

**JOEL P. REGINELLI, MD**Department of Cardiovascular Medicine,
The Cleveland Clinic Foundation**BRIAN GRIFFIN, MD**Department of Cardiovascular Medicine,
The Cleveland Clinic Foundation

The challenge of valvular heart disease: When is it time to operate?

ABSTRACT

In patients with valve disease, operating too soon exposes them to unnecessary surgical risk, but waiting too long may lead to cardiac damage and poor outcome. When to refer a patient for surgery depends on which valve is involved, the type of defect (stenosis or regurgitation), the degree of the defect, and the degree of symptoms or functional impairment.

KEY POINTS

Patients with aortic stenosis should be referred for valve replacement at the onset of symptoms. Other indications include left ventricular dysfunction or plans for other major surgery.

Patients with chronic aortic regurgitation need valve replacement at the onset of symptoms, decreased ejection fraction, or severe left ventricular dilatation.

Patients with mitral stenosis should be considered for intervention when they have moderate symptoms or when stenosis becomes more severe (mitral valve area < 1.5 cm²). Mitral stenosis can be treated effectively by percutaneous balloon valvotomy in many patients.

Patients with chronic mitral regurgitation should be referred for surgery before left ventricular dysfunction develops (ejection fraction < 60%). Patients with flail leaflets may benefit from earlier intervention.

Patients with severe tricuspid regurgitation need referral for surgery when they have symptoms and peripheral edema.

VALVULAR HEART DISEASE poses many challenges, the most vital and perhaps most difficult of which is how to determine the optimal time for surgery.

Performed too soon, surgery needlessly exposes a patient to operative risks. On the other hand, inappropriate delay may lead to irreparable cardiac damage and worse long-term outcome. Therefore, the physician must carefully analyze the available data and weigh the risks inherent in surgery vs a conservative approach of close observation.

The decision to proceed with surgery may be relatively straightforward in patients with symptoms of severe valvular disease, particularly valvular stenosis. However, it is far less clear-cut for patients with severe but asymptomatic defects, or those with severe symptoms but only mild-to-moderate defects.

Guidelines provide a general framework within which to make decisions, but each case requires a tailored approach, taking into account the patient's general medical condition, his or her wishes, the level of complexity, and the challenges posed by each of the various valvular defects.

AORTIC STENOSIS: SYMPTOMS ARE CRUCIAL

Aortic stenosis is the most common valvular abnormality. Most cases are due to calcific degeneration of either a normal trileaflet or a congenitally bicuspid aortic valve.

Typically, there is a long asymptomatic period of progressive valvular narrowing. The hallmark symptoms of angina, dyspnea, and syncope generally do not appear until the valve orifice has become significantly nar-

TABLE 1

Indications for aortic valve replacement in aortic stenosis**Class 1**

Conditions for which there is evidence or general agreement that the procedure is useful and effective

Symptomatic, severe aortic stenosis

Severe aortic stenosis in patients undergoing coronary artery bypass grafting

Severe aortic stenosis in patients undergoing surgery on the aorta or other heart valves

Class 2

Conditions for which there is conflicting evidence or divergence of opinion about the usefulness or efficacy of the procedure

2a

Weight of evidence or opinion is in favor of usefulness or efficacy

Moderate aortic stenosis in patients undergoing coronary artery bypass grafting or surgery on the aorta or other heart valves

Asymptomatic but severe aortic stenosis with:

Left ventricular systolic dysfunction, or

Abnormal response to exercise (eg, hypotension)

2b

Usefulness or efficacy is less well established by evidence or opinion

Asymptomatic but severe aortic stenosis and:

Ventricular tachycardia

Marked or excessive left ventricular hypertrophy (≥ 15 mm)

Valve area < 0.6 cm²

Class 3

Conditions for which there is evidence or general agreement that the procedure is not useful and in some cases may be harmful

Prevention of sudden death in patients with no symptoms and none of the indications above

ADAPTED FROM BONOW RO, CARABELLO B, DE LEON AC, ET AL. ACC/AHA GUIDELINES FOR THE MANAGEMENT OF PATIENTS WITH VALVULAR HEART DISEASE. EXECUTIVE SUMMARY. A REPORT OF THE AMERICAN COLLEGE OF CARDIOLOGY/AMERICAN HEART ASSOCIATION TASK FORCE ON PRACTICE GUIDELINES (COMMITTEE ON MANAGEMENT OF PATIENTS WITH VALVULAR HEART DISEASE). J AM COLL CARDIOL 1998; 32:1486-1588.

Symptoms of aortic valve stenosis—angina, dyspnea, and syncope—appear late in its course

rowed; therefore, the onset of symptoms is critical in deciding to proceed with surgery.

When aortic stenosis is severe, the valve can rarely be repaired. In this situation it is necessary to insert a mechanical valve, a homograft, an autograft, or a bioprosthesis.

Symptomatic aortic stenosis

Untreated, symptomatic aortic stenosis reduces survival: patients with angina due to aortic stenosis have a 50% mortality rate at 5 years, and those with associated heart failure survive an average of less than 2 years.¹⁻³ The American College of Cardiology (ACC) and the American Heart Association (AHA) recommend prompt referral for aortic valve replacement at the onset of symptoms (TABLE 1).⁴

Asymptomatic aortic stenosis

Asymptomatic aortic stenosis usually manifests itself as a typical systolic murmur found during a routine physical examination. Patients with asymptomatic aortic stenosis have a low risk of cardiac death. Studies suggest that when sudden death occurs in an “asymptomatic” patient, a careful review of the history often reveals a prior insidious onset of symptoms. Prospective studies are under way to determine if this is in fact the case.⁵

Patients should be educated about typical symptoms and told to report them should they develop. They should also be advised of the indications for antibiotic prophylaxis to prevent bacterial endocarditis.⁶

Echocardiographic studies provide infor-



mation about the severity of the stenosis before symptoms develop. Symptoms rarely occur⁷ until the aortic valve area is less than 1.0 cm². Although stenosis progresses at different rates in different patients, the average reduction in area is 0.12 cm² per year. A severely calcified valve or a rapid rise in valvular gradient also indicates faster progression and worse outcome.⁸

Continuous-wave Doppler echocardiography, which measures aortic jet velocity, helps identify patients most likely to develop symptoms in the near future. Patients with a high aortic jet velocity (> 4.0 m/s) are more likely to develop symptoms over the ensuing 3 years than those with a lower jet velocity (< 3.0 m/s).⁷

Follow-up is key. The ACC/AHA guidelines recommend annual office visits for patients with asymptomatic aortic stenosis that is mild (valve area > 1.5 cm²), and office visits every 6 months for those with stenosis that is moderate (valve area 1.0–1.5 cm²). If the patient's clinical status does not change, repeat echocardiography is recommended every 5 years for mild aortic stenosis and every 2 years for moderate stenosis.⁹ Annual echocardiography may be reasonable, however, in older patients, particularly those with risk factors for more rapid progression, such as diabetes, coronary artery disease, hyperlipidemia, or hypertension.

Frequent follow-up (at least every 6 months) is extremely important for patients with aortic stenosis that is severe but asymptomatic. They should be questioned intensively at each visit about symptoms and be referred for valve replacement promptly when symptoms develop.

Exercise echocardiography may be useful in excluding severe limitation of functional capacity if this is suspected on the basis of the patient's physical state. Although exercise testing poses a potential risk in aortic stenosis, there are now considerable data to suggest that the risk is low in patients without symptoms.

Surgery for asymptomatic aortic stenosis is controversial. In patients who truly have no symptoms in spite of critical aortic stenosis (valve area < 0.7 cm²), watchful waiting is usually considered the strategy of choice. However, there are specific situations in

which surgery is indicated, even in asymptomatic patients.

Patients with moderate aortic stenosis who require cardiac surgery for another reason should be considered for concomitant aortic valve replacement. This is particularly true for patients who have coronary artery disease, a risk factor for faster progression of aortic stenosis (TABLE 1).¹⁰

Surgery is indicated for patients with severe aortic stenosis who have left ventricular dysfunction attributable to aortic stenosis or an abnormal response to exercise or who require a major noncardiac surgical procedure. There is considerable disagreement over whether severe left ventricular hypertrophy (> 15 mm) or ventricular tachycardia is an appropriate indication for surgery in the absence of symptoms. Increasing evidence suggests that calcification of the valve and rapid increase in valve gradient are associated with a worse outcome in aortic stenosis. We now believe that surgery is indicated in older patients (> 60 years) with these indications who have severe aortic stenosis in the absence of symptoms.

Percutaneous balloon aortic valvotomy was initially seen as a less-invasive alternative to aortic valve replacement, particularly for patients for whom surgery would be risky. The procedure, performed in a cardiac catheterization laboratory, involves placing a dilating balloon across the stenotic aortic valve.

Although effective in children and adolescents, the procedure has largely been abandoned in adults, owing to an unacceptably high complication rate during the procedure and poor long-term efficacy.^{3,11} In rare instances, it may be considered as a palliative measure or as a bridge to surgery in a critically ill patient who may later be well enough for valve replacement.

Statin therapy may slow the progression of aortic stenosis, according to retrospective studies. Prospective studies are now underway to evaluate this.¹²

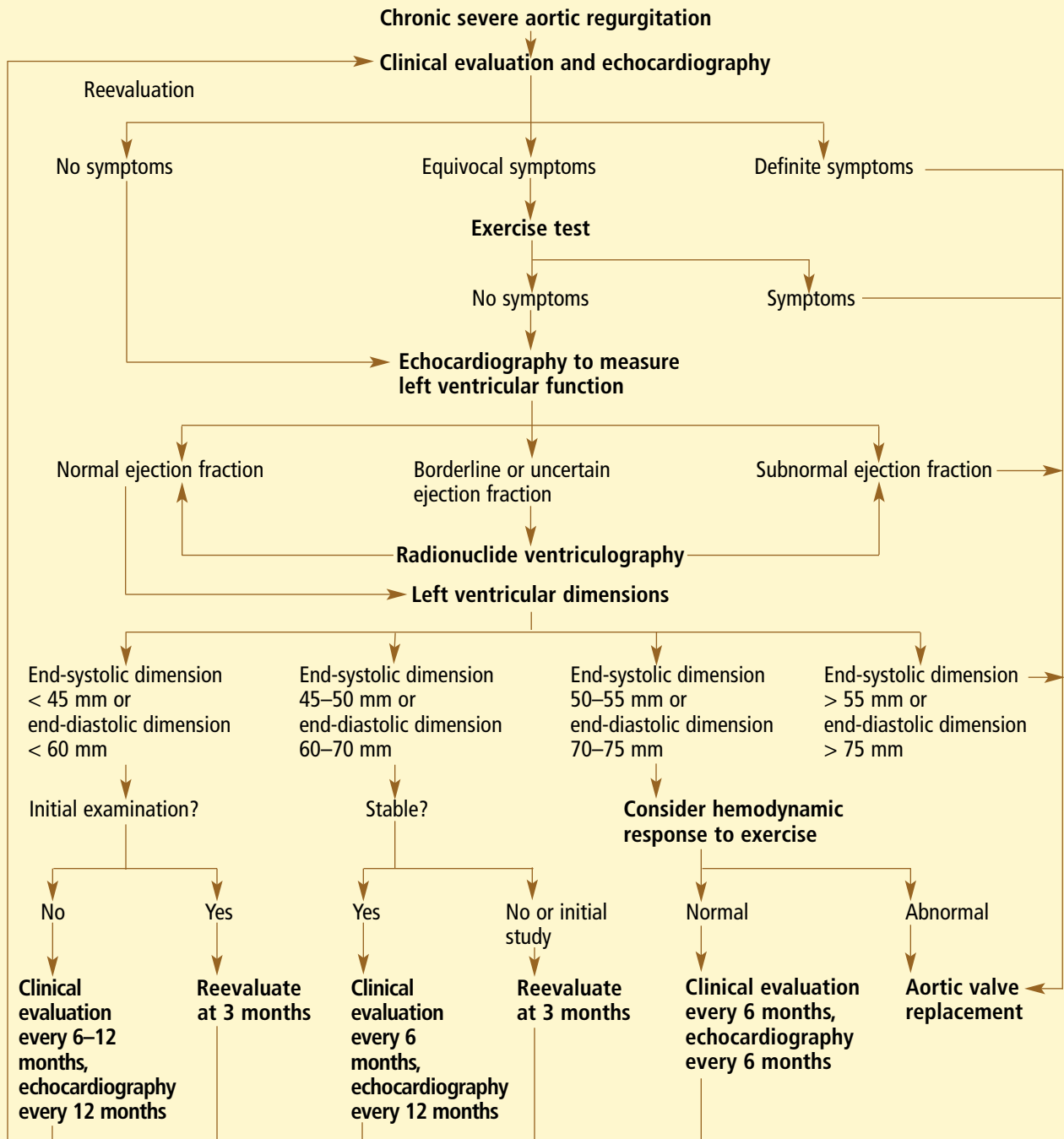
■ AORTIC REGURGITATION

Aortic regurgitation arises from diseases of the aortic root, the aortic valve, or both, which result in poor coaptation or incompetence of

Balloon aortic valvotomy has largely been abandoned in adults



Management strategy for chronic severe aortic regurgitation



ADAPTED FROM BONOW RO, CARABELLO B, DE LEON AC, ET AL. ACC/AHA GUIDELINES FOR THE MANAGEMENT OF PATIENTS WITH VALVULAR HEART DISEASE. EXECUTIVE SUMMARY. A REPORT OF THE AMERICAN COLLEGE OF CARDIOLOGY/AMERICAN HEART ASSOCIATION TASK FORCE ON PRACTICE GUIDELINES (COMMITTEE ON MANAGEMENT OF PATIENTS WITH VALVULAR HEART DISEASE). J AM COLL CARDIOL 1998; 32:1486–1588.

FIGURE 1

the aortic valve leaflets. It causes volume overload of the left ventricle.

Acute aortic regurgitation requires immediate surgery

Acute aortic regurgitation is usually caused by infective endocarditis, aortic dissection, or aortic trauma. The left ventricle cannot compensate for the increased volume, and patients typically present in extremis with pulmonary edema and heart failure.

Acute aortic regurgitation must be treated surgically without delay. Endocarditis—the most common cause of acute aortic regurgitation—is not a contraindication for surgery, as the risk of death without surgery outweighs the risk of developing prosthetic valve endocarditis after surgery.¹³

Chronic aortic regurgitation has a long asymptomatic period

In contrast to acute aortic regurgitation, chronic disease causes a gradual increase in both preload and afterload (due to increased stroke volume), while the left ventricle hypertrophies and dilates to compensate for the increased pressure and volume.¹⁴ Because of these compensatory mechanisms, patients with chronic disease typically have a long asymptomatic period with preserved left ventricular function.

Patients with chronic mild-to-moderate regurgitation and normal left ventricular function are at low risk and are not candidates for aortic valve replacement. Appropriate follow-up consists of an annual history and physical examination and echocardiography every 2 to 3 years.

Patients with severe regurgitation are at high risk, however, and must be evaluated often for symptoms or evidence of left ventricular dysfunction.⁴ Typical symptoms include dyspnea, orthopnea, and paroxysmal nocturnal dyspnea. Angina is also common, even in the absence of coronary artery disease, due to afterload mismatch, ie, the inability of the coronary arteries to adequately supply the excessively increased cardiac muscle mass that is typical of this condition.¹⁵ Patients who develop symptoms or evidence of left ventricular impairment should be referred promptly for valve replacement (FIGURE 1).

Symptomatic chronic aortic regurgitation with normal left ventricular function

As a general rule, all patients with severe aortic regurgitation, normal left ventricular function (ejection fraction > 50%), and symptoms (regardless of severity) warrant consideration for valve replacement (FIGURE 1).

Patients with moderate or severe symptoms (New York Heart Association [NYHA] functional class 3 or 4) clearly have a survival benefit with aortic valve replacement.^{16,17}

On the other hand, patients with severe disease whose symptoms are vague, nonspecific, or mild (NYHA class 2) present a management dilemma. According to the ACC/AHA guidelines, objective evidence of decreased exercise tolerance, left ventricular dilatation, or decreasing ejection fraction (even if in the normal range) constitute a class 1 indication for aortic valve replacement. Without such supporting data, valve replacement is considered a class 2a indication: ie, there is conflicting evidence as to whether replacement is beneficial, but most experts agree it is justified.⁴

Symptomatic chronic aortic regurgitation with decreased left ventricular function

Patients with symptoms of aortic regurgitation and decreased left ventricular function need prompt referral for valve replacement. A patient's preoperative condition largely determines the outcome after valve replacement, so timing is critical.

The poorer the preoperative left ventricular function, the worse the prognosis in terms of postoperative left ventricular function, incidence of congestive heart failure, and survival.^{18–22} Also, patients with severe symptoms have a poorer prognosis than those with mild symptoms for any given degree of preoperative left ventricular dysfunction.^{23,24} In addition, the longer the duration of preoperative left ventricular impairment, the poorer the chances of left ventricular recovery following valve replacement.^{22,25} These findings highlight the importance of close follow-up for patients with severe aortic regurgitation.

Even high-risk patients who have severe aortic regurgitation, advanced symptoms, and markedly reduced left ventricular systolic function should be considered for valve replacement. Although these patients have a

Acute severe aortic regurgitation must be treated surgically without delay

higher risk of surgical complications and death, most experts agree that surgery offers a better long-term prognosis than does long-term medical management.⁴

Severe but asymptomatic aortic regurgitation

Patients with aortic regurgitation that is severe but asymptomatic must be evaluated for evidence of left ventricular dilatation or systolic dysfunction.

Normal left ventricle—low risk. Patients with normal left ventricular function and dimensions are at low risk. In seven studies,⁴ the annual mortality rate was less than 0.2%, the annual rate of progression to symptomatic left ventricular systolic dysfunction 4.3%, and the annual rate of asymptomatic progression to left ventricular systolic dysfunction 1.3%.

The ACC/AHA guidelines recommend that patients with severe asymptomatic aortic regurgitation, normal left ventricular dimensions, and normal left ventricular systolic function undergo clinical follow-up visits every 6 to 12 months and echocardiography annually.⁴ As for all patients with valvular lesions, doctors should emphasize the need for antibiotic prophylaxis and recognition of symptoms related to their condition.

Patients who develop equivocal symptoms should undergo stress testing to unmask underlying functional impairment. Exercise testing is useful but less clear-cut for aortic regurgitation than for other valve lesions: afterload may increase dramatically, so a modest (< 10%) reduction in left ventricular ejection fraction may not indicate that surgery is needed. The time is right for valve replacement, however, if the ejection fraction or exercise capacity declines more significantly, especially if declines occur serially (FIGURE 1).

Left ventricular dilatation increases risk

Patients with asymptomatic severe aortic regurgitation and significant left ventricular dilatation (left ventricular end-systolic diameter > 50 mm and left ventricular end-diastolic diameter > 70 mm) are at higher risk: the rate of progression to symptoms or left ventricular systolic dysfunction is estimated to be 10% to 20% per year.^{16,26}

These patients require more frequent fol-

low-up visits (every 4–6 months) and echocardiography every 6 months.⁴

All patients with asymptomatic severe aortic regurgitation should be referred for valve replacement at the onset of symptoms, left ventricular systolic dysfunction (ejection fraction < 55%), or significant dilatation (left ventricular end-systolic diameter > 55 mm).⁴ These are merely guidelines, and exceptions do exist: eg, many women, as well as men of small build, may have severe left ventricular dilatation with smaller dimensions and should be considered for surgical intervention at lesser degrees of ventricular dilatation.²⁷

Vasodilators may help

There is some evidence that long-term vasodilator therapy may delay the need for valve replacement for patients with severe aortic regurgitation; however, vasodilators should not be used to postpone intervention in those who clearly meet surgical criteria.²⁸

■ MITRAL STENOSIS

Mitral stenosis is most commonly caused by damage to the mitral valve from rheumatic fever, after which there typically is a long period of asymptomatic progressive valve narrowing. Symptoms at rest are rare until the mitral valve area is less than 1.5 cm².

Symptoms include fatigue, dyspnea, orthopnea, and paroxysmal nocturnal dyspnea. These are due to increased left atrial pressure and decreased cardiac output, and usually occur in situations in which flow across the mitral valve is increased or diastolic filling time is decreased (eg, during exercise, pregnancy, or atrial fibrillation).²⁹ In more advanced cases, patients present with signs and symptoms of right-sided heart failure due to long-standing pulmonary hypertension.

Whether intervention is needed is determined by the symptoms, degree of functional impairment, and evidence of significant pulmonary hypertension.

Mitral stenosis can in many instances be effectively treated nonsurgically, ie, by percutaneous balloon valvotomy. The choice between a surgical vs a percutaneous approach depends on the valvular anatomy and the patient's general health.

Symptoms of chronic aortic regurgitation: angina, dyspnea, orthopnea, paroxysmal nocturnal dyspnea

Percutaneous balloon mitral valvotomy

In this procedure, a catheter is threaded from the femoral vein into the right heart, across into the left atrium via puncture of the atrial septum, and across the mitral valve. One or more balloons are then inflated, splitting the commissures and relieving the valvular obstruction. In properly selected patients, the outcome of balloon valvotomy is as good as or better than that of surgery (FIGURE 2).^{30–32}

Before the procedure, the valvular morphology must be assessed thoroughly, particularly the degree of commissural calcification.^{33–35} Poor candidates have heavily calcified, thickened, or noncompliant valves with extensive subvalvular involvement. These patients fare better with surgery (commissurotomy or valve replacement).

Significant mitral regurgitation (> 2+) is also a contraindication to the balloon procedure, because regurgitation is expected to increase by 1 grade, even if the procedure is successful. Other contraindications include left atrial thrombosis, severe tricuspid regurgitation, and severe pulmonary hypertension, because they increase the procedural risk and decrease the chances of a successful long-term outcome.

Symptomatic mitral stenosis

With advanced symptoms (NYHA class 3 or 4), patients with moderate-to-severe mitral stenosis (mitral valve area < 1.5 cm²) have a poor long-term prognosis without treatment and have an ACC/AHA class 1 indication for balloon valvotomy or surgery (FIGURE 3).^{4,36}

A patient with advanced symptoms who has only mild mitral stenosis (as determined by pressure gradient) should have an exercise stress test to determine whether the symptoms are attributable to mitral stenosis. A significant rise in pulmonary artery pressure (> 60 mm Hg) or transmitral gradient (> 15 mm Hg) with exercise suggests that the mitral stenosis is physiologically significant despite a measurement that falls within the “mild” range, and the patient should undergo evaluation for either balloon valvotomy or surgery (FIGURE 3).⁴ On the other hand, a normal exercise response suggests that an alternative etiology is responsible for the patient’s symptoms.

With mild symptoms (NYHA class 2), it is important to determine the severity of mitral stenosis. If the stenosis is moderate-to-severe (mitral valve area < 1.5 cm²), then the valve morphology should be assessed.

If the valve anatomy is favorable, then balloon valvotomy should be considered.⁴ If the anatomy precludes valvotomy, the patient should be followed closely with serial stress echocardiography every 6 to 12 months (FIGURE 3).

Asymptomatic mitral stenosis

Patients with asymptomatic mild mitral stenosis (mitral valve area > 1.5 cm²) have an excellent long-term prognosis, as symptoms do not usually develop for years.^{29,37}

Appropriate management includes an annual history, physical examination, electrocardiography, and chest radiography. Patients should also be taught the symptoms of mitral stenosis, signs of atrial fibrillation, and the need for antibiotic prophylaxis.⁴ Echocardiography is indicated if symptoms develop or if there is a significant change in the physical examination.⁹

Managing patients with asymptomatic moderate-to-severe mitral stenosis (mitral valve area < 1.5 cm²) is more challenging. Exercise stress testing may unmask symptoms in patients who are “asymptomatic” only because they have reduced their activity level. Patients who develop significant symptoms with exercise should be considered for balloon valvotomy or surgery, depending on valve morphology.

If stress testing does not provoke symptoms, but reveals evidence of pulmonary hypertension at rest (> 50 mm Hg) or with stress (> 60 mm Hg), the ACC/AHA guidelines consider this a class 2a indication for balloon valvotomy (FIGURE 3).⁴ Most agree that the overall risk of the procedure is less than the risk of long-standing pulmonary hypertension with subsequent right ventricular failure.

Atrial fibrillation and mitral stenosis

The onset of atrial fibrillation is not an indication for surgical intervention in patients who otherwise have no symptoms.

Long-term anticoagulation therapy is required, however, because patients with both

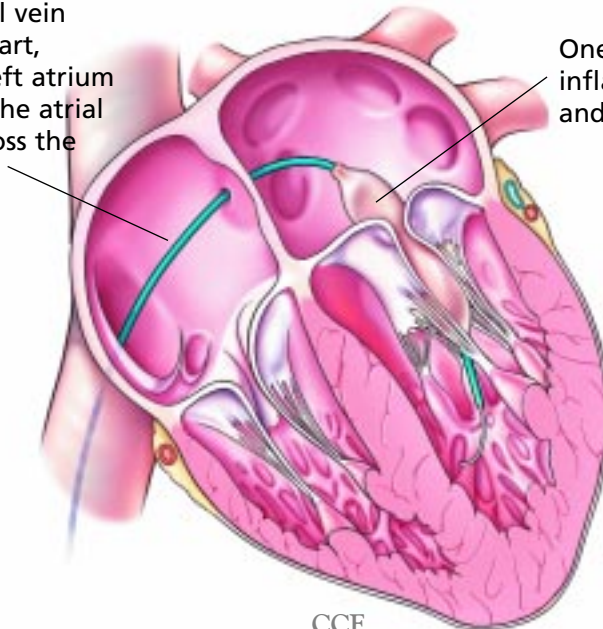
In mitral regurgitation, the ejection fraction does not accurately reflect ventricular function



■ Percutaneous balloon mitral valvotomy

Mitral stenosis can often be treated nonsurgically, ie, by percutaneous balloon valvotomy.

A catheter is threaded from the femoral vein into the right heart, across into the left atrium via puncture of the atrial septum, and across the mitral valve.



One or more balloons are then inflated, splitting the commissures and relieving the obstruction.

In properly selected patients, outcomes are as good as or better than with surgery.

Contraindications:

- Heavily calcified, thickened, or noncompliant valves with extensive subvalvular involvement
- Significant mitral regurgitation (> 2+)
- Left atrial thrombosis
- Severe tricuspid regurgitation
- Severe pulmonary hypertension

CCF
©2004

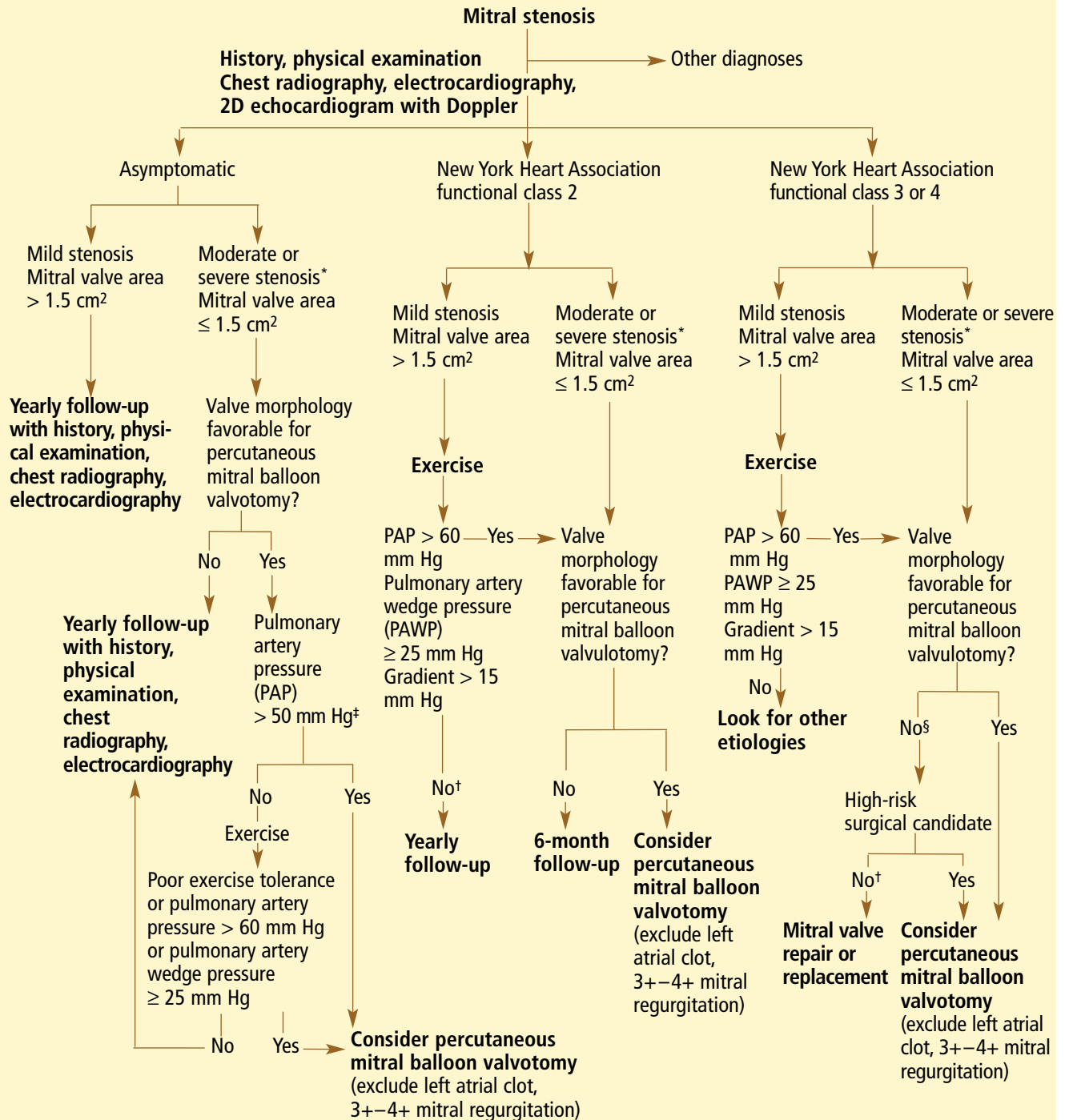
Before

After



FIGURE 2. Short-axis echocardiographic planimetry of mitral valve area before (left) and after (right) percutaneous balloon mitral valvotomy.

Management strategy for mitral stenosis



*Because there may be variability in the measurement of mitral valve area, it is important to consider the mean transmitral gradient, pulmonary artery wedge pressure, and pulmonary artery pressure

[†]There is controversy as to whether patients with severe mitral stenosis (mitral valve area < 1.0 cm²) and severe pulmonary hypertension (pulmonary artery pressure > 60–80 mm Hg) should undergo mitral valve replacement to prevent right ventricular failure

[‡]Assuming no other cause for pulmonary hypertension is present

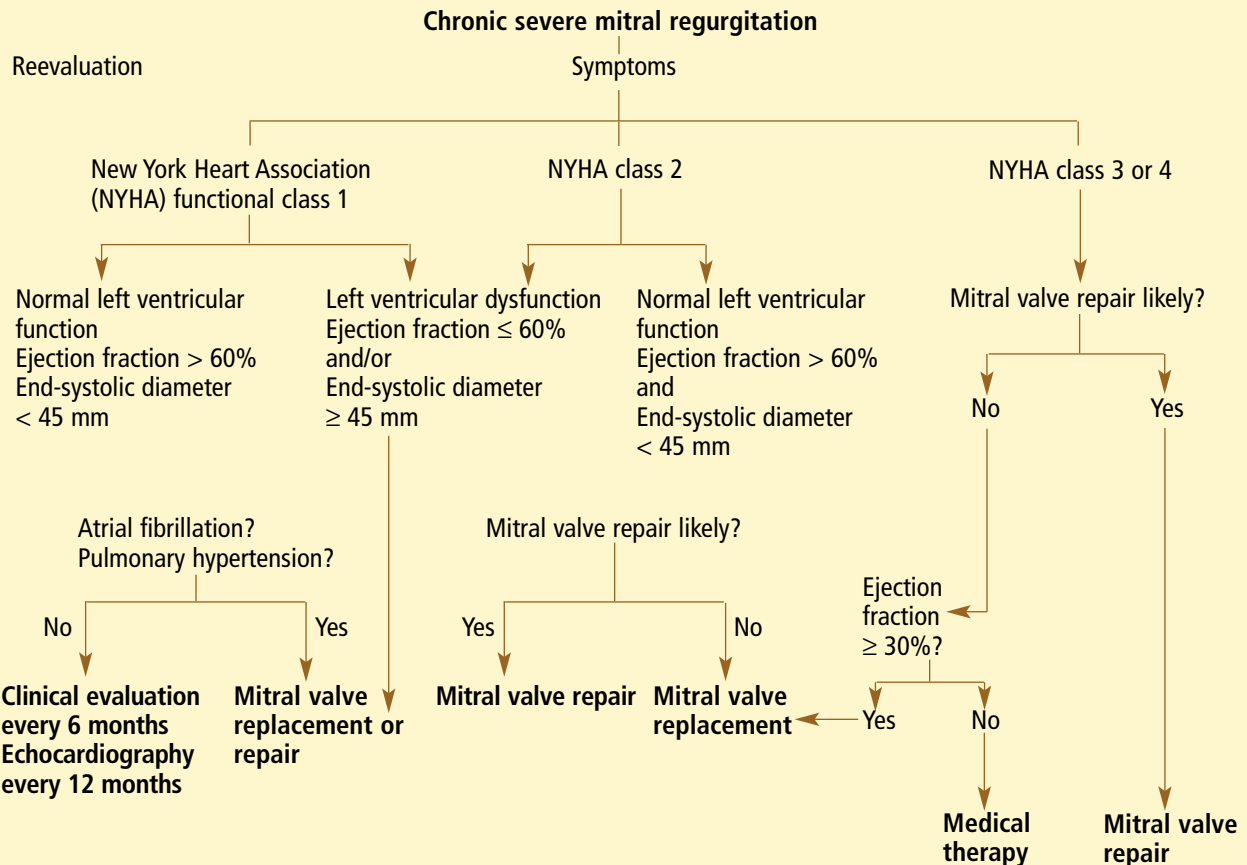
[§]There is controversy as to which patients with less favorable valve morphology should undergo percutaneous mitral balloon valvotomy rather than mitral valve surgery

ADAPTED FROM BONOW RO, CARABELLO B, DE LEON AC, ET AL. ACC/AHA GUIDELINES FOR THE MANAGEMENT OF PATIENTS WITH VALVULAR HEART DISEASE. EXECUTIVE SUMMARY. A REPORT OF THE AMERICAN COLLEGE OF CARDIOLOGY/AMERICAN HEART ASSOCIATION TASK FORCE ON PRACTICE GUIDELINES (COMMITTEE ON MANAGEMENT OF PATIENTS WITH VALVULAR HEART DISEASE). J AM COLL CARDIOL 1998; 32:1486–1588

FIGURE 3



Management strategy for patients with chronic severe mitral regurgitation



ADAPTED FROM BONOW RO, CARABELLO B, DE LEON AC, ET AL. ACC/AHA GUIDELINES FOR THE MANAGEMENT OF PATIENTS WITH VALVULAR HEART DISEASE. EXECUTIVE SUMMARY. A REPORT OF THE AMERICAN COLLEGE OF CARDIOLOGY/AMERICAN HEART ASSOCIATION TASK FORCE ON PRACTICE GUIDELINES (COMMITTEE ON MANAGEMENT OF PATIENTS WITH VALVULAR HEART DISEASE). J AM COLL CARDIOL 1998; 32:1486-1588.

FIGURE 4

mitral stenosis and atrial fibrillation have a very high risk of thromboembolism. Rarely, recurrent thromboembolism occurs despite adequate anticoagulation in a patient with mitral stenosis who has no other symptoms. Such patients require surgery to increase the mitral valve area and to tie off the left atrial appendage, and thus reduce the risk of subsequent embolic events.

■ MITRAL REGURGITATION

Mitral regurgitation occurs when disease of the valve leaflets, annular ring, or subvalvular apparatus causes poor alignment of the valve

leaflets during systole. The regurgitant volume leads to elevated left atrial pressures and volume overload in the left ventricle.

Acute mitral regurgitation

Acute mitral regurgitation is most often caused by chordal rupture in mitral valve prolapse, infective endocarditis, papillary muscle ischemia, or rupture of the posteromedial papillary muscle after a myocardial infarction.

If the onset is acute, the left atrial pressure rises rapidly, and patients typically present in a low-output state with pulmonary edema. Many patients need intra-aortic balloon

Exercise unmasks occult left ventricular dysfunction in chronic mitral regurgitation

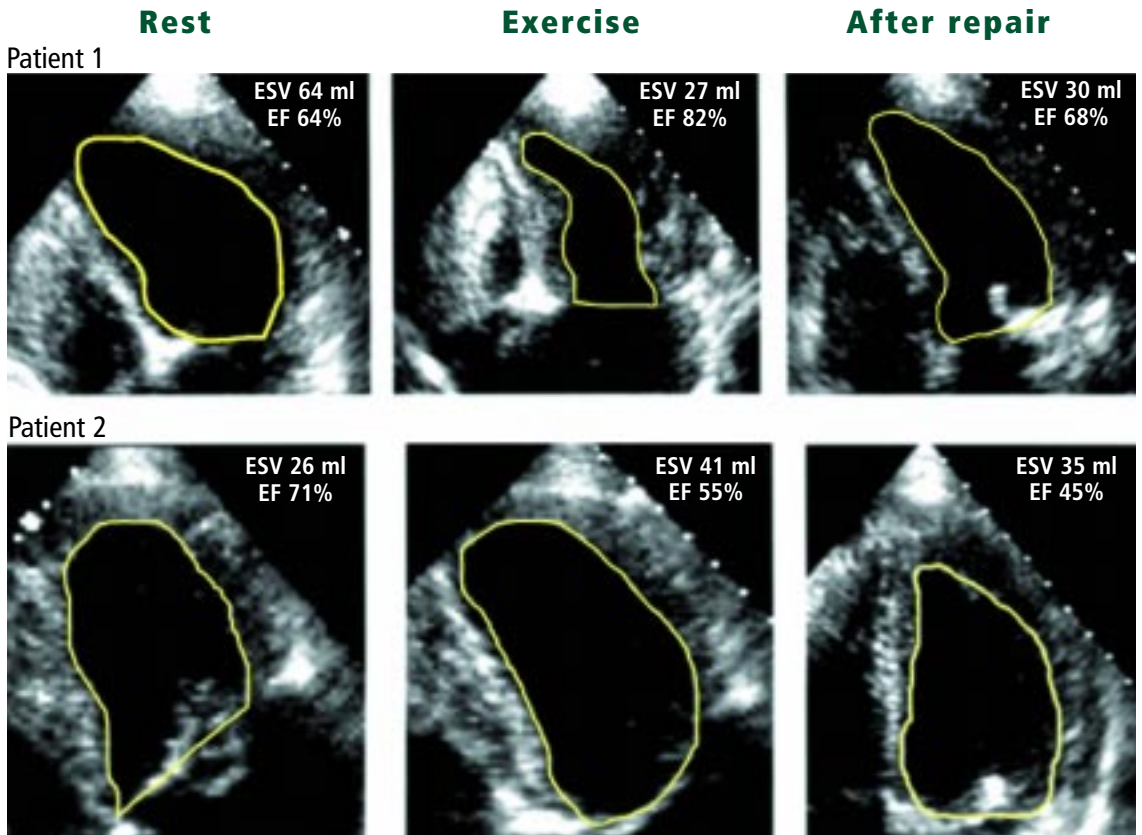


FIGURE 5. Stress echocardiography is useful in detecting occult LV dysfunction even in the setting of normal left ventricular ejection fraction (EF) in chronic mitral regurgitation. The top group of panels are end-systolic images of the stress echocardiogram of Patient 1, with preserved LV systolic function. Upon exercise (middle panel), the end-systolic volume (ESV) declines and the EF increases. After successful repair of the mitral valve, the EF remains in the normal range. On the bottom are images from Patient 2, in whom the resting EF is normal but the end-systolic volume increases and the EF declines on exercise. Following successful mitral valve repair, the EF is abnormal at 45%.

In asymptomatic mitral regurgitation, we obtain echos every 6-12 months

counterpulsation as a bridge to urgent mitral valve repair or replacement. In some patients with otherwise normal ventricles, the left ventricle compensates quickly, and symptoms of heart failure disappear rapidly without intervention.

Chronic mitral regurgitation

Chronic mitral regurgitation usually has a lengthy asymptomatic period because the left ventricle compensates with hypertrophy and dilatation.

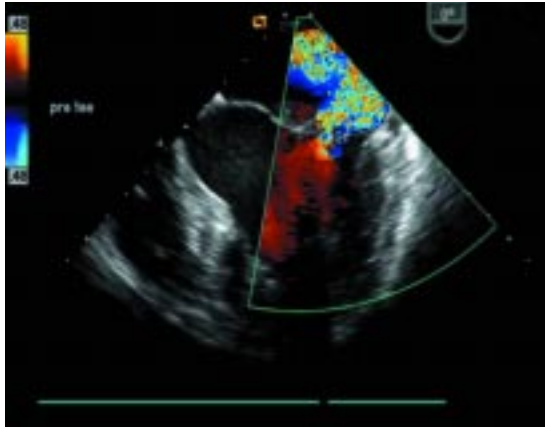
The most common cause of chronic mitral regurgitation is myxomatous degeneration of

the mitral valve leading to mitral valve prolapse, but other causes include rheumatic heart disease, mitral annular calcification, connective tissue disease, and functional mitral regurgitation due to ischemia or cardiomyopathy.

Ejection fraction may be elevated. In the asymptomatic period, preload increases (due to left ventricular dilatation) and afterload decreases (due to the low pressure outlet in the left atrium). At this stage, the cardiac output is normal and the ejection fraction is *above* normal. The ejection fraction does not accurately reflect ventricular func-



Before mitral valve repair



After repair



FIGURE 6. Successful repair of a prolapsing anterior mitral leaflet. Severe mitral regurgitation seen by transesophageal echocardiography before repair (left panel) is only a trace after repair (right panel).

tion in this situation, however, because the left ventricle is pumping a lot of blood into the low-pressure left atrium rather than into the systemic vessels (which are at a higher pressure than the left atrium). In fact, a “normal” ejection fraction in patients with severe chronic mitral regurgitation indicates that there is underlying left ventricular impairment.³⁸

After mitral valve repair or replacement the ejection fraction usually decreases.³⁹

Intervene before left ventricular dysfunction

The preoperative left ventricular function is the single most important predictor of postoperative outcome.^{40–43} Patients with severe mitral regurgitation must be referred for surgery before the left ventricle becomes impaired, regardless of symptoms or functional class.

For patients with severe primary mitral regurgitation (due to disease of the valve alone, such as mitral valve prolapse, and not secondary to ischemic heart disease or cardiomyopathy), a left ventricular ejection fraction of less than 60% should be considered evidence of actual or incipient left ventricular dysfunction, and surgical referral is appropriate before this occurs (FIGURE 4).

Medical treatment with afterload reduction is indicated for most cases of secondary mitral regurgitation.

Symptomatic mitral regurgitation

Symptomatic severe mitral regurgitation is a class 1 indication for surgery if the baseline left ventricular function is no more than moderately reduced (ejection fraction > 30% and left ventricular end-systolic diameter < 55 mm; FIGURE 4).⁴

Patients with severely reduced left ventricular function (ejection fraction < 30%, left ventricular end-systolic diameter > 55 mm) should be considered for mitral valve surgery on a case-by-case basis. Many of them have ischemic mitral regurgitation, and the debate over a strategy of combined revascularization with valve repair or replacement is beyond the scope of this article. Patients with an organic cause of mitral regurgitation (such as mitral valve prolapse), severe left ventricular dysfunction, and a high likelihood of successful valve repair generally fare better with surgery.⁴

Asymptomatic mitral regurgitation

Patients with asymptomatic severe mitral regurgitation who have left ventricular dysfunction (ejection fraction 30%–60%) should be referred at once for surgery (FIGURE 4).

When to refer a symptom-free patient with severe mitral regurgitation and normal left ventricular function (ejection fraction > 65%) is more problematic. The ACC/AHA guidelines advocate a conservative approach with frequent follow-up visits and echocardiography

Data are limited for aggressive repair of asymptomatic mitral regurgitation

every 6 to 12 months.⁴ Patients should be educated about antibiotic prophylaxis and the symptoms of mitral regurgitation and atrial fibrillation. Serial exercise stress testing is recommended to provide an objective measure of functional capacity.

We have found that the response of the left ventricle to stress predicts postoperative left ventricular function better than the resting left ventricular ejection fraction does (FIGURE 5). We perform exercise echocardiography at 6-month to 12-month intervals and assess the left ventricular ejection fraction and left ventricular systolic volume at both rest and peak exercise. Failure of the left ventricular ejection fraction to increase or the end-systolic volume to decrease at peak exercise indicates early left ventricular failure, which we consider an indication for surgical referral.

Other indications for surgery in the absence of symptoms or overt left ventricular dysfunction include (FIGURE 4):

- Significant left ventricular dilatation (left ventricular end-systolic dimension > 4.5 cm)
- Pulmonary hypertension at rest or with exercise (pulmonary artery systolic pressure > 60 mm Hg)
- Atrial fibrillation.

Is earlier surgery beneficial? Over the last decade, due to increasing success with valve repair and a decline in surgical morbidity and mortality, many experts have advocated earlier surgical intervention in asymptomatic patients with normal left ventricular function and dimensions. Data to support this aggressive strategy are limited, however.

Studies of early intervention suggest some benefit for patients who have a flail mitral leaflet. Two single-center retrospective studies of patients with asymptomatic mitral regurgitation due to a flail leaflet demonstrated improved long-term outcomes after early surgery.^{44,45}

However, a flail leaflet does not always lead to severe mitral regurgitation. In the absence of severe regurgitation, we recommend watchful waiting with serial clinical evaluations and stress echocardiography. If significant mitral regurgitation is confirmed

by Doppler echocardiography and left heart enlargement on echocardiography, then elective surgery seems reasonable, even in asymptomatic patients without serious comorbidities, as long as the valve seems likely to be repaired. This strategy has not yet been endorsed in the ACC/AHA guidelines. In all causes of mitral regurgitation, repair when feasible is preferable to valve replacement, as left ventricular function is better preserved with repair than with replacement (FIGURE 6).

■ TRICUSPID REGURGITATION

Tricuspid regurgitation occurs most commonly as a response to right ventricular dilatation and tricuspid annular enlargement in pulmonary hypertension or right ventricular dysfunction. This scenario is common in patients with severe mitral valve disease.

Therefore, patients who are undergoing surgery for mitral valve disease should also have tricuspid valve surgery if regurgitation is severe. Usually a valve repair is performed, but if a valve prosthesis is necessary, a bioprosthesis is favored. Mechanical prostheses have a significant risk of thrombosis at the tricuspid position.

Primary tricuspid regurgitation in the absence of left-sided valve lesions is relatively uncommon. However, other causes include:

- Right-sided endocarditis
- Trauma
- Congenital heart disease (eg, Ebstein anomaly)
- Carcinoid heart disease
- Iatrogenic damage (following percutaneous right ventricular biopsy).

Indications for surgery for tricuspid regurgitation

Patients with symptomatic severe tricuspid regurgitation with evidence of significant right ventricular volume loading, peripheral edema, and low output symptoms are candidates for valve surgery.

The treatment of severe primary tricuspid regurgitation without symptoms is controversial. We advocate elective surgical intervention if there is evidence of signifi-

Mitral repair is preferable to replacement, if feasible



cant right ventricular enlargement and evidence of any right ventricular dysfunction in otherwise healthy patients.

Patients with tricuspid regurgitation secondary to nonvalvular pulmonary hypertension are not usually considered surgical candidates. Instead, the tricuspid regurgitation often responds to therapeutic measures that lower the pulmonary pressures.

■ TRICUSPID STENOSIS

Tricuspid stenosis is usually rheumatic in origin and rarely occurs in patients who have no significant mitral valve disease. Symptomatic tricuspid stenosis is amenable to balloon valvotomy or to surgical commissurotomy. For severely calcified and stenotic valves, a bioprosthesis is required. ■

■ REFERENCES

- Chizner MA, Pearle DL, deLeon AC. The natural history of aortic stenosis in adults. *Am Heart J* 1980; 99:419–424.
- Kennedy KD, Nishimura RA, Holmes DR, Bailey KR. Natural history of moderate aortic stenosis. *J Am Coll Cardiol* 1991; 17:313–319.
- Otto CM, Mickel MC, Kennedy JW, et al. Three-year outcome after balloon aortic valvuloplasty. Insights into prognosis of valvular aortic stenosis. *Circulation* 1994; 89:642–650.
- Bonow RO, Carabello B, de Leon AC, et al. ACC/AHA guidelines for the management of patients with valvular heart disease. Executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Valvular Heart Disease). *J Am Coll Cardiol* 1998; 32:1486–1588.
- Pellikka PA, Nishimura RA, Bailey KR, Tajik AJ. The natural history of adults with asymptomatic, hemodynamically significant aortic stenosis. *J Am Coll Cardiol* 1990; 15:1012–1017.
- Dajani AS, Taubert KA, Wilson W, et al. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. *Circulation* 1997; 96:358–366.
- Otto CM, Burwash IG, Legget ME, et al. Prospective study of asymptomatic valvular aortic stenosis. Clinical, echocardiographic, and exercise predictors of outcome. *Circulation* 1997; 95:2262–2270.
- Rosenhek R, Binder T, Porenta G, et al. Predictors of outcome in severe, asymptomatic aortic stenosis. *N Engl J Med* 2000; 343:611–617.
- Cheitlin MD, Alpert JS, Armstrong WF, et al. ACC/AHA Guidelines for the Clinical Application of Echocardiography. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Clinical Application of Echocardiography). Developed in collaboration with the American Society of Echocardiography. *Circulation* 1997; 95:1686–1744.
- Otto CM. Aortic stenosis. Clinical evaluation and optimal timing of surgery. *Cardiol Clin* 1998; 16:353–373, vii.
- Lieberman EB, Bashore TM, Hermiller JB, et al. Balloon aortic valvuloplasty in adults: failure of procedure to improve long-term survival. *J Am Coll Cardiol* 1995; 26:1522–1528.
- Novaro GM, Tiong IY, Pearce GL, Lauer MS, Sprecher DL, Griffin BP. Effect of hydroxymethylglutaryl coenzyme A reductase inhibitors on the progression of calcific aortic stenosis. *Circulation* 2001; 104:2205–2209.
- al Jubair K, al Fagih MR, Ashmeg A, Belhaj M, Sawyer W. Cardiac operations during active endocarditis. *J Thorac Cardiovasc Surg* 1992; 104:487–490.
- Ricci DR. Afterload mismatch and preload reserve in chronic aortic regurgitation. *Circulation* 1982; 66:826–834.
- Alexopoulos D, Kolovou G, Kyriakidis M, et al. Angina and coronary artery disease in patients with aortic valve disease. *Angiology* 1993; 44:707–711.
- Bonow RO, Lakatos E, Maron BJ, Epstein SE. Serial long-term assessment of the natural history of asymptomatic patients with chronic aortic regurgitation and normal left ventricular systolic function. *Circulation* 1991; 84:1625–1635.
- Borer JS, Hochreiter C, Herrold EM, et al. Prediction of indications for valve replacement among asymptomatic or minimally symptomatic patients with chronic aortic regurgitation and normal left ventricular performance. *Circulation* 1998; 97:525–534.
- Kennedy JW, Doces J, Stewart DK. Left ventricular function before and following aortic valve replacement. *Circulation* 1977; 56:944–950.
- Forman R, Firth BG, Barnard MS. Prognostic significance of preoperative left ventricular ejection fraction and valve lesion in patients with aortic valve replacement. *Am J Cardiol* 1980; 45:1120–1125.
- Carabello BA, Usher BW, Hendrix GH, Assey ME, Crawford FA, Lemann RB. Predictors of outcome for aortic valve replacement in patients with aortic regurgitation and left ventricular dysfunction: a change in the measuring stick. *J Am Coll Cardiol* 1987; 10:991–997.
- Bonow RO, Picone AL, McIntosh CL, et al. Survival and functional results after valve replacement for aortic regurgitation from 1976 to 1983: impact of preoperative left ventricular function. *Circulation* 1985; 72:1244–1256.
- Bonow RO, Dodd JT, Maron BJ, et al. Long-term serial changes in left ventricular function and reversal of ventricular dilatation after valve replacement for chronic aortic regurgitation. *Circulation* 1988; 78:1108–1120.
- Bonow RO, Borer JS, Rosing DR, et al. Preoperative exercise capacity in symptomatic patients with aortic regurgitation as a predictor of postoperative left ventricular function and long-term prognosis. *Circulation* 1980; 62:1280–1290.
- Greves J, Rahimtoola SH, McAnulty JH, et al. Preoperative criteria predictive of late survival following valve replacement for severe aortic regurgitation. *Am Heart J* 1981; 101:300–308.
- Bonow RO, Rosing DR, Maron BJ, et al. Reversal of left ventricular dysfunction after aortic valve replacement for chronic aortic regurgitation: influence of duration of preoperative left ventricular dysfunction. *Circulation* 1984; 70:570–579.
- Tornos MP, Olona M, Permanyer-Miralda G, et al. Clinical outcome of severe asymptomatic chronic aortic regurgitation: a long-term prospective follow-up study. *Am Heart J* 1995; 130:333–339.
- Klodos E, Enriquez-Sarano M, Tajik AJ, Mullany CJ, Bailey KR, Seward JB. Surgery for aortic regurgitation in women. Contrasting indications and outcomes compared with men. *Circulation* 1996; 94:2472–2478.
- 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.
- Selzer A, Cohn KE. Natural history of mitral stenosis: a review. *Circulation* 1972; 45:878–890.
- Reyes VP, Raju BS, Wynne J, et al. Percutaneous balloon valvuloplasty compared with open surgical commissurotomy for mitral stenosis. *N Engl J Med* 1994; 331:961–967.
- Ben Farhat M, Ayari M, Maatouk F, et al. Percutaneous balloon versus surgical closed and open mitral commissurotomy: seven-year follow-up results of a randomized trial. *Circulation* 1998; 97:245–250.
- Palacios IF, Tuzcu ME, Weyman AE, Newell JB, Block PC. Clinical follow-up of patients undergoing percutaneous mitral balloon valvotomy. *Circulation* 1995; 91:671–676.
- Wilkins GT, Weyman AE, Abascal VM, Block PC, Palacios IF. Percutaneous balloon dilatation of the mitral valve: an analysis of echocardiographic variables related to outcome and the mechanism



- of dilatation. *Br Heart J* 1988; 60:299–308.
34. **Cannan CR, Nishimura RA, Reeder GS, et al.** Echocardiographic assessment of commissural calcium: a simple predictor of outcome after percutaneous mitral balloon valvotomy. *J Am Coll Cardiol* 1997; 29:175–180.
 35. **Cohen DJ, Kuntz RE, Gordon SP, et al.** Predictors of long-term outcome after percutaneous balloon mitral valvuloplasty. *N Engl J Med* 1992; 327:1329–1335.
 36. **Oleson K.** The natural history of 271 patients with mitral stenosis under medical treatment. *Br Heart J* 1962; 24:349.
 37. **Rowe J BE, Sprague H.** The course of mitral stenosis without surgery: Ten and twenty year perspectives. *Ann Intern Med* 1960; 52:741–749.
 38. **Wisnibaugh T.** Does normal pump function belie muscle dysfunction in patients with chronic severe mitral regurgitation? *Circulation* 1988; 77:515–525.
 39. **Wisnibaugh T, Spann JF, Carabello BA.** Differences in myocardial performance and load between patients with similar amounts of chronic aortic versus chronic mitral regurgitation. *J Am Coll Cardiol* 1984; 3:916–923.
 40. **Carabello BA, Williams H, Gash AK, et al.** Hemodynamic predictors of outcome in patients undergoing valve replacement. *Circulation* 1986; 74:1309–1316.
 41. **Corin WJ, Sutsch G, Murakami T, Krogmann ON, Turina M, Hess OM.** Left ventricular function in chronic mitral regurgitation: preoperative and postoperative comparison. *J Am Coll Cardiol* 1995; 25:113–121.
 42. **Crawford MH, Soucek J, Oprian CA, et al.** Determinants of survival and left ventricular performance after mitral valve replacement. Department of Veterans Affairs Cooperative Study on Valvular Heart Disease. *Circulation* 1990; 81:1173–1181.
 43. **Enriquez-Sarano M, Tajik AJ, Schaff HV, et al.** Echocardiographic prediction of left ventricular function after correction of mitral regurgitation: results and clinical implications. *J Am Coll Cardiol* 1994; 24:1536–1543.
 44. **Ling LH, Enriquez-Sarano M, Seward JB, et al.** Clinical outcome of mitral regurgitation due to flail leaflet. *N Engl J Med* 1996; 335:1417–1423.
 45. **Ling LH, Enriquez-Sarano M, Seward JB, et al.** Early surgery in patients with mitral regurgitation due to flail leaflets: a long-term outcome study. *Circulation* 1997; 96:1819–1825.

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