GUIDELINES FOR THE MANAGEMENT OF PATIENTS WITH VALVULAR HEART DISEASE

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VALVULAR HEART DISEASE AFFECTS a large number of patients and requires diagnostic procedures and decisions regarding their long-term management. Unlike many other forms of cardiovascular disease, there is a scarcity of large-scale multicenter trials addressing the diagnosis and treatment of patients with valvular heart disease. Recently, the American College of Cardiology (ACC) and the American Heart Association (AHA) jointly published new guidelines for the management of patients with valvular heart disease.1,2 This review is based primarily on these guidelines. It is important to emphasize that these guidelines attempt to define practices that meet the needs of most patients in most circumstances. The ultimate judgment regarding care of a particular patient must be made by the physician looking after the patient.

Specific Valve Lesions

**Aortic Stenosis**

The normal adult aortic valve orifice is ~ 3.0 cm² to 4.0 cm². Aortic stenosis is divided as mild (area > 1.5 cm²), moderate (area > 1.0 cm² to 1.5 cm²), or severe (area ~ 1.0 cm²). When stenosis is severe and cardiac output is normal, the mean transvalvular pressure gradient is generally > 50 mm Hg. Therapeutic decisions, particularly related to corrective surgery, are based largely on the presence or absence of symptoms. Thus the absolute valve area (transvalvular pressure gradient) is not usually the primary determinant of the need for aortic valve replacement (A VR). In most patients, the severity of the stenotic lesion can be defined with Doppler echocardiographic measurements of a mean transvalvular pressure gradient and a derived valve area.2 In some patients, it may be necessary to proceed with cardiac catheterization and coronary angiography at the time of initial evaluation. This is appropriate, for example, if there is a discrepancy between the clinical and echocardiographic examinations, or if the patient is symptomatic and A VR is planned. Exercise testing in adults with aortic stenosis (AS) has been discouraged largely because of concerns about safety. Certainly, it should not be performed in symptomatic patients.4

In the absence of serious comorbid conditions, A VR is indicated in virtually all symptomatic patients with severe AS. However, patients with severe LV dysfunction, particularly those with so called low-gradient AS, represent a difficult management decision.5 A VR should not be performed in such patients when they do not have anatomically severe stenosis. In patients with severe AS, even those with a low transvalvular pressure gradient, A VR results in hemodynamic improvement and better functional status. Patients with severe AS, with or without symptoms who are undergoing coronary artery bypass surgery should undergo A VR at the time of revascularization.

**Acute Aortic Regurgitation**

Many of the characteristic physical findings of chronic AR are modified or absent when valvular regurgitation is acute. Echocardiography is indispensable in confirming the severity and
etiology of valvular regurgitation.

Death from pulmonary edema, ventricular arrhythmias, or circulatory collapse is common in acute severe AR. Early surgical intervention is recommended. Nitroprusside and possibly inotropic agents, such as dopamine or dobutamine, may be helpful in treating the patient temporarily before surgery. Intra-aortic balloon pump is contraindicated. Although β-blockers are often used in treating aortic dissection, they should be used cautiously, if at all, in the setting of acute AR because they will block compensatory tachycardia.

**Chronic Aortic Regurgitations**

A large number of studies have identified LV systolic function and end-systolic size as the most important determinants of survival and postoperative LV function in patients undergoing AVR for chronic AR. Patients with evidence of LV systolic dysfunction, even if asymptomatic or minimally symptomatic, should undergo AVR before more severe symptoms or more severe ventricular dysfunction develops.

If the patient is asymptomatic, leading an active lifestyle and has a preserved systolic function on a good quality echocardiogram, no other testing is necessary. If the patient has severe AR and is sedentary or has equivocal symptoms, exercise testing is helpful to assess functional capacity, symptomatic responses and hemodynamic effects of exercise. When patients are symptomatic, it is reasonable to proceed directly with cardiac catheterization and angiography if the echocardiogram is of insufficient quality to assess LV function or severity of AR.

**Medical Therapy**

Therapy with vasodilating agents is designed to improve forward stroke volume and reduce regurgitant volume. These effects have been observed in patients who received oral therapy with hydralazine and long-acting nifedipine. Less consistent results have been reported with ACE inhibitors. Chronic vasodilator therapy is recommended in: 1) patients with severe AR or who have symptoms and/or LV dysfunction when surgery is not recommended because of additional factors; 2) asymptomatic patients with severe AR who have LV dilatation but normal systolic function; 3) asymptomatic patients with hypertension and any degree of regurgitation; and 4) patients with persistent LV systolic dysfunction after, AVR. Long-term ACE inhibitor therapy should be considered.

Vasodilator therapy is not recommended for asymptomatic patients with mild AR and normal LV function in the absence of systemic hypertension. It is not an alternative to surgery for asymptomatic or symptomatic patients with severe AR and LV systolic dysfunction.

**Serial follow-up**

Asymptomatic patients with mild AR, little or no LV dilatation, and normal LV systolic function can be seen on a yearly basis with instructions to alert the physician if symptoms develop in the interim. A routine echocardiography can be performed every 2 to 3 years in such patients. 1 Asymptomatic patients with normal systolic function but severe AR and significant LV dilatation (end-diastolic dimension > 60 mm) require more frequent and careful reevaluation, with a history and physical examination every 6 months and echocardiography every 6 to 12 months. It is reasonable to obtain serial echocardiograms as often as every 4 to 6 months in patients with more advanced LV dilatation (end-diastolic dimension > 70 mm or end-systolic dimension > 50 mm). Patients with echocardiographic evidence of progressive ventricular dilatation or declining systolic function have a greater likelihood of developing symptoms or LV dysfunction, and should have more frequent followup examinations (every 6 months) than those with stable LV function.

**Indications for cardiac catheterization**

Cardiac catheterization is not required in patients with chronic AR unless there are questions about the severity of AR, hemodynamic abnormalities, or LV dysfunction despite physical examination and non-invasive testing or unless AVR is contemplated and there is a need to assess coronary anatomy.

**Recommendations for aortic valve replacement in chronic severe aortic regurgitation**

A VR is recommended in the following group of patients with pure severe aortic regurgitation: 1) patients with NYHA functional class III or IV symptoms and preserved LV systolic function, defined as normal ejection fraction (EF) at rest (ejection fraction ~ 0.50); 2) patients with NYHA functional class II symptoms and preserved LV
systolic function (EF ≈ 0.50 at rest) but with progressive LV dilatation or declining EF at rest on serial studies or declining effort tolerance on exercise testing; 3) asymptomatic or symptomatic patients with mild to moderate LV dysfunction at rest (EF 0.25 to 0.49); 12 and 4) patients with severe LV dilatation (end-diastolic dimension > 75 mm or end-systolic dimension > 55 mm), even if EF is normal. 10

Even in patients with NYHA functional class IV symptoms and EF < 0.25, the high risks associated with AVR and subsequent medical management of LV dysfunction are usually a better alternative than the higher risks of long-term medical management alone. 3

Women tend to develop symptoms and/or LV systolic dysfunction with less LV dilatation than men 14 - this appears to be related to body size. Hence, LV dimensions alone may be misleading in small patients of either gender, and the threshold values of end-diastolic and end-systolic dimension recommended for AVR in asymptomatic patients (75 mm and 55 mm, respectively) may need to be reduced for such patients.

An echocardiogram should be performed soon after surgery to assess the results of surgery. A good predictor of subsequent LV systolic function is the reduction in LV end-diastolic dimension, which declines significantly within the first week or two of operation. This is an excellent marker of the functional success of AVR. IS

Mitral Stenosis

The normal mitral valve area is 4.0 cm² to 5.0 cm². Narrowing of the valve area to < 2.5 cm² must occur before development of symptoms. A mitral valve area > 1.5 cm² usually does not produce symptoms at rest. The diagnostic tool of choice in the evaluation of a patient with MS is 2-D and Doppler echocardiography.

Evaluation and management of the asymptomatic patient

In the asymptomatic patient who has documented mild MS (valve area > 1.5 cm² and mean gradient < 5 mm Hg), no further evaluation is needed on the initial work-up. If ~ is more significant, further evaluation should be considered if the mitral valve morphology appears to be suitable for mitral valvotomy. Patients with moderate pulmonary hypertension at rest (pulmonary artery systolic pressure > 50 mm Hg) and pliable mitral valve leaflets may be considered for percutaneous mitral valvotomy even if they deny symptoms. In patients who lead a sedentary lifestyle, an exercise test with Doppler echocardiography is useful. 16 A rise in transmural gradient > 15 mm Hg and pulmonary artery systolic pressure > 60 mm Hg may be an indication to consider percutaneous valvotomy if mitral valve morphology is suitable. 2

Medical therapy

Beta-blockers or calcium channel blockers may be of benefit in patients with sinus rhythm who have exertional symptoms. Digitalis does not benefit patients with MS in sinus rhythm unless there is left and/or right ventricular dysfunction. Salt-restriction and intermittent administration of a diuretic are useful if there is evidence of pulmonary vascular congestion.

Atrial fibrillation develops in 30% to 40% of patients with symptomatic MS, and systemic embolization may occur in 10% to 20% of patients with MS. Anticoagulation is recommended for patients with atrial fibrillation, paroxysmal or chronic, and for patients with a prior embolic event. 2

Indications for surgical or percutaneous valvotomy

Percutaneous mitral balloon valvotomy has become an accepted alternative to surgical approaches in selected patients. Overall, 80% to 95% of patients may have a successful procedure, which is defined as a mitral valve area > 1.5 cm² and a decrease in left atrial pressure to ≤ 18 mm Hg in the absence of complications. The most common acute complications include severe MR (2% to 10%), and a residual atrial septal defect (ASD). A large ASD (> 1.5:1 left-to-right shunt) occurs in up to 12% of patients with double balloon technique and in < 5% with Inoue balloon technique. The mortality for patients who undergo balloon valvotomy has ranged from 1% to 2%. 17

Recommendations for percutaneous mitral balloon valvotomy

1) Symptomatic patients (NYHA functional class II, III, or IV), moderate or severe MS (mitral valve area ≤ 1.5 cm²), and valve morphology favorable for percutaneous balloon valvotomy in the absence of left atrial thrombus or moderate to severe MR; 2) asymptomatic patients with moderate or severe MS
(mitral valve area ≤ 1.5 cm²) and valve morphology favorable for percutaneous balloon valvotomy who have pulmonary hypertension (pulmonary artery systolic pressure > 50 mm Hg at rest or 60 mm Hg with exercise) in the absence of left atrial thrombus or moderate to severe MR. 3) patients with NYHA functional class III to IV symptoms, moderate or severe MS (mitral valve area ≤ 1.5 cm²) and a non-pliable calcified valve who are at high risk for surgery in the absence of left atrial thrombus or moderate to severe MR (class IIa recommendation).

Recommendations for mitral valve repair for mitral stenosis.

1) Patients with NYHA functional class III to IV symptoms, moderate or severe MS (mitral valve area ≤ 1.5 cm²), and valve morphology favorable for repair if percutaneous mitral balloon valvotomy is not available; 2) patients with NYHA functional class III to class IV symptoms, moderate or severe MS (mitral valve area ≤ 1.5 cm²), and valve morphology favorable for repair if a left atrial thrombus is present despite anticoagulation; 3) patients with NYHA functional class III to class IV symptoms, moderate or severe MS (mitral valve area ≤ 1.5 cm²), and a non-pliable or calcified valve with the decision to proceed with either repair or replacement made at the time of the operation.

Mitral valve replacement (MVR)
The risk of MVR is dependent on multiple factors. In the young healthy person, MVR can be performed with a risk of < 5%. However, in the older patients with concomitant medical problems or pulmonary hypertension at systolic levels, the risk of MVR may be 10% to 20%.

Recommendations for mitral valve replacement for mitral stenosis.

1) Patients with moderate or severe MS (mitral valve area ≤ 1.5 cm²), and NYHA functional class III to IV symptoms who are not considered candidates for percutaneous balloon valvotomy or mitral valve repair; 2) patients with moderate MS (mitral valve area ≤ 1.5 cm²) and severe pulmonary hypertension (PASP > 60 to 80 mg Hg) with NYHA functional class I to II symptoms who are not considered for percutaneous balloon valvotomy or mitral valve repair.

Management of patients after valvotomy
A baseline echocardiogram should be performed after the procedure to assess hemodynamics as well as to exclude significant complications. The echocardiogram should be performed ~ 72 hours after the procedure because acute changes in atrial and ventricular compliance immediately after the procedure affect the reliability of the half-time method in calculating valve area. Patients with severe MR, or large atrial septal defect should be considered for early operation. However, the majority of small left-to-right shunts at the atrial level will close spontaneously over the course of 6 months. In patients with a history of atrial fibrillation, warfarin should be restarted 1 to 2 days after the procedure.

Mitral Valve Prolapse (MVP)
MVP is the most common form of Valvular heart disease and occurs in 2% to 6% of the population. In most patient studies, the MVP syndrome is associated with a benign prognosis. The age-adjusted survival rate of both men and women with MVP is similar to that of individuals without this common clinical entity.

Management of the asymptomatic patient
All patients with MVP should have an initial echocardiogram. Serial echocardiograms are not usually necessary in the asymptomatic patient with MVP unless there are clinical indications for severe or worsening MR. Reassurance is a major part of the management of patients with MVP, most of whom are asymptomatic or have no cardiac symptoms and lack a high-risk profile. A normal lifestyle and regular exercise is encouraged. Antibiotic prophylaxis for prevention of infective endocarditis is indicated in: 1) patients with characteristic systolic click-murmur complex; 2) patients with isolated systolic click and echo cardiographic evidence of MVP and MR; and 3) patients with isolated systolic click and echocardiographic evidence of high risk MVP such as leaflet thickening, elongated chordae, left atrial enlargement or LV dilatation.

Management of the symptomatic patient
Patients with MVP and palpitations associated with mild tachyarrhythmias and those with chest pain, anxiety, or fatigue often respond to therapy
with β-blockers. However, in many cases, the cessation of stimulants such as caffeine, alcohol, and cigarettes may be sufficient to control symptoms. In patients with recurrent palpitations, continuous or event-activated ambulatory monitoring may reveal whether arrhythmias are the cause of symptoms and indicate appropriate treatment of existing arrhythmias. The indications for electrophysiological testing are similar to those in the general population.21

Dysrhythmias

Daily aspirin therapy (80 to 325 mg/day) is recommended for patients with MVP and documented focal neurological events who are in sinus rhythm with no atrial thrombi. Such patients should avoid smoking cigarettes and using oral contraceptives. Long-term anticoagulation with warfarin is recommended for post-stroke patients with MVP and patients with MVP and recurrent transient ischemic attacks while receiving aspirin (INR 2 to 3). Warfarin is indicated in patients >65 years with MVP and atrial fibrillation and those with MR, hypertension, or a history of heart failure. Aspirin therapy is satisfactory in patients with atrial fibrillation who are < 65, have no MR, and have no history of hypertension or heart failure.22

Asymptomatic patients with MVP and no significant MR can be clinically evaluated every 3 to 5 years. Serial echocardiography is performed only if there is development of symptoms consistent with cardiovascular disease and a change in physical findings suggesting development of significant MR, and in patients with high-risk characteristics observed on the initial echocardiogram. Patients with high-risk characteristics, including those with moderate to severe MR, should receive a follow-up once a year:

Mitral Regurgitation

Acute severe mitral regurgitation

In acute severe MR, the hemodynamic overload cannot often be tolerated, and mitral valve repair or replacement must often be performed urgently. In a normotensive patient with acute severe MR, nitroprusside is the drug of choice. However, it should not be administered alone to patients with hypotension. Combination therapy with an inotropic agent (such as dobutamine) and nitroprusside is of benefit in some patients. In such patients, aortic balloon counterpulsation may be helpful. These measures can be used to stabilize hemodynamics while preparing for surgery.

Chronic mitral regurgitation

The duration of the compensated phase of MR varies but may last for many years. Asymptomatic patients with mild MR and no evidence of LV enlargement or dysfunction or pulmonary hypertension can be followed up on a yearly basis with instructions to alert the physician if symptoms develop in the interim. In patients with moderate MR, clinical evaluation should be performed annually, and echocardiography is not necessary more than once a year. Asymptomatic patients with severe MR should be followed up with a history, physical examination, and echocardiography every 6 to 12 months. Preoperative ejection fraction is an important predictor of postoperative survival in patients with chronic MR.

Echocardiographic LV end-systolic dimension can be used in the timing of mitral valve surgery. End-systolic dimension should be < 45 mm before surgery to ensure normal postoperative LV function.23 If patients become symptomatic, they should undergo mitral valve surgery, even if LV function is normal.

Medical therapy

For the asymptomatic patient with chronic MR, there is no generally accepted medical therapy. The use of vasodilators may appear to be logical for the same reasons that they are effective in acute MR and chronic AR. However, in the absence of systemic hypertension, there is no known indication for the use of vasodilating drugs in asymptomatic patients with preserved LV function. Although the risk of embolism with the combination of MR and atrial fibrillation may be less than that of MS and atrial fibrillation, INR should be maintained between 2 and 3 in patients with MR who develop atrial fibrillation.

In patients with MR who develop symptoms but have preserved LV function, surgery is the most appropriate therapy.

Recommendations for mitral valve surgery in non ischemic severe mitral regurgitation

1) Acute symptomatic MR in which repair is likely;
2) Patients with severe MR and NYHA functional class II, III, or IV symptoms despite normal LV function on echocardiography (ejection fraction
> 0.60 and end-systolic dimension < 45 mm;
3) Symptomatic or asymptomatic patients with mild LV dysfunction (ejection fraction 0.50 to 0.60, and end-systolic dimension 45 to 50 mm);
4) Symptomatic or asymptomatic patients with moderate LV dysfunction (ejection fraction 0.30 to 0.50, and/or end-systolic dimension 50 to 55 mm);
5) Asymptomatic patients with preserved LV function and atrial fibrillation (recommendation class IIa);
6) Asymptomatic patients with preserved LV function and pulmonary hypertension (PASP > 50 mm Hg at rest or > 60 mm Hg with exercise) (recommendation class IIa); and
7) Patients with severe LV dysfunction (ejection fraction < 0.30 and/or end-systolic dimension > 55 mm) in whom chordal preservation is highly likely (recommendation class IIa). I

Ischemic Mitral Regurgitation
Correction of acute severe ischemic MR usually requires valve surgery. Unlike non-ischemic MR in which mitral repair is clearly the operation of choice, the best operation for ischemic MR is controversial. 2

Multiple Valve Disease
Unlike the management of a severe pure valve lesion, solid guidelines for mixed disease are difficult to establish. The most logical approach is to surgically correct disease that produces more than mild symptoms or, in the case of AS-dominant aortic valve disease, to operate in the presence of even mild symptoms. In regurgitant dominant lesions surgery can be delayed until symptoms develop or asymptomatic LV dysfunction as defined by markers used in pure regurgitant disease, become apparent. The use of vasodilators to delay surgery in patients with asymptomatic mixed disease is untested.

Combined Mitral Stenosis and Aortic Regurgitation
Mechanical correction of both lesions is eventually necessary in most patients. Development of symptoms or pulmonary hypertension is the usual indication for intervention. When mechanical correction is anticipated in predominant MS, balloon mitral valvotomy followed by AVR, obviates the need for double-valve replacement which has a higher risk of complications than single-valve replacement. In most cases, it is advisable to perform mitral valvotomy first and then follow the patient for symptomatic improvement. If symptoms disappear, correction of AR can be delayed.

Combined Mitral Stenosis and Tricuspid Regurgitation
If the mitral valve anatomy is favorable for percutaneous balloon valvotomy and there is concomitant pulmonary hypertension, valvotomy should be performed regardless of symptoms status. After successful mitral valvotomy, pulmonary hypertension and TR almost always diminish.25

If mitral valve surgery is performed, concomitant tricuspid annuloplasty should be considered, especially if there are preoperative signs or symptoms of right-heart failure, rather than risking severe persistent TR, which may necessitate a second operation.26 However, TR that seems severe on echocardiography but does not cause elevation of right atrial or right ventricular diastolic pressure will generally improve greatly after MVR. If intraoperative assessment suggests that TR is functional without significant dilatation of the tricuspid annulus, it may not be necessary to perform an annuloplasty.

Combined Mitral and Aortic Regurgitation
The most logical approach is the same as for mixed single valve disease, i.e., to determine which lesion is dominant and to treat primarily according to that lesion.

Combined Mitral and Aortic Stenosis
If the AS appears mild and the mitral valve is acceptable for balloon valvotomy, this should be attempted first. If mitral balloon valvotomy is successful, the aortic valve should then be reevaluated.

Combined Aortic Stenosis and Mitral Regurgitation
Patients with severe AS and severe MR with symptoms, LV dysfunction, or pulmonary hypertension should undergo combined A VR and
MVR or mitral valve repair. However, in patients with severe AS and lesser degree of MR, the severity of MR improves greatly after isolated A VR. Intraoperative transesophageal echocardiography and, if necessary, visual inspection of the mitral valve should be performed at the time of A VR to determine whether additional mitral valve surgery is warranted in these patients.

In patients with mild to moderate AS and severe MR in whom surgery on the mitral valve is indicated because of symptoms, LV dysfunction, or pulmonary hypertension, preoperative assessment of the severity of AS may be difficult because of reduced forward stroke volume. If the mean aortic valve gradient is ~30 mm Hg, A VR should be performed.

Tricuspid Valve Disease

Patients with severe TR of any cause have a poor long-term outcome because of RV dysfunction and/or systemic venous congestion. Annuloplasty is recommended for severe TR and pulmonary hypertension in patients with mitral valve disease requiring mitral valve surgery. When the valve leaflets themselves are diseased, abnormal or destroyed, valve replacement is often necessary. Biological prosthesis is preferred.

Management of Valvular Disease in Pregnancy

Most experts would agree that pregnancy should be discouraged for some conditions, such as cyanotic heart disease, Eisenmenger syndrome, or severe pulmonary hypertension. Valvular heart lesions associated with increased maternal and fetal risk during pregnancy include severe AS, MR or AR with NYHA functional class III & IV symptoms, MS with NYHA functional class II to IV symptoms, valve disease resulting in severe pulmonary hypertension (pulmonary pressure >75% of systemic pressures), valves disease with severe LV dysfunction (EF <0.40), mechanical prosthetic valves requiring anticoagulation, and AR in Marfan syndrome.

Mitral stenosis

Young pregnant women with a previous history of acute rheumatic fever and carditis should continue to receive penicillin prophylaxis as indicated in the non-pregnant state. Patients with mild to moderate MS can almost always be managed with judicious use of diuretics and β-blockers. Patients with severe MS should be considered for percutaneous balloon mitral valvotomy before conception. Patients with severe MS who develop NYHA functional class III to IV symptoms during pregnancy should undergo percutaneous balloon valvotomy.

Mitral regurgitation

Mitril regurgitation can usually be managed medically, although on rare occasions mitral valve surgery is required.

Aortic stenosis

Patient with mild to moderate obstruction and normal LV Systolic function can usually be managed conservatively through the entire pregnancy. Patients with more severe obstruction (pressure gradient >50 mm Hg) or symptoms should be advised to delay conception until relief of AS can be obtained. For those rare women with severe AS whose disease is first diagnosed during pregnancy, consideration may have to be given to either percutaneous aortic balloon valvotomy or surgery before labor. These procedures are fraught with danger to both the mother and fetus.

Management of Valvular Disease in Pregnancy

Aortic regurgitation

Isolated AR, like MR, can usually be managed medically with a combination of diuretics and if necessary vasodilatory therapy.

Anticoagulation during pregnancy

The true incidence of warfarin embryopathy is estimated at 4% to 10%. The risk may be dose related and appears to be highest if exposure occurs the 6th to 12th week of gestation. On the other hand, the incidence of thromboembolic complications, including fatal valve thrombosis in high-risk pregnant women managed with subcutaneous heparin is 12% to 24%.

Recommendations for Anticoagulation During Pregnancy: Week 1 Through 35 in Patients with Mechanical Prosthetic Valves

1) The decision whether to use heparin during the first trimester or to continue oral anticoagulation throughout pregnancy should be made after full
discussion with the patient and her partner. If she choose to change to heparin for the first trimester, she should be made aware that heparin is less safe for her, with a higher risk of both thrombosis and bleeding, and that any risk to the mother also jeopardizes the baby; 2) high-risk women (a history of thromboembolism or an older generation mechanical prosthesis in the mitral position) who choose not to take warfarin during the first trimester should receive continuous unfractionated heparin intravenously in a dose to prolong the mid-interval (6 hours after dosing) a PT or 2 to 3 times control. Transition to warfarin can occur thereafter; 3) in patients receiving warfarin, INR should be maintained between 2.0 and 3.0 with the lowest possible dose of warfarin, and low-dose aspirin should be added.

Low-molecular weight (LMW) heparins offer several potential advantages over unfractionated heparin. LMW heparins do not cross the placenta. Although they have been used to treat deep venous thrombosis in pregnant patients, there is no data to guide their use in the management of patients with mechanical heart valves.30 Dip–damole is not an acceptable alternative to aspirin because of its harmful effects on the fetus. Neither warfarin nor heparin is contraindicated in postpartum mothers who breast-feed.31

Management of Patients with Prosthetic Heart Valves

Antibiotic prophylaxis

All patients with prosthetic valves need appropriate antibiotics for prophylaxis against infective endocarditis. Patients with rheumatic heart disease continue to need antibiotics for prophylaxis against recurrence of rheumatic carditis.

Antithrombotic therapy

All patients with mechanical valves require warfarin therapy. The risk of embolism is greater with a valve in the mitral position (mechanical or biological) compared with a valve in the aortic position:32

1. Mechanical valves: For mechanical prosthesis in the mitral position, INR should be maintained between 2.5 and 3.5 for all mechanical valves. The addition of low-dose aspirin (80 to 100 mg/day) to warfarin therapy (INR 2.0 to 3.5) further decreases the risk of thromboembolism and should be strongly considered unless there is a contraindication to the use of aspirin.34 A slight increase in risk of bleeding with this combination should be kept in mind.35

2. Biological valves: Because of an increased risk of thromboembolism in the first 3 months after implantation of a biological prosthetic valve, anticoagulation with warfarin is usually recommended, although in several centers, only aspirin is used for biological valves in the aortic position. Risk is particularly high in the first few days after surgery, and heparin should be started as soon as the risk of increased surgical bleeding is reduced. After three months, the biological valves can be treated like native valve disease.3

3. Excessive anticoagulation: Patients with prosthetic heart valves with INR in the range of 5 to 10 who are not bleeding can be managed by withholding warfarin and administering 2.5 mg of vitamin K, orally.37 INR should be determined after 24 hours and subsequently as needed. In emergency situation, the use of fresh frozen plasma is preferable to high dose vitamin K, especially if given parenterally.

4. Antithrombotic therapy in patients requiring noncardiac surgery/dental care: For most patients on warfarin, the drug should be stopped before the procedure so that the INR is ≤ 1.5 (which is often 48 to 72 hours after warfarin is discontinued). The risk of stopping warfarin is relatively slight if the drug is withheld for only a few days. However, individuals at very high risk should be treated with heparin therapy until INR returns to the desired range. Admission to the hospital or a delay in discharge to given heparin is usually unnecessary. Heparin can usually be reserved for those who had recent thrombosis or embolus (arbitrarily within 1 year), those with demonstrated thrombotic problems when previously off therapy, those with the Bjork-Shiley valve, and those ~ 3 "risk factors". Risk factors are atrial fibrillation, previous thromboembolism, a hypercoagulable condition, mechanical prosthesis and LV dysfunction (ejection fraction < 0.30).1
5. Antithrombotic therapy in patients needing cardiac catheterization/angiography: Most centers stop heparin six hours before cardiac catheterization and resume it 12 hours after the procedure. In an emergent or semi-emergent situation, cardiac catheterization can be performed with a patient taking warfarin, but preferably the drug should be stopped ~72 hours before the procedure so that INR is ~1.5. The drug should be restarted as soon as the procedure is completed. If a patient has one or more risk factors that predispose to thromboembolism, heparin should be started when INR falls below 2.0 and continued before the procedure so that INR is achieved. For patients with a large clot or evidence of valve obstruction and who are in NYHA functional class III or IV because of prosthetic thrombosis should undergo early/immediate re-operation. Thrombolytic therapy in such patients is reserved for those for whom surgical intervention carries high risk and those with contraindications to surgery. Streptokinase and urokinase are most frequently used, thrombolytic agents. Thrombolytic therapy should be stopped at 24 hours if there is no hemodynamic improvement or after 72 hours even if hemodynamic recovery is incomplete. If thrombolytic therapy is successful, it should be followed with intravenous heparin until warfarin achieves an INR of 3 to 4 for aortic prosthetic valves and 3.5 to 4.5 for mitral prosthetic valves. Patients with "small clot" who are in NYHA function class I or II and those with LV dysfunction should have in hospital short-term intravenous heparin therapy. If this is unsuccessful, they may receive a trial of continuous infusion thrombolytic therapy over several days. If this is unsuccessful they may need re-operation. 

6. Thrombosis of prosthetic heart valves: Patients who have a large clot or evidence of valve obstruction and who are in NYHA functional class III or IV because of prosthetic thrombosis should undergo early/immediate re-operation. Thrombolytic therapy in such patients is reserved for those for whom surgical intervention carries high risk and those with contraindications to surgery. Streptokinase and urokinase are most frequently used, thrombolytic agents. Thrombolytic therapy should be stopped at 24 hours if there is no hemodynamic improvement or after 72 hours even if hemodynamic recovery is incomplete. If thrombolytic therapy is successful, it should be followed with intravenous heparin until warfarin achieves an INR of 3 to 4 for aortic prosthetic valves and 3.5 to 4.5 for mitral prosthetic valves. Patients with "small clot" who are in NYHA function class I or II and those with LV dysfunction should have in hospital short-term intravenous heparin therapy. If this is unsuccessful, they may receive a trial of continuous infusion thrombolytic therapy over several days. If this is unsuccessful they may need re-operation.

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