Current medical management of valvular heart disease

ABSTRACT

Drug therapy plays a key role in the management of valvular heart disease, though in many cases it does not alter its course or delay the need for surgery. The importance of drug therapy lies in stabilizing the patient’s condition when the disease is due to abnormal valve structure, and in treating the underlying condition when the condition is due to a functional abnormality. Drug therapy also lowers the risk of bacterial endocarditis and rheumatic fever.

KEY POINTS

Data are conflicting regarding the hemodynamic benefits of long-term angiotensin-converting enzyme (ACE) inhibitor therapy in mitral regurgitation.

Patients with mitral stenosis and a history of rheumatic heart disease should continue antibiotic prophylaxis for at least 5 years after their most recent attack of rheumatic fever.

RUG THERAPY HAS IMPORTANT ROLES in the management of valvular heart disease: stabilization of patients until the time of surgery, treatment of the underlying cause, and prevention of bacterial endocarditis and rheumatic fever (TABLE 1). On the other hand, it is still not proven to alter the course of valvular heart disease or the time of surgery when a serious structural abnormality is the cause.

TRENDS IN VALVE DISEASE

Valvular heart disease is a diverse group of diseases. Management depends on the cause and the nature of the valvular abnormality.

Rheumatic fever no longer the predominant cause in developed countries

The prevalence of valve disease as a sequela of rheumatic fever has steadily decreased in developed countries but remains a significant health problem in developing countries, occurring in 12% to 65% of all cardiac patients and having a mortality rate of 0.9 to 8 per 100,000.1

Valvular disease is now more often the result of a degenerative condition, ischemia, or calcificiation or is functional. And it is seen more often in older patients. The prevalence of at least moderate calcific aortic valve stenosis is estimated to be 5% in the elderly, and the prevalence of at least moderate mitral valve regurgitation is 11.2%.2,3

Increasing role of medical therapy in congenital valve disorders

While drug therapy plays a central role in the management of secondary (ie, functional) valve disease, it does not alter the natural his-
Primary valve disease comprises conditions in which valve structural abnormalities lead to abnormal function: mitral regurgitation, aortic regurgitation, mitral stenosis, and aortic stenosis.

Mitral regurgitation
The most common cause of mitral regurgitation in the United States is myxomatous degeneration. Other causes include rheumatic heart disease, infective endocarditis, and ischemic and nonischemic cardiomyopathy. Management depends on whether mitral regurgitation is chronic or acute. (The management of ischemic and functional forms of mitral regurgitation, which are considered secondary valve disease, is discussed separately below.)

Chronic mitral regurgitation. Chronic mitral regurgitation is a volume overload state which, if left untreated, leads to progressive left ventricular enlargement, diminished systolic function, and congestive heart failure.

Data on the hemodynamic benefits of long-term angiotensin-converting enzyme (ACE) inhibitor therapy conflict. One study of quinapril showed a decrease in regurgitant fraction, ventricular volumes, mass, and degree of left ventricular hypertrophy, while a study of captopril showed no effect.

No study has yet shown that ACE inhibitors alter the natural course of the disease, alleviate symptoms, or delay the need for surgery. Moreover, the current data do not support the routine use of vasodilators—ACE inhibitors or others—in asymptomatic patients with chronic, severe mitral regurgitation. Yet vasodilators may have a role in patients with symptomatic congestive heart failure and reduced left ventricular systolic function, in patients who are not good candi-
dates for surgery,7 or in patients with coexisting systemic hypertension.

**A cute mitral regurgitation.** A cute mitral regurgitation is often seen after myocardial infarction or infective endocarditis, both of which may result in rupture of the valve, papillary muscle, or chordae tendineae. A cute mitral regurgitation is characterized by marked acute hemodynamic effects. A cute pulmonary edema and diminished forward cardiac output result from the sudden regurgitant volume load on the non-compensated left ventricle.

Intravenous vasodilators, such as sodium nitroprusside, and intra-aortic balloon counterpulsion may be used to stabilize the patient prior to mitral valve repair or replacement, which is often required on an urgent basis.

**Aortic regurgitation**

The most common causes of aortic regurgitation are congenital heart disease (most often of a bicuspid aortic valve), calcific degeneration, rheumatic heart disease, infective endocarditis, and diseases of the proximal aorta, such as dissection and Marfan syndrome.

Aortic regurgitation leads to volume and pressure overload of the left ventricle and secondary increased left ventricular mass, which over time leads to decreased systolic function and symptoms of congestive heart failure.

The vasodilators hydralazine and nifedipine and ACE inhibitors have been shown to decrease left ventricular end-diastolic volumes, improve ejection fraction, decrease left ventricular mass, and decrease the degree of left ventricular hypertrophy in aortic regurgitation.4,8–12

In addition, in a randomized trial of patients with severe but asymptomatic aortic regurgitation and normal left ventricular ejec tion fraction, nifedipine was shown to reduce or delay the need for aortic valve replacement when compared with digoxin.**[FIGURE 1]**

Therefore, vasodilator therapy with either a calcium channel blocker or an ACE inhibitor is useful in patients with chronic, severe asymptomatic aortic regurgitation with preserved left ventricular function.

Patients with mild to moderate aortic regurgitation should receive vasodilator therapy if they have concomitant hypertension. Vasodilators may also be used in patients with chronic, severe aortic regurgitation and decreased left ventricular function who are not candidates for aortic valve surgery.

Beta-blockers and rate-controlling calcium-channel blockers should not be used in patients with aortic regurgitation and severe aortic insufficiency, as this may lead to a decrease in cardiac output and an increase in the regurgitant fraction. This effect may be attributed to the negative inotropic properties of these drugs and to their ability to increase the duration of diastole.

**Mitral stenosis**

Given the mechanical nature of mitral inflow obstruction in mitral stenosis, medical therapy neither alters the natural history nor delays the need for surgery. Medical management primarily involves giving diuretics to alleviate pulmonary congestion, treating atrial fibrilla-
Atrial fibrillation. The development of atrial fibrillation, with resultant decreased diastolic filling time and loss of the atrial contribution to ventricular filling, may lead to a decrease in cardiac output and to pulmonary congestion. Beta-blockers, calcium-channel blockers, or digoxin may be used to achieve ventricular rate control. Sinus rhythm should be restored via either direct-current cardioversion or antiarrhythmic drugs.

Given the high rate of peripheral and cerebrovascular embolization observed in patients with mitral stenosis and atrial fibrillation, all patients with a history of atrial fibrillation or prior arterial embolism should receive long-term anticoagulation with warfarin. We have no prospective clinical trial data to support routine anticoagulation of patients with mitral stenosis but with no history of atrial fibrillation or prior embolic event.

Long-term anticoagulation. While echocardiographic predictors of left atrial thrombus formation—eg, left atrial spontaneous echo contrast (“smoke”) and marked left atrial cavity enlargement—have been identified, long-term anticoagulation in these patients is controversial.

Physical exertion. Patients with severe mitral stenosis should be counseled to avoid particularly strenuous physical activity, which decreases diastolic filling time and may result in left atrial hypertension and pulmonary congestion. Beta-blockers or calcium channel blockers decrease the heart rate and increase the diastolic filling time and so may be useful in patients with exertional symptoms related to sinus tachycardia.

Rheumatic fever prophylaxis. Since the most common cause of mitral stenosis is rheumatic carditis, secondary prophylaxis of rheumatic fever is recommended for all valve disease patients who do not have another obvious cause. Intramuscular benzathine penicillin G is the preferred method of prophylaxis due to enhanced compliance compared with oral regimens (Table 2). Patients with a history of rheumatic heart disease should continue antibiotic prophylaxis for at least 5 years after their most recent attack of rheumatic fever. Patients at increased risk for exposure to group A streptococci, such as child care workers, may be candidates for longer periods of antibiotic prophylaxis.

Aortic stenosis

Calcific stenosis of either a tri-leaflet or bicuspid aortic valve is the most common cause of aortic stenosis in the United States, while rheumatic involvement of the aortic valve is a more common cause worldwide. While the mechanisms that lead to calcific aortic stenosis are not fully understood, evidence is increasing for the role of hyperlipidemia in its pathogenesis.

Aortic stenosis is a mechanical disorder for which surgery is the primary treatment available. No medical treatment is known to alter the natural history, timing, or need for surgery. Vasodilators, which may cause severe hypotension, should generally be avoided, especially in critical aortic stenosis. However, ACE inhibitors may be considered in patients who are not good surgical candidates and who

---

**Table 2**

<table>
<thead>
<tr>
<th>Recommendations for secondary prevention of rheumatic fever*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AGENT</strong></td>
</tr>
<tr>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>One of the following:</strong></td>
</tr>
<tr>
<td>Benzathine penicillin G</td>
</tr>
<tr>
<td>Penicillin V</td>
</tr>
<tr>
<td>Sulfadiazine</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>If allergic to penicillin and sulfadiazine:</strong></td>
</tr>
<tr>
<td>Erythromycin</td>
</tr>
</tbody>
</table>

*Patients with a history of rheumatic heart disease should continue antibiotic prophylaxis for at least 5 years after their most recent attack of rheumatic fever. Patients at increased risk for exposure to group A streptococci, such as child care workers, may be candidates for longer periods of antibiotic prophylaxis.

have a dilated, poorly functioning left ventricle, as a few small studies have shown an improvement in cardiac output without serious resultant hypotension.20 As with other acquired valvular diseases, antibiotic prophylaxis of bacterial endocarditis is necessary.

### SECONDARY VALVULAR HEART DISEASE

In secondary valve disease, valve structure is essentially normal, while abnormalities in valve function occur secondary to various underlying cardiovascular diseases, such as aortic root dilation and aortic insufficiency.

#### Ischemic mitral regurgitation

Ischemic mitral regurgitation results from scarring of the papillary muscles from ischemia or infarction, and even more commonly from infarction of the adjacent wall associated with the papillary muscle. Ischemic mitral regurgitation is usually treated medically, unless it is severe or surgery is necessary for treatment of the underlying coronary artery disease. In these situations, mitral valve repair is indicated.

Medical treatment is based on afterload reduction with ACE inhibitors or other vasodilators that act to reduce left ventricular size, which produces a concomitant reduction in mitral valve annular size and the degree of mitral regurgitation. Anti-ischemic agents, such as nitrates and beta-blockers, may be used additionally in the rare situation when the mitral regurgitation is worsened by ischemia.

#### Functional mitral regurgitation

Significant mitral regurgitation may accompany ischemic and nonischemic dilated cardiomyopathy due to changes in ventricular shape and secondary failure of mitral leaflet coaptation.21 Patients with cardiomyopathy and mitral regurgitation have a significantly worse prognosis than those without associated mitral regurgitation.22,23

Medical treatment should be directed toward treatment of the underlying cardiomyopathy, including the use of ACE inhibitors, beta-blockers, digoxin, and diuretics. ACE inhibitors and beta-blockers have also been

---

**TABLE 3**

**Recommended prophylactic regimens for dental, oral, respiratory tract, and esophageal procedures in adults and children with valvular disease**

<table>
<thead>
<tr>
<th>SITUATION</th>
<th>AGENT</th>
<th>REGIMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard general prophylaxis</td>
<td>Amoxicillin</td>
<td>Adults 2.0 g; children 50 mg/kg orally 1 h before procedure</td>
</tr>
<tr>
<td>Unable to take oral medications</td>
<td>Ampicillin</td>
<td>Adults 2.0 g intramuscularly (IM) or intravenously (IV); Children 50 mg/kg IM or IV within 30 minutes before procedure</td>
</tr>
<tr>
<td>Allergic to penicillin</td>
<td>Clindamycin</td>
<td>Adults 600 mg; children 20 mg/kg orally 1 h before procedure</td>
</tr>
<tr>
<td></td>
<td>Cephalexin or cefadroxil</td>
<td>Adults 2.0 g; children 50 mg/kg orally 1 h before procedure</td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>Adults 2.0 g; children 50 mg/kg orally 1 h before procedure</td>
</tr>
<tr>
<td></td>
<td>Azithromycin or clarithromycin</td>
<td>Adults 500 mg; children 15 mg/kg orally 1 h before procedure</td>
</tr>
<tr>
<td>Allergic to penicillin and unable to take oral medications</td>
<td>Clindamycin</td>
<td>Adults 600 mg; children 20 mg/kg IV within 30 min before procedure</td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>Adults 1.0 g; children 25 mg/kg IM or IV within 30 min before procedure</td>
</tr>
</tbody>
</table>

**Long-term prophylaxis for all mitral stenosis patients is controversial**
shown to reduce the degree of mitral regurgitation.\textsuperscript{24–26}

Surgical repair of the mitral valve may be considered in patients with end-stage cardiomyopathy who have symptomatic heart failure despite maximal medical therapy.\textsuperscript{27}

Tricuspid regurgitation may be secondary to primary tricuspid valve disease, such as with rheumatic heart disease, myxomatous degeneration, or infective endocarditis. However, secondary (functional) tricuspid regurgitation is much more common.

Functional tricuspid regurgitation is seen in a variety of disorders that result in elevated pulmonary artery pressure, including chronic pulmonary disease, primary pulmonary hypertension, and left ventricular and left-sided valvular heart disease.

Treatment should be aimed at the underlying cause of pulmonary hypertension: for example, treating chronic obstructive lung disease with supplemental oxygen. Diuretics are often required to manage the effects of elevated systemic venous pressure, such as leg edema and hepatic congestion, which often accompany severe pulmonary hypertension and right ventricular failure. While high doses of loop and thiazide diuretics may be needed to minimize chronic edema, care should be taken to avoid over-diuresis and the resultant metabolic abnormalities.

Functional tricuspid regurgitation

Tricuspid regurgitation may be secondary to primary tricuspid valve disease, such as with rheumatic heart disease, myxomatous degeneration, or infective endocarditis. However, secondary (functional) tricuspid regurgitation is much more common.

Functional tricuspid regurgitation is seen in a variety of disorders that result in elevated pulmonary artery pressure, including chronic pulmonary disease, primary pulmonary hypertension, and left ventricular and left-sided valvular heart disease.

Treatment should be aimed at the underlying cause of pulmonary hypertension: for example, treating chronic obstructive lung disease with supplemental oxygen. Diuretics are often required to manage the effects of elevated systemic venous pressure, such as leg edema and hepatic congestion, which often accompany severe pulmonary hypertension and right ventricular failure. While high doses of loop and thiazide diuretics may be needed to minimize chronic edema, care should be taken to avoid over-diuresis and the resultant metabolic abnormalities.

Aortic insufficiency related to aortic disease

Dilatation of the aortic root secondary to connective tissue diseases (eg, in Marfan syndrome) or to atherosclerotic disease of the aorta can lead to aortic insufficiency by failure of aortic valve coaptation.

Aggressive treatment of hypertension is important in patients with aortic insufficiency from aortic root enlargement. The target blood pressure is 120/80 mm Hg. Beta-blockers have been shown to slow the rate of aortic dilatation in patients with Marfan syndrome\textsuperscript{28–30} and should be used during the period when surgical replacement of the aortic root is not yet indicated. Direct arterial vasodilators, especially without the concomitant use of beta-blockers, should be avoided as they may enhance sympathetic activity and increase wall stress.

In ischemic mitral regurgitation, vasodilators help reduce LV size

| TABLE 4 |

<table>
<thead>
<tr>
<th>SITUATION</th>
<th>AGENTS</th>
<th>REGIMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk patients\textsuperscript{*}</td>
<td>Ampicillin + gentamicin</td>
<td>Ampicillin 2.0 g intramuscularly (IM) or intravenously (IV) + gentamicin 1.5 mg/kg (not to exceed 120 mg) within 30 min of starting procedure; 6 h later, ampicillin 1 g IM/IV or amoxicillin 1 g orally</td>
</tr>
<tr>
<td>High-risk + allergic to ampicillin or amoxicillin</td>
<td>Vancomycin + gentamicin</td>
<td>Vancomycin 1.0 g IV over 1-2 h + gentamicin 1.5 mg/kg (not to exceed 120 mg); complete injection/infusion within 30 min of starting procedure</td>
</tr>
<tr>
<td>Moderate-risk patients‡</td>
<td>Amoxicillin or ampicillin</td>
<td>Amoxicillin 2.0 g orally 1 h before procedure, or amoxicillin 2.0 g IM/IV within 30 min of starting procedure</td>
</tr>
<tr>
<td>Moderate-risk patients allergic to ampicillin or amoxicillin</td>
<td>Vancomycin</td>
<td>Vancomycin 1.0 g IV over 1-2 h; complete infusion within 30 min of starting procedure</td>
</tr>
</tbody>
</table>

\textsuperscript{*} High risk: prior endocarditis, prosthetic valve

\textsuperscript{‡} Moderate risk: all native valve disease and no prior endocarditis
ANTIBIOTIC PROPHYLAXIS OF BACTERIAL ENDOCARDITIS

Patients with underlying congenital and acquired valvular heart disease are at increased risk for developing bacterial endocarditis. TABLES 3 AND 4 summarize the guidelines for antibiotic prophylaxis for dental and other invasive procedures during which transient bacteremia is likely to occur.31

REFERENCES


ADDRESS: Brian Griffin, MD, Department of Cardiology, F15, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail griffinb@ccf.org.