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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.

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DRUG 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 calicification 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-

TABLE 1

Recommended medical treatments for valvular heart disease

	VASODILATORS	BETA-BLOCKERS	DIURETICS	ANTIBIOTIC PROPHYLAXIS OF RHEUMATIC FEVER	ANTIBIOTIC PROPHYLAXIS OF BACTERIAL ENDOCARDITIS
Primary valvular heart disease					
Mitral regurgitation	No	No	No	?*	Yes
Aortic regurgitation	Yes	No	No	?*	Yes
Mitral stenosis	No	Yes	Yes†	Yes	Yes
Aortic stenosis	No‡	No	No	?*	Yes
Secondary valvular heart disease					
Ischemic mitral regurgitation	Yes	Yes§	No	No	Yes
Functional mitral regurgitation	Yes	Yes	Yes	No	No
Functional tricuspid regurgitation	No	No	Yes‖	No	No
Aortic insufficiency from aortic disease	No	Yes¶	No	No	Yes

*Prophylaxis is indicated if echocardiography shows evidence of a rheumatic etiology of valve disease
†To alleviate pulmonary congestion
‡ACE inhibitors may be considered if surgery is contraindicated
§May be used in the rare situation when mitral regurgitation is worsened by ischemia
‖To manage edema and hepatic congestion
¶Should not be used in severe aortic regurgitation

All patients with mitral stenosis plus atrial fibrillation should receive warfarin

tory or the timing of surgery in patients with primary (structural) valve disease such as calcific aortic stenosis. Yet even in primary valve disease, drug therapy is useful in stabilizing function in patients until surgical intervention becomes necessary.

PRIMARY VALVE DISEASE

Primary valve disease comprises conditions in which valve structural abnormalities lead to abnormal function: ie, 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,[4,5] while a study of captopril showed no effect.[6]

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.

Acute mitral regurgitation. Acute 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. Acute mitral regurgitation is characterized by marked acute hemodynamic effects. Acute 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 counterpulsation 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 ejection fraction, nifedipine was shown to reduce or delay the need for aortic valve replacement when compared with digoxin (FIGURE 1).[13]

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.

Nifedipine delays the need for aortic valve replacement

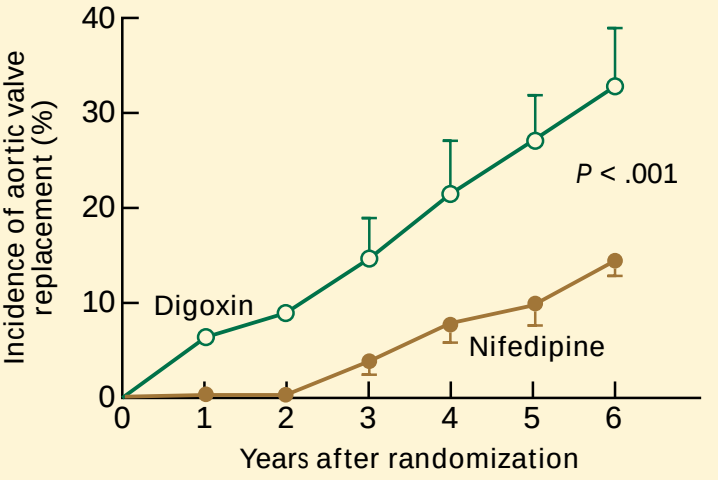

FIGURE 1. Cumulative actuarial incidence of progression to aortic valve replacement in 143 patients with asymptomatic aortic regurgitation: 69 patients received nifedipine 20 mg twice daily, and 74 patients received digoxin 0.25 mg daily. The need for aortic valve replacement was significantly lower at all times in those taking nifedipine.

REPRINTED FROM SCOGNAMIGLIO R. RAHIMTOOLA SH. FASOLI G. NISTRI S. DALLA VOLTA S. NIFEDIPINE IN ASYMPTOMATIC PATIENTS WITH SEVERE AORTIC REGURGITATION AND NORMAL LEFT VENTRICULAR FUNCTION. N ENGL J MED 1994:331:689-694, WITH PERMISSION

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-

TABLE 2

Recommendations for secondary prevention of rheumatic fever*

AGENT	RECOMMENDED DOSAGE
One of the following:	
Benzathine penicillin G	1.2 million units intramuscularly every 4 weeks
Penicillin V	250 mg by mouth twice daily
Sulfadiazine	< 60 lb: 0.5 g by mouth once daily ≥ 60 lb: 1.0 g by mouth once daily
If allergic to penicillin and sulfadiazine:	
Erythromycin	250 mg by mouth twice daily

*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.

ADAPTED FROM DAJANI AS, BISNO AL, CHUNG KJ, ET AL. PREVENTION OF RHEUMATIC FEVER: A STATEMENT FOR HEALTH PROFESSIONALS BY THE COMMITTEE ON RHEUMATIC FEVER, ENDOCARDITIS, AND KAWASAKI DISEASE OF THE COUNCIL ON CARDIOVASCULAR DISEASE IN THE YOUNG, THE AMERICAN HEART ASSOCIATION. PED INFECT DIS J 1989; 8:263–266.

Continue rheumatic heart disease prophylaxis at least 5 years

tion, and giving anticoagulants to patients at increased risk of arterial embolic events.

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,[14] 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,[15–17] 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).[18]

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. However, controversy exists regarding whether long-term prophylaxis is required for all patients with mitral stenosis.

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.[19]

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 3

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

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

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

Long-term prophylaxis for all mitral stenosis patients is controversial

TABLE 4

Prophylactic regimens for genitourinary and nonesophageal gastrointestinal procedures in adults with valvular heart disease

SITUATION	AGENTS	REGIMEN
High-risk patients*	Ampicillin + gentamicin	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
High-risk + allergic to ampicillin or amoxicillin	Vancomycin + gentamicin	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
Moderate-risk patients†	Amoxicillin or ampicillin	Amoxicillin 2.0 g orally 1 h before procedure, or ampicillin 2.0 g IM/IV within 30 min of starting procedure
Moderate-risk patients allergic to ampicillin or amoxicillin	Vancomycin	Vancomycin 1.0 g IV over 1-2 h; complete infusion within 30 min of starting procedure

*High risk: prior endocarditis, prosthetic valve
†Moderate risk: all native valve disease and no prior endocarditis

In ischemic mitral regurgitation, vasodilators help reduce LV size

shown to reduce the degree of mitral regurgitation.[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.[27]

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 leaflet 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[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.

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

1. Strategy for controlling rheumatic fever/rheumatic heart disease, with emphasis on primary prevention: memorandum from a joint WHO/ISFC meeting. Bull WHO 1995; 73:583–587.
2. **Lindroos M, Kupari M, Heikkila J, Tilvis R.** Prevalence of aortic valve abnormalities in the elderly: an echocardiographic study of a random population sample. J Am Coll Cardiol 1993; 21:1220–1225.
3. **Singh JP, Evans JC, Levy D, et al.** Prevalence and clinical determinants of mitral, tricuspid, and aortic regurgitation (the Framingham Heart Study) [published erratum appears in Am J Cardiol 1999; 84:1143]. Am J Cardiol 1999; 83:897–902.
4. **Schon HR.** Hemodynamic and morphologic changes after long-term angiotensin-converting enzyme inhibition in patients with chronic valvular regurgitation. J Hypertens 1994; 12 (suppl):95–104.
5. **Schon HR, Schroter G, Barthel P, Schomig A.** Quinapril therapy in patients with chronic mitral regurgitation. J Heart Valve Dis 1994; 3:303–312.
6. **Wisenbaugh T, Sinovich V, Dullabh A, Sareli P.** Six-month pilot study of captopril for mildly symptomatic, severe isolated mitral, and isolated aortic regurgitation. J Heart Valve Dis 1994; 3:197–204.
7. **Greenberg BH, DeMots H, Murphy E, Rahimtoola SH.** Arterial dilators in mitral regurgitation: effects on rest and exercise hemodynamics and long-term clinical follow-up. Circulation 1982; 65:181–187.
8. **Schon HR, Dorn R, Barthel P, Schomig A.** Effects of 12-month quinapril therapy in asymptomatic patients with chronic aortic regurgitation. J Heart Valve Dis. 1994; 3:500–509.
9. **Greenberg BH, Rahimtoola SH.** Long-term vasodilator therapy in aortic insufficiency. Evidence for regression of left ventricular dilatation and hypertrophy and improvement in systolic pump function. Ann Intern Med 1980; 93:440–442.
10. **Greenberg B, Massie B, Bristow JD, et al.** Long-term vasodilator therapy of chronic aortic insufficiency. A randomized double-blinded, placebo-controlled clinical trial. Circulation 1988; 78:92–103.
11. **Scognamiglio R, Fasoli G, Ponchia A, Dalla-Volta S.** Long-term nifedipine unloading therapy in asymptomatic patients with chronic severe aortic regurgitation. J Am Coll Cardiol 1990; 16:424–429.
12. **Lin M, Chiang HT, Lin SL, et al.** Vasodilator therapy in chronic asymptomatic aortic regurgitation: enalapril versus hydralazine therapy. J Am Coll Cardiol 1994; 24:1046–1053.
13. **Scognamiglio R, Rahimtoola SH, Fasoli G, Nistri S, Dalla Volta S.** Nifedipine in asymptomatic patients with severe aortic regurgitation and normal left ventricular function. N Engl J Med 1994; 331:689–694.
14. **Fleming HA, Bailey SM.** Mitral valve disease, systemic embolism and anticoagulants. Postgrad Med J 1971; 47:599–604.
15. **Chiang CW, Lo SK, Kuo CT, Cheng NJ, Hsu TS.** Noninvasive predictors of systemic embolism in mitral stenosis. An echocardiographic and clinical study of 500 patients. Chest 1994; 106:396–399.
16. **Rittoo D, Sutherland GR, Currie P, Starkey IR, Shaw TR.** A prospective study of left atrial spontaneous echo contrast and thrombus in 100 consecutive patients referred for balloon dilation of the mitral valve. J Am Soci Echocardiogr 1994; 7:516–527.
17. **Daniel WG, Nellessen U, Schroder E, et al.** Left atrial spontaneous echo contrast in mitral valve disease: an indicator for an increased thromboembolic risk. J Am Coll Cardiol 1988; 11:1204–1211.
18. **Dajani AS, Bisno AL, Chung KJ, et al.** Prevention of rheumatic fever: a statement for health professionals by the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease of the Council on Cardiovascular Disease in the Young, the American Heart Association. Ped Infect Dis J 1989; 8:263–266.
19. **Otto CM, Kuusisto J, Reichenbach DD, Gown AM, O'Brien KD.** Characterization of the early lesion of "degenerative" valvular aortic stenosis. Histological and immunohistochemical studies. Circulation 1994; 90:844–853.
20. **Martinez Sanchez C, Henne O, Arceo A, et al.** Hemodynamic effects of oral captopril in patients with critical aortic stenosis. Arch Inst Cardiol Mex 1996; 66:322–330.
21. **Kono T, Sabbah HN, Stein PD, Brymer JF, Khaja F.** Left ventricular shape as a determinant of functional mitral regurgitation in patients with severe heart failure secondary to either coronary artery disease or idiopathic dilated cardiomyopathy. Am J Cardiol 1991; 68:355–359.
22. **Blondheim DS, Jacobs LE, Kotler MN, Costacurta GA, Parry WR.** Dilated cardiomyopathy with mitral regurgitation: decreased survival despite a low frequency of left ventricular thrombus. Am Heart J 1991; 122 (3 Pt 1):763–771.
23. **Junker A, Thayssen P, Nielsen B, Andersen PE.** The hemodynamic and prognostic significance of echo-Doppler-proven mitral regurgitation in patients with dilated cardiomyopathy. Cardiology 1993; 83:14–20.
24. **Lowes BD, Gill EA, Abraham WT, et al.** Effects of carvedilol on left ventricular mass, chamber geometry, and mitral regurgitation in chronic heart failure. Am J Cardiol 1999; 83:1201–1205.
25. **Levine AB, Muller C, Levine TB.** Effects of high-dose lisinopril-isosorbide dinitrate on severe mitral regurgitation and heart failure remodeling. Am J Cardiol 1998; 82:1299–1301.
26. **Evangelista-Masip A, Bruguera-Cortada J, Serrat-Serradell R, et al.** Influence of mitral regurgitation on the response to captopril therapy for congestive heart failure caused by idiopathic dilated cardiomyopathy. Am J Cardiol 1992; 69:373–376.
27. **Bach DS, Bolling SF.** Early improvement in congestive heart failure after correction of secondary mitral regurgitation in end-stage cardiomyopathy. Am Heart J 1995; 129:1165–1170.
28. **Rossi-Foulkes R, Roman MJ, Rosen SE, et al.** Phenotypic features and impact of beta-blocker or calcium antagonist therapy on aortic lumen size in the Marfan syndrome. Am J Cardiol 1999; 83:1364–1368.
29. **Shores J, Berger KR, Murphy EA, Pyeritz RE.** Progression of aortic dilatation and the benefit of long-term beta-adrenergic blockade in Marfan syndrome. N Engl J Med 1994; 330:1335–1341.
30. **Salim MA, Alpert BS, Ward JC, Pyeritz RE.** Effect of beta-adrenergic blockade on aortic root rate of dilation in the Marfan syndrome. Am J Cardiol 1994; 74:629–633.
31. **Dajani AS, Taubert KA, Wilson W, et al.** Prevention of bacterial endocarditis. Recommendations by the American Heart Association. JAMA 1997; 277:1794–1801.

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