenicity with use of these agents, although some question remains about an association with intrauterine growth restriction.²⁰ For unstable patients with ventricular tachycardia or those with ventricular fibrillation, electrical cardioversion is required at energy levels of 200 to 400 joules.

Wolff-Parkinson-White Syndrome

Wolff-Parkinson-White syndrome is seen most often in patients without underlying cardiac disease, although it has been associated with Ebstein's anomaly, hypertrophic cardiomyopathy, levotransposition of the great arteries with ventricular inversion, and mitral valve prolapse.²⁷ Treatment of arrhythmias related to WPW syndrome in pregnant patients is similar to that in non-pregnant patients. Adenosine has been successfully used to control supraventricular tachycardia in pregnant patients with WPW syndrome.^{28,29,32} Electrical cardioversion may be required.^{27,30,31}

Atrioventricular Conduction Block

Pregnant patients with first- and second-degree heart block are treated in the same way as non-pregnant patients. More than 100 case reports of third-degree heart block in pregnancy have been published.³³ The severity of symptoms depends on the level of the heart block (at or below the atrioventricular node). Mendelson described 21 cases of complete heart block in pregnancy and found that almost half of these patients had an associated ventricular septal defect.²² Patients who have undergone previous open-heart surgery are also at risk for complete heart block.³⁴

Pregnant women with advanced atrioventricular conduction block may remain completely asymptomatic during pregnancy; however, caution is advised at the time of labour and delivery. The increased vagal tone associated with the Valsalva manoeuvre in labour may precipitate significant ventricular bradycardia and symptoms of presyncope or syncope. Continuous cardiac monitoring in labour is recommended with the availability of a temporary pacemaker, if necessary.^{34,35} The increased cardiac output normally seen in labour cannot be compensated for by an increase in heart

rate in this population—only by an increase in stroke volume. Therefore, judicious attention must be paid to fluid management, because these patients are at considerable risk of pulmonary edema.³⁴

Some authors suggest that pacemakers should not be placed in the breast or abdominal areas in young women, as the pregnancy-associated changes in these areas can lead to skin tension and ulceration over the pacemaker unit.^{36,37} However, others have described successful pregnancies with pacemakers placed in the standard subpectoral pouch.³⁴

Electrical Cardioversion in Pregnancy

Electrical cardioversion appears to be safe in pregnancy, although the overall experience is limited. Sanchez-Diaz et al. reported 20 cases in which electrical cardioversion was used on an emergency basis during pregnancy.³⁸ All of the patients were successfully cardioverted, and no immediate adverse effects were reported. Ueland et al. reviewed 15 cases of electrical cardioversion use in pregnancy.³⁹ The cardioversion was successful in 13 of the 15 cases, using energy levels of 50 to 300 joules. One fetus developed a non-reactive heart rate tracing after cardioversion and emergency Caesarean section was subsequently performed for suspected fetal distress, which in fact was not present. One patient underwent electrical cardioversion seven times in three pregnancies for control of paroxysmal atrial tachycardia that was refractory to conventional medical therapy.³⁹ Each cardioversion was performed at an energy level of 100 joules without maternal or fetal complication. Although inducing fetal arrhythmia by electrical discharge is theoretically possible, this has not been reported. Work in animal models suggests that the fetal heart may have a higher threshold for fibrillation than the adult heart.⁴⁰ Indications for the use of electrical cardioversion in pregnancy include hemodynamically unstable arrhythmias and those refractory to medical therapy.

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