

## 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)

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### I. Introduction

This executive summary and recommendations appears in the November 3, 1998, issue of *Circulation*. The guidelines in their entirety, including the ACC/AHA Class I, II, and III recommendations, are published in the November 1, 1998, issue of the *Journal of the American College of Cardiology*. Reprints of both the full text and the executive summary and recommendations are available from both organizations.

During the past 2 decades, major advances have occurred in diagnostic techniques, the understanding of natural history, and interventional cardiologic and surgical procedures for

patients with valvular heart disease. The information base from which to make clinical management decisions has greatly expanded in recent years, yet in many situations, management issues remain controversial or uncertain. Unlike many other forms of cardiovascular disease, there is a scarcity of large-scale multicenter trials addressing the diagnosis and treatment of valvular disease from which to derive definitive conclusions, and the literature represents primarily the experiences reported by single institutions in relatively small numbers of patients.

The Committee on Management of Patients With Valvular Disease was given the task of reviewing and compiling this information base and making recommendations for diagnostic testing, treatment, and physical activity. These guidelines follow the format established in previous American College of Cardiology/American Heart Association (ACC/AHA) guidelines for classifying indications for diagnostic and therapeutic procedures:

**Class I:** Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective

**Class II:** Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment

Ia. Weight of evidence/opinion is in favor of usefulness/efficacy

Ib. Usefulness/efficacy is less well established by evidence/opinion.

**Class III:** Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful and in some cases may be harmful.

This task force report overlaps with several previously published ACC/AHA guidelines for cardiac imaging and diagnostic testing, including the Guidelines for Clinical Use of Cardiac Radionuclide Imaging,<sup>1</sup> the Guidelines for the Clinical Application of Echocardiography,<sup>2</sup> the Guidelines for Exercise Testing,<sup>3</sup>

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"Guidelines for the Management of Patients With Valvular Heart Disease: Executive Summary" was approved by the American College of Cardiology in August 1998 and the American Heart Association Science Advisory and Coordinating Committee in July 1998.

A single reprint of this document (Executive Summary) is available by calling 800-242-8721 (US only) or writing the American Heart Association, Public Information, 7272 Greenville Avenue, Dallas, TX 75231-4596. Ask for reprint No. 71-0154. To obtain a reprint of the full text of the Guidelines published in the November 1998 issue of the *Journal of the American College of Cardiology*, ask for reprint No. 71-0153. To purchase additional reprints, specify version and reprint number: up to 999 copies, call 800-611-6083 (US only) or fax 413-665-2671; 1000 or more copies, call 214-706-1466, fax 214-691-6342, or E-mail pubauth@amhrt.org. To make photocopies for personal or educational use, call the Copyright Clearance Center, 978-750-8400.

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and the Guidelines for Coronary Angiography.<sup>4</sup> Although these guidelines are not intended to include detailed information covered in previous guidelines on the use of imaging and diagnostic testing, a discussion of the indications for these tests in the evaluation and treatment of patients with valvular heart disease is an essential component of this summary.

The committee emphasizes the fact that many factors ultimately determine the most appropriate treatment of individual patients with valvular heart disease in individual communities. These factors include the availability of diagnostic equipment and expert diagnosticians, the expertise of interventional cardiologists and surgeons, and notably the wishes of well-informed patients. Therefore, deviation from these guidelines may be appropriate in some circumstances. These guidelines are written with the assumption that a diagnostic test can be performed and interpreted with skill levels consistent with previously reported ACC training and competency statements and ACC/AHA guidelines, that interventional cardiological and surgical procedures can be performed by highly trained practitioners within acceptable safety standards, and that the resources necessary to perform these diagnostic procedures and provide this care are readily available. This is not true in all geographic areas, which further underscores the committee's position that these recommendations are guidelines and not rigid requirements.

## II. General Principles

### A. Evaluation of the Patient With a Cardiac Murmur

A heart murmur may have no pathological significance or may be an important clue to the presence of valvular, congenital, or other structural abnormalities of the heart. Most systolic heart murmurs do not signify cardiac disease, and many are related to physiological increases in blood flow velocity. In other instances, a heart murmur may be an important clue to the diagnosis of undetected cardiac disease that may be important even when asymptomatic or that may define the reason for cardiac symptoms. In these situations, various noninvasive or invasive cardiac tests may be necessary to establish a firm diagnosis and form the basis for rational treatment of an underlying disorder. Two-dimensional (2-D) and Doppler echocardiography is particularly useful in this regard. Diastolic murmurs virtually always represent pathological conditions and require further cardiac evaluation, as do most continuous murmurs. Continuous "innocent" murmurs include venous hums and mammary soufflés.

An important consideration in a patient with a cardiac murmur is the presence or absence of symptoms. Many asymptomatic children and young adults with grade 2/6 midsystolic murmurs and no other cardiac physical findings need no further cardiac workup after the initial history and physical examination. A particularly important group is the large number of *asymptomatic* elderly patients, many with systemic hypertension, who have midsystolic murmurs related to sclerotic aortic valve leaflets, flow into tortuous, noncompliant great vessels, or a combination of these. Such murmurs must be distinguished from murmurs caused by mild to severe valvular aortic stenosis (AS), which is prevalent in this age group.

Although echocardiography usually provides more specific and often quantitative information about the significance of a heart murmur and may be the only test needed, the electrocardiogram (ECG) and chest x-ray are readily available and may have already been obtained. The absence of ventricular hypertrophy, atrial abnormality, arrhythmias, conduction abnormalities, prior myocardial infarction, and evidence of active ischemia on the ECG provides useful negative information at a relatively low cost. Abnormal findings on the ECG such as ventricular hypertrophy or a prior infarction should lead to a more extensive evaluation, including 2-D and Doppler echocardiography.

### Echocardiography

Echocardiography is an important noninvasive method for assessing the significance of cardiac murmurs. 2-D echocardiography may indicate abnormal valvular motion and morphology but usually does not indicate the severity of valvular stenosis or regurgitation except in mitral stenosis (MS). Doppler echocardiography identifies increased velocity of flow across stenotic valves from which the severity of stenosis may be determined. The presence of an abnormal regurgitant jet on Doppler color flow imaging indicates valvular regurgitation and provides semiquantitative information about its severity.

Although 2-D echocardiography and color flow Doppler imaging can provide important information on patients with cardiac murmurs, these tests are not necessary for all patients with cardiac murmurs and usually add little but expense in the evaluation of asymptomatic patients with short grade 1 to 2 midsystolic murmurs and otherwise normal physical findings. Alternatively, if the diagnosis is still questionable after transthoracic echocardiography, transesophageal echocardiography or cardiac catheterization may be appropriate. Many recent studies indicate that Doppler ultrasound devices are very sensitive and may detect valvular regurgitation through the tricuspid and pulmonic valves in a large percentage of healthy subjects and through left-sided valves (particularly the mitral) in a variable but lower percentage.

General recommendations for performing 2-D and Doppler echocardiography in asymptomatic and symptomatic patients with heart murmurs follow. Of course, individual exceptions to these indications may exist.

### Recommendations for Echocardiography in Asymptomatic Patients With Cardiac Murmurs

Indication	Class
1. Diastolic or continuous murmurs.	I
2. Holosystolic or late systolic murmurs.	I
3. Grade 3 or greater midsystolic murmurs.	I
4. Murmurs associated with abnormal physical findings on cardiac palpation or auscultation.	IIa
5. Murmurs associated with an abnormal ECG or chest x-ray.	IIa
6. Grade 2 or softer midsystolic murmur identified as innocent or functional by an experienced observer.	III
7. To detect "silent" aortic regurgitation or mitral regurgitation in patients without cardiac murmurs, then recommend endocarditis prophylaxis.	III

## Recommendations for Echocardiography in Symptomatic Patients With Cardiac Murmurs

Indication	Class
1. Symptoms or signs of congestive heart failure, myocardial ischemia, or syncope.	I
2. Symptoms or signs consistent with infective endocarditis or thromboembolism.	I
3. Symptoms or signs likely due to noncardiac disease with cardiac disease not excluded by standard cardiovascular evaluation.	IIa
4. Symptoms or signs of noncardiac disease with an isolated midsystolic "innocent" murmur.	III

There are very few data addressing the cost-effectiveness of various approaches to the patient undergoing medical evaluation of a cardiac murmur. Optimal auscultation by well-trained examiners who can recognize an insignificant midsystolic murmur with confidence results in less frequent use of expensive additional testing to define murmurs that do not indicate cardiac pathology.

Many murmurs in asymptomatic adults are innocent and have no functional significance. Such murmurs have the following characteristics: (1) grade 1 to 2 intensity at the left sternal border, (2) a systolic ejection pattern, (3) normal intensity and splitting of the second heart sound, (4) no other abnormal sounds or murmurs, and (5) no evidence of ventricular hypertrophy or dilatation and the absence of increased murmur intensity with the Valsalva maneuver. Such murmurs are especially common in high-output states such as pregnancy.

In the evaluation of heart murmurs, the purposes of echocardiography are to (1) define the primary lesion in terms of etiology and severity, (2) define hemodynamics, (3) define coexisting abnormalities, (4) detect secondary lesions, (5) evaluate cardiac chamber size and function, (6) establish a reference point for future comparisons, and (7) reevaluate the patient after an intervention.

## B. Endocarditis and Rheumatic Fever Prophylaxis

### 1. Endocarditis Prophylaxis

Endocarditis is a serious illness associated with significant mortality. Its prevention by appropriate administration of antibiotics before procedures expected to produce bacteremia merits serious consideration. Several issues must be considered in generating recommendations for endocarditis prophylaxis. It has been suggested that the risk of endocarditis in patients with preexisting cardiac disorders be classified as relatively high risk, moderate risk, and low or negligible risk, as determined by the cardiac disorder. Guidelines for the prevention of endocarditis have been issued by the American Heart Association,<sup>5</sup> and the current committee endorses those guidelines, with the following comments:

- This committee recommends prophylaxis in hypertrophic cardiomyopathy only when there is latent or resting obstruction.
- Patients with mitral valve prolapse (MVP) without regurgitation require additional clinical judgment. Indications for antibiotic prophylaxis in MVP are discussed in section III.D. Patients who do not have mitral regurgitation (MR) but do have echocardiographic evidence of thickening

and/or redundancy of the valve leaflets and especially men  $\geq 45$  years may be at increased risk for bacterial endocarditis.<sup>5</sup> Additionally, approximately one third of patients with MVP without MR at rest may have exercise-induced MR. Some patients may exhibit MR at rest on 1 occasion and none on others. There are no data available to address this latter issue, and at present, the decision must be left to clinical judgment, taking into account the nature of the invasive procedure, the previous history of endocarditis, and the presence or absence of valve thickening and/or redundancy.

- In patients with echocardiographic evidence of physiological MR in the absence of a murmur and with structurally normal valves, prophylaxis is not recommended. The committee also does *not* recommend prophylaxis for physiological tricuspid and pulmonary regurgitation detected by Doppler in the absence of a murmur, as such findings occur in a large number of normal individuals and the risk of endocarditis is extremely low. Recommendations regarding Doppler echocardiography for purposes of antibiotic prophylaxis in patients who have received anorectic drugs are given in section III.H. of these guidelines.

Various dental and/or surgical procedures are associated with varying degrees and frequencies of bacteremia. Recommendations for endocarditis prophylaxis, as determined by the dental and/or surgical procedure, are provided in full in the AHA recommendations for prevention of bacterial endocarditis<sup>5</sup> and the full text of these guidelines.

### 2. Rheumatic Fever Prophylaxis

Rheumatic fever is an important cause of valvular heart disease worldwide. In the United States (and Western Europe), cases of acute rheumatic fever have been uncommon since the 1970s. However, starting in 1987, an increase in cases has been observed.

Patients who have had an episode of rheumatic fever are at high risk of developing recurrent episodes of acute rheumatic fever. Patients who develop carditis are especially prone to similar episodes with subsequent attacks. Thus, secondary prevention of subsequent rheumatic fever recurrences is of great importance. Continuous antimicrobial prophylaxis has been shown to be effective. Anyone who has had rheumatic fever with or without carditis (including MS) should have prophylaxis for recurrent rheumatic fever. Lifelong prophylaxis is recommended for patients who have had carditis and residual valve disease and are likely to come in contact with populations with a high prevalence of streptococcal infections, such as teachers and day-care workers. Guidelines for primary and secondary prevention have been published by the AHA<sup>6</sup> and are reproduced in the full text of these guidelines.

## III. Specific Valve Lesions

### A. Aortic Stenosis

#### Grading the Degree of Stenosis

The aortic valve area must be reduced to one fourth its normal size before significant changes in the circulation occur. Because the normal adult valve orifice is  $\approx 3.0$  to  $4.0$   $\text{cm}^2$ , an area  $\geq 0.75$  to  $1.0$   $\text{cm}^2$  is usually not considered severe AS. In large patients, a valve area of  $1.0$   $\text{cm}^2$  may be severely stenotic, whereas a valve area of  $0.7$   $\text{cm}^2$  may be adequate for a smaller patient.

The committee used a variety of hemodynamic and natural history data to grade the degree of AS as mild (area  $> 1.5$   $\text{cm}^2$ ), moderate (area  $> 1.0$  to  $1.5$   $\text{cm}^2$ ), or severe (area  $\leq 1.0$

cm<sup>2</sup>). When stenosis is severe and cardiac output is normal, the mean transvalvular pressure gradient is generally >50 mm Hg. Some patients with severe AS remain asymptomatic, whereas others with only moderate stenosis develop symptoms. Therapeutic decisions, particularly those related to corrective surgery, are based largely on the presence or absence of symptoms. Thus, the absolute valve area (or transvalvular pressure gradient) is not usually the primary determinant of the need for aortic valve replacement (AVR).

An ejection systolic murmur may be heard in the presence of a normal valve, one that is thickened and minimally calcified, and one that is stenotic. The 3 conditions must be distinguished.

#### **Natural History**

The natural history of AS in the adult consists of a prolonged latent period in which morbidity and mortality are very low. The rate of progression of the stenotic lesion has been estimated in a variety of hemodynamic studies performed largely in patients with moderate AS. Cardiac catheterization and Doppler echocardiographic studies indicate that some patients exhibit a decrease in valve area of 0.1 to 0.3 cm<sup>2</sup> per year; the average rate of change is ≈0.12 cm<sup>2</sup> per year. The systolic pressure gradient across the valve may increase by as much as 10 to 15 mm Hg per year. However, more than half of the reported patients showed little or no progression over a 3- to 9-year period. Although it appears that progression of AS can be more rapid in patients with degenerative calcific disease than in those with congenital or rheumatic disease, it is not possible to predict the rate of progression in an individual patient.

Eventually, symptoms of angina, syncope, or heart failure develop after a long latent period, and the outlook changes dramatically. After onset of symptoms, average survival is <2 to 3 years. Thus, the development of symptoms identifies a critical point in the natural history of AS.

Many asymptomatic patients with severe AS develop symptoms within a few years and require surgery. The incidence of angina, dyspnea, or syncope in asymptomatic patients with Doppler outflow velocities ≥4 m/s has been reported to be as high as 38% after 2 years and 79% after 3 years. Therefore, patients with severe AS require careful monitoring for development of symptoms and progressive disease.

Sudden death is known to occur in patients with severe AS but has rarely been documented to occur without prior symptoms. Recent prospective echocardiographic studies provide important data on the rarity of sudden death in asymptomatic patients. Although sudden death does occasionally occur in the absence of preceding symptoms in patients with AS, it must be an uncommon event—probably <1% per year.

#### **Management of the Asymptomatic Patient**

Patients with the physical findings of AS should undergo selected laboratory examinations, including an ECG, a chest x-ray, and an echocardiogram. The 2-D echocardiogram is valuable for confirming the presence of aortic valve disease and determining left ventricular (LV) size and function,

degree of hypertrophy, and presence of other associated valve disease. In most patients, the severity of the stenotic lesion can be defined with Doppler echocardiographic measurements of a mean transvalvular pressure gradient and a derived valve area as discussed in the ACC/AHA Guidelines for the Clinical Application of Echocardiography.<sup>2</sup>

#### **Recommendations for Echocardiography in Aortic Stenosis**

Indication	Class
1. <b>Diagnosis and assessment of severity of AS.</b>	I
2. <b>Assessment of LV size, function, and/or hemodynamics.</b>	I
3. <b>Reevaluation of patients with known AS with changing symptoms or signs.</b>	I
4. <b>Assessment of changes in hemodynamic severity and ventricular compensation in patients with known AS during pregnancy.</b>	I
5. <b>Reevaluation of asymptomatic patients with severe AS.</b>	I
6. <b>Reevaluation of asymptomatic patients with mild to moderate AS and evidence of LV dysfunction or hypertrophy.</b>	IIa
7. <b>Routine reevaluation of asymptomatic adult patients with mild AS having stable physical signs and normal LV size and function.</b>	III

From the ACC/AHA Guidelines for the Clinical Application of Echocardiography.<sup>2</sup>

In some patients, it may be necessary to proceed with cardiac catheterization and coronary angiography at the time of initial evaluation. This is appropriate, for example, if there is a discrepancy between the clinical and echocardiographic examinations or if the patient is symptomatic and AVR is planned.

Exercise testing in adults with AS has been discouraged largely because of concerns about safety. Furthermore, when used to assess the presence or absence of coronary artery disease (CAD), the test has limited diagnostic accuracy. Certainly, exercise testing should not be performed in symptomatic patients. However, in asymptomatic patients, exercise testing is safe and may provide information not uncovered during the initial clinical evaluation. Exercise testing in asymptomatic patients should be performed only under the supervision of an experienced physician, with close monitoring of blood pressure and the ECG. Such testing can identify patients who have a limited exercise capacity or even exercise-induced symptoms despite a negative medical history. An abnormal hemodynamic response (eg, hypotension) in a patient with severe AS is sufficient reason to consider AVR.

The frequency of follow-up visits to the physician depends on the severity of valvular stenosis and in part on the presence of comorbid conditions. Recognizing that an optimal schedule for repeated medical examinations has not been defined, many physicians perform an annual history and physical examination on patients with mild AS. Those with moderate and severe AS should be examined more frequently. Patients should be advised to promptly report the development of any exertional chest discomfort, dyspnea, lightheadedness, or syncope.

Echocardiographic studies can be an important part of an integrated approach to the asymptomatic patient. Current understanding of the natural history of AS and indications for surgical intervention do not support the use of annual echocardiographic studies to assess changes in valve area. However, serial echocardiograms are helpful for assessing changes in LV hypertrophy and function. Therefore, in patients with severe AS, a yearly echocardiogram may be appropriate. In patients with moderate AS, serial studies every 2 years or so are satisfactory, and in patients with mild AS, serial studies can be performed every 5 years. Echocardiography should be performed more frequently if there is a change in clinical findings.

Recommendations for activity are based on the clinical examination, with special emphasis on the hemodynamic severity of the stenotic lesion. Recommendations regarding participation in competitive athletics have been published by the Task Force on Acquired Valvular Heart Disease of the 26th Bethesda Conference.<sup>7</sup> Patients with severe AS should be advised to limit activity to relatively low levels.

#### **Indications for Cardiac Catheterization**

In patients with AS, the indications for cardiac catheterization and angiography are to assess the coronary circulation and confirm or clarify the clinical diagnosis. In preparation for AVR, coronary angiography is indicated in patients suspected of having CAD, as discussed in section VIII. If the clinical and echocardiographic data are typical of severe isolated AS, coronary angiography may be all that is needed before AVR. Complete left- and right-heart catheterization may be necessary to assess the hemodynamic severity of AS if there is a discrepancy between clinical and echocardiographic data or evidence of associated valvular or congenital disease or pulmonary hypertension.

#### **Recommendations for Cardiac Catheterization in Aortic Stenosis**

Indication	Class
1. Coronary angiography before AVR in patients at risk for CAD (see section VIII.B. of these guidelines).	I
2. Assessment of severity of AS in symptomatic patients when AVR is planned or when noninvasive tests are inconclusive or there is a discrepancy with clinical findings regarding severity of AS or need for surgery.	I
3. Assessment of severity of AS before AVR when noninvasive tests are adequate and concordant with clinical findings and coronary angiography is not needed.	IIb
4. Assessment of LV function and severity of AS in asymptomatic patients when noninvasive tests are adequate.	III

The pressure gradient across a stenotic valve is related to the valve orifice area and transvalvular flow. Thus, in the presence of depressed cardiac output, relatively low pressure gradients are frequently obtained in patients with severe AS. On the other hand, during exercise or other high-flow states, systolic gradients can be measured in minimally stenotic valves. For these reasons, complete assessment of AS requires (1) measurement of transvalvular flow, (2) determina-

tion of the transvalvular pressure gradient, and (3) calculation of the effective valve area. Careful attention to detail with accurate measurements of pressure and flow is important, especially in patients with low cardiac output or a low transvalvular pressure gradient.

Patients with severe AS and low cardiac output often present with only modest transvalvular pressure gradients (ie, <30 mm Hg). Such patients can be difficult to distinguish from those with low cardiac output and only mild to moderate AS. In both situations, the low-flow state and low pressure gradient contribute to a calculated effective valve area that can meet criteria for severe AS. The standard valve area formula is less accurate and is known to underestimate the valve area in low-flow states; under such conditions, it should be interpreted with caution. Although valve resistance is less sensitive to flow than valve area, resistance calculations have not been proved to be substantially better than valve area calculations.

In patients with low gradient stenosis and what appears to be moderate to severe AS, it may be useful to determine the transvalvular pressure gradient and calculate valve area and resistance during a baseline state and again during exercise or pharmacological (ie, dobutamine infusion) stress. Patients who do not have true, anatomically severe stenosis exhibit an increase in the valve area during an increase in cardiac output. In patients with severe AS, these changes may result in a calculated valve area that is higher than the baseline calculation but that remains in the severe range, whereas in patients without severe AS, the calculated valve area will fall outside the severe range with administration of dobutamine and indicate that severe AS is not present.

#### **Indications for Aortic Valve Replacement**

In the vast majority of adults, AVR is the only effective treatment for severe AS. However, younger patients may be candidates for valvotomy (see section VI.A.).

*1. Symptomatic Patients.* Patients with angina, dyspnea, or syncope exhibit symptomatic improvement and an increase in survival after AVR. Outcome is similar in patients with normal LV function and those with moderate depression of contractile function. The depressed ejection fraction in many patients in this latter group is caused by excessive afterload (afterload mismatch), and LV function improves after AVR in such patients. If LV dysfunction is not caused by afterload mismatch, then improvement in LV function and resolution of symptoms may not be complete after valve replacement. Survival is still improved in this setting with the possible exception of patients with severe LV dysfunction caused by CAD. Therefore, in the absence of serious comorbid conditions, AVR is indicated in virtually all symptomatic patients with severe AS. However, patients with severe LV dysfunction, particularly those with so-called low gradient AS, represent a difficult management decision (see above). AVR should not be performed in such patients when they do not have anatomically severe stenosis. In patients with severe AS, even those with a low transvalvular pressure gradient, AVR results in hemodynamic improvement and better functional status.

2. *Asymptomatic Patients.* Management decisions in asymptomatic patients are more controversial. The combined risk of surgery and late complications of a prosthesis generally exceed the possibility of preventing sudden death and prolonging survival in all asymptomatic patients, as discussed previously. Despite these considerations, some difference of opinion persists regarding indications for AVR in asymptomatic patients. It is reasonable to attempt to identify patients who may be at especially high risk of sudden death without surgery, although data supporting this approach are limited. Patients in this subgroup include those with an abnormal response to exercise (eg, hypotension), LV systolic dysfunction or marked/excessive LV hypertrophy, or evidence of severe AS. However, it should be recognized that such “high-risk” patients are rarely asymptomatic.

3. *Patients Undergoing Coronary Artery Bypass Surgery.* Patients with severe AS, with or without symptoms, who are undergoing coronary artery bypass surgery should undergo AVR at the time of revascularization. Similarly, patients with severe AS undergoing surgery on other valves (such as mitral valve repair) or the aortic root should also undergo AVR as part of the surgical procedure. Patients with moderate AS (for example, gradient  $\geq 30$  mm Hg) may warrant AVR at the time of coronary artery bypass surgery or surgery on the mitral valve or aortic root. However, controversy persists regarding indications for concomitant AVR at the time of coronary artery bypass surgery in patients with milder forms of AS as discussed in section VIII.D.

#### Recommendations for Aortic Valve Replacement in Aortic Stenosis

Indication	Class
1. Symptomatic patients with severe AS.	I
2. Patients with severe AS undergoing coronary artery bypass surgery.	I
3. Patients with severe AS undergoing surgery on the aorta or other heart valves.	I
4. Patients with moderate AS undergoing coronary artery bypass surgery or surgery on the aorta or other heart valves (see sections III.F. and VIII.D.).	IIa
5. Asymptomatic patients with severe AS and	
• LV systolic dysfunction	IIa
• Abnormal response to exercise (eg, hypotension)	IIa
• Ventricular tachycardia	IIb
• Marked or excessive LV hypertrophy ( $\geq 15$ mm)	IIb
• Valve area $< 0.6$ cm <sup>2</sup>	IIb
6. Prevention of sudden death in asymptomatic patients with none of the findings listed under indication 5.	III

#### Aortic Balloon Valvotomy

Percutaneous balloon aortic valvotomy has an important role in treatment of adolescents and young adults with AS (see section VI.A.) but a very limited role in older adults. Immediate hemodynamic results include a moderate reduction in the transvalvular pressure gradient, but the postvalvot-

omy valve area is rarely  $> 1.0$  cm<sup>2</sup>. However, serious complications occur with a frequency of  $> 10\%$ , and restenosis and clinical deterioration occur within 6 to 12 months in most patients. Therefore, in adults with AS, balloon valvotomy is not a substitute for AVR.

Balloon valvotomy can play a temporary role in the management of some symptomatic patients who are not initially candidates for AVR. For example, patients with severe AS and refractory pulmonary edema or cardiogenic shock may benefit from aortic valvuloplasty as a “bridge” to surgery; an improved hemodynamic state may reduce the risks of AVR. Indications for palliative valvotomy in patients with serious comorbid conditions are less well established, but most patients can expect temporary relief of symptoms despite a very limited life expectancy. Asymptomatic patients with severe AS who require urgent noncardiac surgery may be candidates for valvotomy, but most such patients can be successfully treated with more conservative measures.

#### Recommendations for Aortic Balloon Valvotomy in Adults With Aortic Stenosis\*

Indication	Class
1. A “bridge” to surgery in hemodynamically unstable patients who are at high risk for AVR.	IIa
2. Palliation in patients with serious comorbid conditions.	IIb
3. Patients who require urgent noncardiac surgery.	IIb
4. An alternative to AVR.	III

\*Recommendations for aortic balloon valvotomy in adolescents and young adults with AS are provided in section VI.A.

#### Special Considerations in the Elderly

Because there is no effective medical therapy and balloon valvotomy is not an acceptable alternative to surgery, AVR must be considered in all elderly patients who have symptoms caused by AS. AVR is technically possible at any age, but the decision to proceed with such surgery depends on many factors, including the patient’s wishes and expectations.

In addition to the confounding effects of CAD and the potential for stroke, other considerations are specific to older patients. For example, a narrow LV outflow tract and small aortic annulus sometimes present in elderly women may require enlargement of the annulus. Heavy calcification of the valve, annulus, and aortic root may require debridement. Occasionally, a composite valve-aortic graft is needed. Excessive or inappropriate hypertrophy associated with valvular stenosis can be a marker for perioperative morbidity and mortality. Preoperative recognition of elderly patients with marked LV hypertrophy followed by appropriate perioperative management may substantially reduce this morbidity and mortality.

## B. Aortic Regurgitation

### 1. Acute Aortic Regurgitation

In acute severe aortic regurgitation (AR), the sudden large regurgitant volume is imposed on a left ventricle of normal size that has not had time to accommodate to the volume overload. LV end-diastolic and left atrial pressures may increase rapidly and dramatically. The Frank-Starling mechanism is used, but the inability of the ventricle to develop

compensatory chamber dilatation acutely results in a decrease in forward stroke volume. Although tachycardia develops as a compensatory mechanism to maintain cardiac output, this is often insufficient. Hence, patients frequently present with pulmonary edema and/or cardiogenic shock.

#### *Diagnosis*

Many of the characteristic physical findings of chronic AR are modified or absent when valvular regurgitation is acute, which may lead to underestimation of its severity. Echocardiography is indispensable in confirming the presence and severity of valvular regurgitation, determining its etiology, estimating the degree of pulmonary hypertension (if tricuspid regurgitation [TR] is present), and determining whether there is rapid equilibration of aortic and LV diastolic pressure. Evidence for rapid pressure equilibration includes short AR diastolic half-time (<300 ms), short mitral deceleration time (<150 ms), or premature closure of the mitral valve.

Acute AR caused by aortic root dissection is a surgical emergency that requires prompt identification and management. Transesophageal echocardiography is indicated when aortic dissection is suspected. If the diagnosis remains uncertain, cardiac catheterization and aortography should be performed. Coronary angiography is an important component of the evaluation of aortic dissection and acute AR and should be performed, provided that it does not delay urgent surgery.

#### *Treatment*

Death from pulmonary edema, ventricular arrhythmias, electromechanical dissociation, or circulatory collapse is common in acute severe AR, even with intensive medical management. Early surgical intervention is recommended. Nitroprusside and possibly inotropic agents such as dopamine or dobutamine to augment forward flow and reduce LV end-diastolic pressure may be helpful to treat the patient temporarily before surgery. Intra-aortic balloon counterpulsation is contraindicated. Although  $\beta$ -blockers are often used in treating aortic dissection, they should be used cautiously, if at all, in the setting of acute AR because they will block compensatory tachycardia.

### **2. Chronic Aortic Regurgitation**

Chronic AR represents a condition of combined volume overload and pressure overload. As the disease progresses, recruitment of preload reserve and compensatory hypertrophy permit the ventricle to maintain normal ejection performance despite the elevated afterload. The majority of patients remain asymptomatic throughout this compensated phase, which may last for decades. Vasodilator therapy has the potential to reduce the hemodynamic burden in such patients.

For the purposes of subsequent discussion, patients with normal LV systolic function are defined as those with normal LV ejection fraction at rest. It is recognized that overall LV function is usually not "normal" in chronic severe AR and that the hemodynamic abnormalities noted above may be considerable. It is also recognized that the transition to LV systolic dysfunction represents a continuum and that no single hemodynamic measurement represents the absolute boundary between normal LV systolic function and LV systolic dysfunction.

The balance between afterload excess, preload reserve, and hypertrophy cannot be maintained indefinitely in many patients, and afterload mismatch and/or depressed contractility ultimately result in a reduction in ejection fraction, first into the low normal range and then below normal. At this point in the natural history, patients often develop dyspnea, which is related to declining systolic function or elevated filling pressures. However, this transition may be much more insidious, and it is possible for patients to remain asymptomatic until severe LV dysfunction has developed.

LV systolic dysfunction (defined as an ejection fraction below normal at rest) is initially a reversible phenomenon predominantly related to afterload excess, and full recovery of LV size and function is possible with AVR. With time, during which the ventricle develops progressive chamber enlargement and a more spherical geometry, depressed myocardial contractility predominates over excessive loading as the cause of progressive systolic dysfunction. This can progress to the extent that the full benefit of surgical correction of the regurgitant lesion in terms of recovery of LV function and improved survival can no longer be achieved.

A large number of studies have identified LV systolic function and end-systolic size as the most important determinants of survival and postoperative LV function in patients undergoing AVR for chronic AR.

Several factors are associated with worse functional and survival results after AVR for chronic AR in patients with preoperative LV systolic dysfunction. These include severity of symptoms, the severity of LV systolic dysfunction, and the duration of preoperative systolic dysfunction. Taken together, these observations support the recommendation that patients with evidence of LV systolic dysfunction, even if asymptomatic or minimally symptomatic, should undergo AVR before more severe symptoms or more severe ventricular dysfunction develop.

#### *Natural History*

*1. Asymptomatic Patients With Normal Left Ventricular Function.* The current recommendations are derived from 7 published series involving a total of 490 patients with a mean follow-up period of 6.4 years. The rate of progression to symptoms and/or LV systolic dysfunction averaged 4.3% per year. Sudden death occurred in 6 of the 490 patients, an average mortality rate of <0.2% per year. Six of the 7 studies reported the rate of development of asymptomatic LV dysfunction; 36 of a total of 463 patients developed depressed systolic function at rest without symptoms during a mean 5.9-year follow-up period, a rate of 1.3% per year.

*2. Asymptomatic Patients With Depressed Systolic Function.* The limited data in asymptomatic patients with depressed LV ejection fraction indicate that the majority develop symptoms warranting surgery within 2 to 3 years. The average rate of symptom onset in such patients is >25% per year.

*3. Symptomatic Patients.* There are no recent large-scale studies of the natural history of symptomatic patients with chronic AR, because the onset of angina or significant dyspnea is usually an indication for valve replacement. Data from the presurgical era indicate that symptomatic patients have a poor outcome with medical therapy, which is analo-

gous to that of patients with symptomatic AS, with mortality rates of >10% per year in patients with angina pectoris and >20% per year in those with heart failure.

#### *Diagnosis and Initial Evaluation of the Asymptomatic Patient*

The diagnosis of chronic severe AR can usually be made on the basis of physical examination. The chest x-ray and ECG are helpful in evaluating overall heart size and rhythm, evidence of LV hypertrophy, and evidence of conduction disorders.

Echocardiography is indicated to confirm the diagnosis of AR if there is an equivocal diagnosis based on physical examination; assess the cause of AR as well as valve morphology; provide a semiquantitative estimate of severity of regurgitation; assess LV dimension, mass, and systolic function; and assess aortic root size. In asymptomatic patients with preserved systolic function, these initial measurements represent the baseline information with which future serial measurements can be compared.

#### Recommendations for Echocardiography in Aortic Regurgitation

Indication	Class
1. Confirm presence and severity of acute AR.	I
2. Diagnosis of chronic AR in patients with equivocal physical findings.	I
3. Assessment of etiology of regurgitation (including valve morphology and aortic root size and morphology).	I
4. Assessment of LV hypertrophy, dimension (or volume), and systolic function.	I
5. Semiquantitative estimate of severity of AR.	I
6. Reevaluation of patients with mild, moderate, or severe regurgitation with new or changing symptoms.	I
7. Reevaluation of LV size and function in asymptomatic patients with severe regurgitation.	I
8. Reevaluation of asymptomatic patients with mild, moderate, or severe regurgitation and enlarged aortic root.	I
9. Yearly reevaluation of asymptomatic patients with mild to moderate regurgitation with stable physical signs and normal or near-normal LV chamber size.	III

If the patient is asymptomatic and leads an active lifestyle and the echocardiogram is of good quality, no other testing is necessary. If the patient has severe AR and is sedentary or has equivocal symptoms, exercise testing is helpful to assess functional capacity, symptomatic responses, and hemodynamic effects of exercise. If the echocardiogram is of insufficient quality to assess LV function, radionuclide angiography should be used in asymptomatic patients to measure LV ejection fraction at rest and estimate LV volumes. When patients are symptomatic on initial evaluation, it is reasonable to proceed directly with cardiac catheterization and angiography if the echocardiogram is of insufficient quality to assess LV function or severity of AR.

The exercise ejection fraction and change in ejection fraction from rest to exercise are often abnormal, even in asymptomatic patients. However, these have not been proved to have independent diagnostic or prognostic value

when LV function at rest and severity of LV volume overload by echocardiography are already known.

#### Recommendations for Exercise Testing in Chronic Aortic Regurgitation\*

Indication	Class
1. Assessment of functional capacity and symptomatic responses in patients with a history of equivocal symptoms.	I
2. Evaluation of symptoms and functional capacity before participation in athletic activities.	IIa
3. Prognostic assessment before AVR in patients with LV dysfunction.	IIa
4. Exercise hemodynamic measurements to determine the effect of AR on LV function.	IIb
5. Exercise radionuclide angiography for assessing LV function in asymptomatic or symptomatic patients.	IIb
6. Exercise echocardiography or dobutamine stress echocardiography for assessing LV function in asymptomatic or symptomatic patients.	III

\*These recommendations differ from the ACC/AHA Guidelines for Exercise Testing.<sup>3</sup> The committee believes that indications 1, 2, and 3 above warrant a higher recommendation than IIb.

#### Recommendations for Radionuclide Angiography in Aortic Regurgitation

Indication	Class
1. Initial and serial assessment of LV volume and function at rest in patients with suboptimal echocardiograms or equivocal echocardiographic data.*	I
2. Serial assessment of LV volume and function at rest when serial echocardiograms are not used.*	I
3. Assessment of LV volume and function in asymptomatic patients with moderate to severe regurgitation when echocardiographic evidence of declining LV function is suggestive but not definitive.*	I
4. Confirmation of subnormal LV ejection fraction before recommending surgery in an asymptomatic patient with borderline echocardiographic evidence of LV dysfunction.*	I
5. Assessment of LV volume and function in patients with moderate to severe regurgitation when clinical assessment and echocardiographic data are discordant.*	I
6. Routine assessment of exercise ejection fraction.	IIb
7. Quantification of AR in patients with unsatisfactory echocardiograms.	IIb
8. Quantification of AR in patients with satisfactory echocardiograms.	III
9. Initial and serial assessment of LV volume and function at rest in addition to echocardiography.	III

\*In centers with expertise in cardiac magnetic resonance imaging (MRI), cardiac MRI may be used in place of radionuclide angiography for these indications.

Asymptomatic patients with normal LV systolic function may participate in all forms of normal daily physical activity, including mild-intensity forms of exercise and in some cases competitive athletics. Isometric exercise should be avoided. Recommendations for participation in competitive athletics



were published by the Task Force on Acquired Valvular Heart Disease of the 26th Bethesda Conference.<sup>7</sup>

*Medical Therapy*

Therapy with vasodilating agents is designed to improve forward stroke volume and reduce regurgitant volume. These effects should translate into reductions in LV end-diastolic volume, wall stress, and afterload, resulting in preservation of LV systolic function and reduction in LV mass. These effects have been observed in small numbers of patients who received oral therapy with hydralazine and nifedipine for 1 to 2 years. Less consistent results have been reported with angiotensin converting enzyme (ACE) inhibitors, depending on the degree of reduction in arterial pressure and end-diastolic volume.

Only 1 study, in which long-acting nifedipine was compared with digoxin therapy in 143 patients followed up for 6 years, has evaluated whether vasodilating therapy alters the long-term natural history of chronic asymptomatic AR in a favorable manner. Over 6 years, long-acting nifedipine reduced the need for valve replacement from 34% to 15%. Moreover, when patients who received nifedipine did undergo AVR because of symptoms or impaired systolic function, all survived surgery, and LV size and function improved considerably in all patients.

The goal of vasodilator therapy is to reduce systolic blood pressure. Drug dosage should be increased until there is a measurable decrease in systolic blood pressure or the patient develops side effects. It is rarely possible to decrease systolic blood pressure to normal because of the increased LV stroke volume, and drug dosage should not be increased excessively in an attempt to achieve this goal. Vasodilator therapy is of unknown benefit and is not indicated in patients with normal blood pressure and/or normal cavity size.

Vasodilator therapy is not recommended for asymptomatic patients with mild AR and normal LV function in the absence of systemic hypertension, as these patients have an excellent outcome with no therapy. Vasodilator therapy is not an alternative to surgery for asymptomatic or symptomatic patients with severe AR and LV systolic dysfunction. Whether symptomatic patients who have preserved systolic function can be safely treated with aggressive medical management and whether aggressive medical management is as good or better than AVR have not been determined. It is recommended that symptomatic patients undergo surgery rather than long-term medical therapy.

**Recommendations for Vasodilator Therapy for Chronic Aortic Regurgitation**

Indication	Class
1. <b>Chronic therapy in patients with severe regurgitation who have symptoms and/or LV dysfunction when surgery is not recommended because of additional cardiac or noncardiac factors.</b>	I
2. <b>Long-term therapy in asymptomatic patients with severe regurgitation who have LV dilatation but normal systolic function.</b>	I
3. <b>Long-term therapy in asymptomatic patients with hypertension and any degree of regurgitation.</b>	I

Indication	Class
4. <b>Long-term ACE inhibitor therapy in patients with persistent LV systolic dysfunction after AVR.</b>	I
5. <b>Short-term therapy to improve the hemodynamic profile of patients with severe heart failure symptoms and severe LV dysfunction before proceeding with AVR.</b>	I
6. <b>Long-term therapy in asymptomatic patients with mild to moderate AR and normal LV systolic function.</b>	III
7. <b>Long-term therapy in asymptomatic patients with LV systolic dysfunction who are otherwise candidates for valve replacement.</b>	III
8. <b>Long-term therapy in symptomatic patients with either normal LV function or mild to moderate LV systolic dysfunction who are otherwise candidates for valve replacement.</b>	III

*Serial Testing*

In general, the stability and chronicity of the regurgitant lesion and the LV response to the volume load must be established when the patient first presents to the physician, especially if AR is moderate to severe. If the chronic nature of the lesion is uncertain and the patient does not present initially with 1 or more indications for surgery, the physical examination and echocardiogram should be repeated 2 to 3 months after the initial evaluation to ensure that a subacute process with rapid progression is not under way. Once the chronicity and stability of the process have been established, the frequency of clinical reevaluation and repeat noninvasive testing depends on severity of valvular regurgitation, degree of LV dilatation, level of systolic function, and whether previous serial studies have revealed progressive changes in LV size or function. In most patients, serial testing during the long-term follow-up period should include a detailed history, physical examination, and echocardiography. Serial chest x-rays and ECGs are of less value but are helpful in selected patients.

Asymptomatic patients with mild AR, little or no LV dilatation, and normal LV systolic function can be seen on a yearly basis with instructions to alert the physician if symptoms develop in the interim. Yearly echocardiography is not necessary unless there is clinical evidence that regurgitation has worsened. Routine echocardiography can be performed every 2 to 3 years in such patients.

Asymptomatic patients with normal systolic function but severe AR and significant LV dilatation (end-diastolic dimension >60 mm) require more frequent and careful reevaluation, with a history and physical examination every 6 months and echocardiography every 6 to 12 months, depending on severity of dilatation and stability of measurements. If the patient's condition is stable, echocardiographic measurements are not required more frequently than every 12 months. It is reasonable to obtain serial echocardiograms as often as every 4 to 6 months in patients with more advanced LV dilatation (end-diastolic dimension >70 mm or end-systolic dimension >50 mm) for whom the risk of developing symptoms or LV dysfunction ranges from 10% to 20% per

year. Serial chest x-rays and ECGs are of less value but are helpful in selected patients.

Chronic AR may develop from disease processes involving the proximal ascending aorta. In patients with aortic root dilatation, serial echocardiograms are indicated to evaluate aortic root size as well as LV size and function.

Repeat echocardiograms are also recommended when the patient has onset of symptoms, there is an equivocal history of changing symptoms or exercise tolerance, or there are clinical findings suggesting worsening regurgitation or progressive LV dilatation. Patients with echocardiographic evidence of progressive ventricular dilatation or declining systolic function have a greater likelihood of developing symptoms or LV dysfunction and should have more frequent follow-up examinations (every 6 months) than those with stable LV function.

In some centers with expertise in nuclear cardiology, serial radionuclide ventriculography to assess LV volume and function at rest may be an accurate and cost-effective alternative to serial echocardiography. However, there is no justification for routine serial testing with both echocardiography and radionuclide ventriculography. Serial radionuclide ventriculograms are also recommended in patients with suboptimal echocardiograms and when there is a discrepancy between clinical assessment and echocardiographic data. In centers with specific expertise in cardiac MRI, serial MRI may be performed in place of radionuclide angiography for the indications listed above.

#### *Indications for Cardiac Catheterization*

Cardiac catheterization is not required in patients with chronic AR unless there are questions about the severity of AR, hemodynamic abnormalities, or LV systolic dysfunction despite physical examination and noninvasive testing or unless AVR is contemplated and there is a need to assess coronary anatomy (see section VIII).

#### **Recommendations for Cardiac Catheterization in Chronic Aortic Regurgitation**

Indication	Class
1. Coronary angiography before AVR in patients at risk for CAD (see section VIII.B.).	I
2. Assessing severity of regurgitation when noninvasive tests are inconclusive or discordant with clinical findings regarding severity of regurgitation or need for surgery.	I
3. Assessing LV function when noninvasive tests are inconclusive or discordant with clinical findings regarding LV dysfunction and need for surgery in patients with severe AR.	I
4. Assessment of LV function and severity of regurgitation before AVR when noninvasive tests are adequate and concordant with clinical findings and coronary angiography is not needed.	Ib
5. Assessment of LV function and severity of regurgitation in asymptomatic patients when noninvasive tests are adequate.	III

Hemodynamic and angiographic assessment of severity of AR and LV function may be necessary in some patients being

considered for surgery when there are conflicting data between clinical assessment and noninvasive tests. Hemodynamic measurements during exercise are occasionally helpful in determining the effect of AR on LV function or in making decisions about medical or surgical therapy. In selected patients with severe AR, borderline or normal LV systolic function, and LV chamber enlargement that is approaching the threshold for operation (defined below), measurement of cardiac output and LV filling pressures at rest and during exercise with a right-heart catheter may be valuable for identifying patients with severe hemodynamic abnormalities in whom surgery is warranted.

#### *Indications for Aortic Valve Replacement*

In patients with pure chronic AR, AVR should be considered only if AR is severe. Patients with only mild AR are not candidates for valve replacement, and if they have symptoms or LV dysfunction, other causes should be considered, such as CAD, hypertension, or cardiomyopathic processes. The following discussion applies only to those patients with pure severe AR.

*1. Symptomatic Patients With Normal Left Ventricular Systolic Function.* AVR is indicated in patients with normal systolic function (defined as ejection fraction  $\geq 0.50$  at rest) who have New York Heart Association (NYHA) functional Class III or IV symptoms or Canadian Heart Association functional Class II to IV angina pectoris. In many patients with NYHA functional Class II dyspnea, the cause of symptoms is often unclear, and it may be difficult to differentiate the effects of deconditioning or aging from true cardiac symptoms. In such patients, exercise testing may be valuable. If the cause of these mild symptoms is uncertain and if they are not severe enough to interfere with the patient's lifestyle, a period of observation may be reasonable. However, new onset of mild dyspnea has different implications in severe AR, especially in patients with increasing LV chamber size or evidence of declining LV systolic function into the low normal range. Mild symptoms are an indication for AVR in such patients.

*2. Symptomatic Patients With Left Ventricular Dysfunction.* Patients with NYHA functional Class II, III, or IV symptoms and mild to moderate LV systolic dysfunction (ejection fraction 0.25 to 0.49) should undergo AVR. Patients with functional Class IV symptoms have worse postoperative survival rates and lower likelihood of recovery of systolic function than patients with less severe symptoms, but AVR will improve ventricular loading conditions and expedite subsequent management of LV dysfunction. Symptomatic patients with advanced LV dysfunction (ejection fraction  $< 0.25$  and/or end-systolic dimension  $> 60$  mm) present difficult management issues, as many have developed irreversible myocardial changes. AVR should be more strongly considered in patients with NYHA functional Class II and III symptoms, especially if (1) symptoms and evidence of LV dysfunction are of recent onset and (2) intensive short-term therapy with vasodilators, diuretics, and/or intravenous positive inotropic agents results in substantial improvement in hemodynamics or systolic function. However, even in pa-

tients with NYHA functional Class IV symptoms and ejection fraction <0.25, the high risks associated with AVR and subsequent medical management of LV dysfunction are usually a better alternative than the higher risks of long-term medical management alone.

3. *Asymptomatic Patients.* AVR in asymptomatic patients remains a controversial topic, but it is generally agreed that valve replacement is indicated in patients with LV systolic dysfunction. As noted previously, for the purposes of these guidelines, LV systolic dysfunction is defined as an ejection fraction below normal at rest, ie, ≤0.50. It is recognized that this lower limit is technique dependent and may vary among institutions. Valve replacement is also recommended in patients with severe LV dilatation (end-diastolic dimension >75 mm or end-systolic dimension >55 mm), even if ejection fraction is normal. Such patients appear to represent a high-risk group with an increased incidence of sudden death, and thus far the results of valve replacement have been excellent. In contrast, postoperative mortality is considerable once patients with severe LV dilatation develop symptoms and/or LV systolic dysfunction.

Women tend to develop symptoms and/or LV dysfunction with less LV dilatation than men; this appears to be related to body size, as these differences are not apparent when LV dimensions are corrected for body surface area. Hence, LV dimensions alone may be misleading in small patients of either gender, and the threshold values of end-diastolic and end-systolic dimension recommended for AVR in asymptomatic patients (75 mm and 55 mm, respectively) may need to be reduced for such patients. There are no data from which to derive guidelines for LV dimensions corrected for body size, and clinical judgment is required.

**Recommendations for Aortic Valve Replacement in Chronic Severe Aortic Regurgitation**

Indication	Class
1. Patients with NYHA functional Class III or IV symptoms and preserved LV systolic function, defined as normal ejection fraction at rest (ejection fraction ≥0.50).	I
2. Patients with NYHA functional Class II symptoms and preserved LV systolic function (ejection fraction ≥0.50 at rest) but with progressive LV dilatation or declining ejection fraction at rest on serial studies or declining effort tolerance on exercise testing.	I
3. Patients with Canadian Heart Association functional Class II or greater angina with or without CAD.	I
4. Asymptomatic or symptomatic patients with mild to moderate LV dysfunction at rest (ejection fraction 0.25 to 0.49).	I
5. Patients undergoing coronary artery bypass surgery or surgery on the aorta or other heart valves.	I
6. Patients with NYHA functional Class II symptoms and preserved LV systolic function (ejection fraction ≥0.50 at rest) with stable LV size and systolic function on serial studies and stable exercise tolerance.	Ila
7. Asymptomatic patients with normal LV systolic function (ejection fraction >0.50) but with severe LV dilatation (end-diastolic dimension >75 mm or end-systolic dimension >55 mm).*	Ila

Indication	Class
8. Patients with severe LV dysfunction (ejection fraction <0.25).	Ilb
9. Asymptomatic patients with normal systolic function at rest (ejection fraction >0.50) and progressive LV dilatation when the degree of dilatation is moderately severe (end-diastolic dimension 70 to 75 mm, end-systolic dimension 50 to 55 mm).	Ilb
10. Asymptomatic patients with normal systolic function at rest (ejection fraction >0.50) but with decline in ejection fraction during	III
• Exercise radionuclide angiography	Ilb
• Stress echocardiography	III
11. Asymptomatic patients with normal systolic function at rest (ejection fraction >0.50) and LV dilatation when degree of dilatation is not severe (end-diastolic dimension <70 mm, end-systolic dimension <50 mm).	III

\*Consider lower threshold values for patients of small stature of either gender. Clinical judgment is required.

*Concomitant Aortic Root Disease*

In addition to causing acute AR, diseases of the proximal aorta may also contribute to chronic AR. If AR is mild and/or the left ventricle is only mildly dilated, management should focus on treating the underlying aortic root disease, which is beyond the scope of these guidelines. However, in many patients, AR may be severe, in which case decisions about medical therapy and timing of surgery must take into account both conditions. In general, AVR and aortic root reconstruction are indicated in patients with disease of the proximal aorta and AR of any severity when the degree of aortic root dilatation is ≥50 mm by echocardiography.

*Evaluation of Patients After Aortic Valve Replacement*

After AVR, careful follow-up is necessary during the early and long-term postoperative course to evaluate prosthetic valve function and assess LV function, as discussed in detail in section VII.C. An echocardiogram should be performed soon after surgery to assess the results of surgery on LV size and function and to serve as a baseline for comparison of subsequent echocardiograms. In the first few weeks after surgery, there is little change in LV systolic function, and ejection fraction may deteriorate, compared with preoperative values, because of the reduced preload. A better predictor of subsequent LV systolic function is the reduction in LV end-diastolic dimension, which declines significantly within the first week or two of operation. This is an excellent marker of the functional success of AVR, as the magnitude of early reduction in end-diastolic dimension after operation correlates with the magnitude of late increase in ejection fraction.

Patients with persistent LV dilatation on the initial postoperative echocardiogram should receive the same treatment, including ACE inhibitors, as any other patient with symptomatic or asymptomatic LV dysfunction.

**C. Mitral Stenosis**

The normal mitral valve area is 4.0 to 5.0 cm<sup>2</sup>. Narrowing of the valve area to <2.5 cm<sup>2</sup> must occur before development of symptoms.

A mitral valve area  $>1.5$  cm<sup>2</sup> usually does not produce symptoms at rest. However, if there is an increase in transmitral flow or a decrease in the diastolic filling period, there will be a rise in left atrial pressure and development of symptoms. Thus, the first symptoms of dyspnea in patients with mild MS are usually precipitated by exercise, emotional stress, infection, pregnancy, or atrial fibrillation with a rapid ventricular response.

#### **Natural History**

MS is a continuous, progressive, lifelong disease, usually consisting of a slow, stable course in the early years and progressive acceleration later in life. In developed countries, there is a long latent period of 20 to 40 years from the occurrence of rheumatic fever to onset of symptoms. Once symptoms develop, there is another period of almost a decade before symptoms become disabling. Overall, the 10-year survival of untreated patients with MS is 50% to 60%, depending on symptoms at presentation. In the asymptomatic or minimally symptomatic patient, survival is  $>80\%$  at 10 years, with 60% of patients having no progression of symptoms. However, once significant limiting symptoms occur, there is a dismal 10-year survival rate of 0% to 15%, and when there is severe pulmonary hypertension, mean survival drops to  $<3$  years. Mortality of untreated patients with MS is caused by progressive heart failure in 60% to 70%, systemic embolism in 20% to 30%, pulmonary embolism in 10%, and infection in 1% to 5%.

#### **Evaluation and Management of the Asymptomatic Patient**

The diagnosis of MS should be based on the history, physical examination, chest x-ray, and ECG. The diagnostic tool of choice in the evaluation of a patient with MS is 2-D and Doppler echocardiography. The morphological appearance of the mitral valve apparatus should be assessed by 2-D echocardiography, including leaflet mobility, leaflet thickness, leaflet calcification, subvalvular fusion, and appearance of the commissures. These features may be important when considering the timing and type of intervention to be performed. Chamber size and function as well as other structural valvular, myocardial, or pericardial abnormalities should also be assessed.

The hemodynamic severity of the obstruction should be assessed with Doppler echocardiography. The mean transmitral gradient can be accurately and reproducibly measured from the continuous wave Doppler signal across the mitral valve with the modified Bernoulli equation, and the mitral valve area can be noninvasively measured by either the diastolic half-time method or the continuity equation. The half-time method may be inaccurate in patients with abnormalities of left atrial or LV compliance, those with associated AR, and those with previous mitral valvotomy. Doppler echocardiography should also be used when possible to estimate pulmonary artery systolic pressure from the TR velocity signal and assess severity of concomitant MR or AR. Formal hemodynamic exercise testing can be done noninvasively by either a supine bicycle or upright treadmill with Doppler recordings of transmitral and tricuspid velocities. This allows measurement of both the transmitral gradient and pulmonary artery systolic pressure at rest and with exercise. Dobutamine stress testing with Doppler recordings may also be performed.

#### **Recommendations for Echocardiography in Mitral Stenosis**

Indication	Class
1. <b>Diagnosis of MS, assessment of hemodynamic severity (mean gradient, mitral valve area, pulmonary artery pressure), and assessment of right ventricular size and function.</b>	I
2. <b>Assessment of valve morphology to determine suitability for percutaneous mitral balloon valvotomy.</b>	I
3. <b>Diagnosis and assessment of concomitant valvular lesions.</b>	I
4. <b>Reevaluation of patients with known MS with changing symptoms or signs.</b>	I
5. <b>Assessment of hemodynamic response of mean gradient and pulmonary artery pressures by exercise Doppler echocardiography in patients when there is a discrepancy between resting hemodynamics and clinical findings.</b>	IIa
6. <b>Reevaluation of asymptomatic patients with moderate to severe MS to assess pulmonary artery pressure.</b>	IIb
7. <b>Routine reevaluation of the asymptomatic patient with mild MS and stable clinical findings.</b>	III

#### **Recommendations for Transesophageal Echocardiography in Mitral Stenosis**

Indication	Class
1. <b>Assess for presence or absence of left atrial thrombus in patients being considered for percutaneous mitral balloon valvotomy or cardioversion.</b>	IIa
2. <b>Evaluate mitral valve morphology and hemodynamics when transthoracic echocardiography provides suboptimal data.</b>	IIa
3. <b>Routine evaluation of mitral valve morphology and hemodynamics when complete transthoracic echocardiographic data are satisfactory.</b>	III

In the asymptomatic patient who has documented mild MS (valve area  $>1.5$  cm<sup>2</sup> and mean gradient  $<5$  mm Hg), no further evaluation is needed on the initial workup. These patients usually remain stable for many years. If MS is more significant, further evaluation should be considered if the mitral valve morphology appears to be suitable for mitral valvotomy with pliable, noncalcified valves with little or no subvalvular fusion and no calcification in the commissures. Patients with moderate pulmonary hypertension at rest (pulmonary artery systolic pressure  $>50$  mm Hg) and pliable mitral valve leaflets may be considered for percutaneous mitral valvotomy even if they deny symptoms. In patients who lead a sedentary lifestyle, a hemodynamic exercise test with Doppler echocardiography is useful. Objective limitation of exercise tolerance with a rise in transmitral gradient  $>15$  mm Hg and pulmonary artery systolic pressure  $>60$  mm Hg may be an indication to consider percutaneous valvotomy if mitral valve morphology is suitable.

All patients should be informed that any change in symptoms warrants reevaluation. In the asymptomatic patient, yearly reevaluation is recommended; at this time, a history, physical examination, chest x-ray, and ECG should be ob-

tained. A yearly echocardiogram is not recommended unless there is a change in clinical status. Ambulatory ECG monitoring to detect paroxysmal atrial fibrillation is indicated in patients with palpitations.

### Medical Therapy

**1. General Principles.** Because MS is primarily caused by rheumatic fever, prophylaxis against rheumatic fever is recommended. Appropriate endocarditis prophylaxis is also recommended. Patients who have more than a mild degree of MS should be counseled to avoid unusual physical stresses. Agents with negative chronotropic properties, such as  $\beta$ -blockers or calcium channel blockers, may be of benefit in patients with sinus rhythm who have exertional symptoms if the symptoms occur with high heart rates. Salt restriction and intermittent administration of a diuretic are useful if there is evidence of pulmonary vascular congestion. Digitalis does not benefit patients with MS in sinus rhythm unless there is left and/or right ventricular dysfunction.

**2. Atrial Fibrillation.** Atrial fibrillation develops in 30% to 40% of patients with symptomatic MS. Significant hemodynamic consequences may result from acute development of atrial fibrillation, with loss of atrial contribution to LV filling, and from the rapid ventricular rate. Atrial fibrillation occurs more commonly in older patients and is associated with a poorer prognosis, with a 10-year survival rate of 25% compared with 46% in patients who remain in sinus rhythm. The risk of arterial embolization, especially stroke, is significantly increased in patients with atrial fibrillation. Treatment of an acute episode of rapid atrial fibrillation consists of anticoagulation with heparin and control of the heart rate response. Intravenous digoxin, calcium channel blockers, or  $\beta$ -blockers should be used to control ventricular response. If there is hemodynamic instability, electrical cardioversion should be undertaken urgently, with intravenous heparin before, during, and after the procedure. Patients who have been in atrial fibrillation >24 to 48 hours without anticoagulation are at an increased risk for embolic events after cardioversion, but patients may also have an embolic event with <24 hours of atrial fibrillation. The decision to proceed with elective cardioversion depends on multiple factors, including duration of atrial fibrillation, hemodynamic response to onset of atrial fibrillation, documented history of prior episodes of atrial fibrillation, and history of prior embolic events. If the decision has been made to proceed with elective cardioversion in a patient who has had documented atrial fibrillation for >24 to 48 hours and who has not been on long-term anticoagulation, 1 of 2 approaches is recommended, based on data from patients with nonrheumatic atrial fibrillation. The first is anticoagulation with warfarin for  $\geq 3$  weeks, followed by elective cardioversion. The second is anticoagulation with heparin and transesophageal echocardiography to look for left atrial thrombus. In the absence of left atrial thrombus, cardioversion is performed with intravenous heparin before, during, and after the procedure. It is important to continue anticoagulation after cardioversion to prevent thrombus formation caused by atrial mechanical inactivity and to then maintain the patient on long-term warfarin unless there is a strong contraindication to anticoagulation. Controversy surrounds whether percutaneous mitral valvotomy should be performed in patients with new-onset atrial fibrillation and moderate to severe MS who are otherwise asymptomatic.

**3. Prevention of Systemic Embolization.** Systemic embolization may occur in 10% to 20% of patients with MS. The risk of embolization is related to age, the presence of atrial fibrillation, and history of previous embolic events. One third of embolic events occur  $\leq 1$  month after onset of atrial fibrillation, and two thirds occur within 1 year. The frequency of embolic events does not seem to be related to severity of MS, cardiac output, size of left atrium, or presence of symptoms. An embolic event may thus be the initial manifestation of MS. In patients who have experienced an embolic event, the frequency of recurrence is as high as 15 to 40 events per 100 patient months. There are no data to support the concept that oral anticoagulation is beneficial in patients with MS who have not had atrial fibrillation or an embolic event. It is controversial whether patients who have not had atrial fibrillation or an embolic event and who might be at higher risk for future embolic events (ie, severe stenosis or enlarged left atrium) should be considered for long-term warfarin therapy.

### Recommendations for Anticoagulation in Mitral Stenosis

Indication	Class
1. Patients with atrial fibrillation, paroxysmal or chronic.	I
2. Patients with a prior embolic event.	I
3. Patients with severe MS and left atrial dimension $\geq 55$ mm by echocardiography.*	IIb
4. All other patients with MS.	III

\*Based on a grade C recommendation given this indication by American College of Chest Physicians Fourth Consensus Conference on Antithrombotic Therapy. The Working Group of the European Society of Cardiology recommended a lower threshold of left atrial dimension (>50 mm) for recommending anticoagulation.

### Physical Activity and Exercise

The 26th Bethesda Conference on Recommendations for Determining Eligibility for Competition in Athletes With Cardiovascular Abnormalities has published guidelines for patients with MS who wish to engage in competitive athletics.<sup>7</sup>

### Evaluation of the Symptomatic Patient

Patients who develop symptoms should undergo evaluation with a history, physical examination, ECG, chest x-ray, and echocardiography to evaluate mitral valve morphology, mitral valve hemodynamics, and pulmonary artery pressure. Patients with NYHA functional Class II symptoms and moderate or severe stenosis (mitral valve area  $\leq 1.5$  cm<sup>2</sup> or mean gradient  $\geq 5$  mm Hg) may be considered for mitral balloon valvotomy if they have suitable mitral valve morphology. Patients with NYHA functional Class III or IV symptoms and evidence of severe MS have a poor prognosis if left untreated, and intervention with either balloon valvotomy or surgery should be considered.

A subset of patients have significant limiting symptoms yet resting hemodynamics that do not indicate moderate to severe MS. If there is a discrepancy between symptoms and hemodynamic data, formal exercise testing or dobutamine stress testing may be useful to differentiate symptoms caused by MS from other causes. Exercise tolerance, heart rate and blood pressure response, transmitral gradient, and pulmonary artery pressure can be obtained at rest and during exercise.

This can usually be accomplished by either supine bicycle or upright exercise with Doppler recording of TR and transmitral velocities. Right- and left-heart catheterization with exercise may also be helpful. Patients who are symptomatic with a significant elevation of pulmonary artery pressure ( $>60$  mm Hg), mean transmitral gradient ( $>15$  mm Hg), or pulmonary artery wedge pressure ( $\geq 25$  mm Hg) on exertion have hemodynamically significant MS and should be considered for further intervention. Alternatively, patients who do not manifest elevation in pulmonary artery, pulmonary artery wedge, or transmitral pressures coincident with development of exertional symptoms most likely would not benefit from intervention on the mitral valve.

#### **Indications for Cardiac Catheterization**

In most instances, Doppler measurements of transmitral gradient, valve area, and pulmonary pressure correlate well with each other. Catheterization is indicated to assess hemodynamics when there is a discrepancy between Doppler-derived hemodynamics and the clinical status of a symptomatic patient. Absolute left- and right-sided pressure measurements should be obtained by catheterization when there is elevation of pulmonary artery pressure out of proportion to mean gradient and valve area. Catheterization including left ventriculography (to evaluate severity of MR) is indicated when there is a discrepancy between Doppler-derived mean gradient and valve area. Coronary angiography may be required in selected patients who may need to undergo intervention (see section VIII).

#### **Recommendations for Cardiac Catheterization in Mitral Stenosis**

Indication	Class
1. Perform percutaneous mitral balloon valvotomy in properly selected patients.	I
2. Assess severity of MR in patients being considered for percutaneous mitral balloon valvotomy when clinical and echocardiographic data are discordant.	IIa
3. Assess pulmonary artery, left atrial, and LV diastolic pressures when symptoms and/or estimated pulmonary artery pressure are discordant with the severity of MS by 2-D and Doppler echocardiography.	IIa
4. Assessment of hemodynamic response of pulmonary artery and left atrial pressures to stress when clinical symptoms and resting hemodynamics are discordant.	IIa
5. Assessment of mitral valve hemodynamics when 2-D and Doppler echocardiographic data are concordant with clinical findings.	III

#### **Indications for Surgical or Percutaneous Valvotomy**

With the development of cardiopulmonary bypass in the 1960s, open mitral commissurotomy and replacement of the mitral valve became the surgical procedures of choice for treatment of MS. Percutaneous mitral balloon valvotomy emerged in the mid 1980s. This procedure has become an accepted alternative to surgical approaches in selected patients. The procedure itself is technically challenging and involves a steep learning curve. There is a higher success rate and lower complication rate in experienced high-volume

centers. Thus, results of the procedure are highly dependent on the experience of the operators, which must be taken into consideration when making recommendations for proceeding with this technique.

The immediate results of percutaneous mitral valvotomy are similar to those of mitral commissurotomy. The mean valve area usually doubles (from  $1.0$   $\text{cm}^2$  to  $2.0$   $\text{cm}^2$ ), with a 50% to 60% reduction in transmitral gradient. Overall, 80% to 95% of patients may have a successful procedure, which is defined as a mitral valve area  $>1.5$   $\text{cm}^2$  and a decrease in left atrial pressure to  $\leq 18$  mm Hg in the absence of complications. The most common acute complications reported in large series include severe MR, which occurs in 2% to 10%, and a residual atrial septal defect. A large atrial septal defect ( $>1.5:1$  left-to-right shunt) occurs in up to 12% of patients with the double balloon technique and in  $<5\%$  with the Inoue balloon technique. Smaller atrial septal defects may be detected by transesophageal echocardiography in larger numbers of patients. Less frequent complications include perforation of the left ventricle (0.5% to 4.0%), embolic events (0.5% to 3%), and myocardial infarction (0.3% to 0.5%). The mortality for patients who undergo balloon valvotomy in larger series has ranged from 1% to 2%; however, with increasing experience in the procedure, percutaneous mitral valvotomy can be done in selected patients with a mortality of  $<1\%$ .

Follow-up information after percutaneous balloon valvotomy is limited. Event-free survival (freedom from death, repeat valvotomy, or mitral valve replacement) overall is 50% to 65% over 3 to 7 years, with an event-free survival of 80% to 90% in patients with favorable mitral valve morphology. More than 90% of patients free of events remain in NYHA functional Class I or II after percutaneous mitral valvotomy. Randomized trials have compared percutaneous balloon valvotomy with both closed and open surgical commissurotomy. There was no significant difference in acute hemodynamic results or complication rate between percutaneous mitral valvotomy and surgery, and early follow-up data indicate no difference in hemodynamics, clinical improvement, or exercise time. However, longer-term follow-up studies at 3 to 7 years indicate more favorable hemodynamic and symptomatic results with percutaneous balloon valvotomy than with closed commissurotomy and results equivalent to those of open commissurotomy.

The immediate results, acute complications, and follow-up results of percutaneous balloon valvotomy depend on multiple factors. It is of utmost importance that this procedure be performed in centers with skilled, experienced operators. Other factors include age, NYHA functional class, severity of stenosis, LV end-diastolic pressure, cardiac output, and pulmonary artery wedge pressure. The underlying mitral valve morphology is the most important factor in determining outcome, and patients with valvular calcification, thickened fibrotic leaflets with decreased mobility, and subvalvular fusion have a higher incidence of acute complications and a higher rate of recurrent stenosis on follow-up. In patients with noncalcified pliable valves and no calcium in the commis-

tures, the procedure can be performed with a high success rate (>90%), low complication rate (<2% to 3%), and sustained improvement in 80% to 90% over a 3- to 7-year follow-up period.

Relative contraindications to percutaneous balloon valvotomy include the presence of a left atrial thrombus and significant (3+ to 4+) MR. Transesophageal echocardiography is frequently performed before the procedure to determine the presence of left atrial thrombus, specifically examining the left atrial appendage. If a thrombus is found, 3 months of anticoagulation with warfarin may result in resolution of the thrombus.

In centers with skilled, experienced operators, percutaneous balloon valvotomy should be considered the initial procedure of choice for symptomatic patients with moderate to severe MS who have a favorable valve morphology in the absence of significant MR or a left atrial thrombus. In asymptomatic patients with a favorable valve morphology, percutaneous mitral valvotomy may be considered if there is evidence of a hemodynamic effect on left atrial pressure (new-onset atrial fibrillation) or pulmonary circulation (pulmonary artery pressure >50 mm Hg at rest or >60 mm Hg with exercise). The strength of evidence for this recommendation is low because there are no data comparing the results of percutaneous balloon valvotomy and medical therapy in such patients. It is controversial whether severely symptomatic patients with less favorable valve morphology should undergo this catheter-based procedure. Although there is a higher acute complication rate and lower event-free survival (approximately 50% at 5 years in these patients, compared with 80% to 90% in patients with favorable valve morphology), this must be weighed against the risks and potential complications of surgical mitral valve replacement.

**Recommendations for Percutaneous Mitral Balloon Valvotomy**

Indication	Class
1. Symptomatic patients (NYHA functional Class II, III, or IV), moderate or severe MS (mitral valve area $\leq 1.5$ cm <sup>2</sup> ),* and valve morphology favorable for percutaneous balloon valvotomy in the absence of left atrial thrombus or moderate to severe MR.	I
2. Asymptomatic patients with moderate or severe MS (mitral valve area $\leq 1.5$ cm <sup>2</sup> )* and valve morphology favorable for percutaneous balloon valvotomy who have pulmonary hypertension (pulmonary artery systolic pressure >50 mm Hg at rest or 60 mm Hg with exercise) in the absence of left atrial thrombus or moderate to severe MR.	IIa
3. Patients with NYHA functional Class III-IV symptoms, moderate or severe MS (mitral valve area $\leq 1.5$ cm <sup>2</sup> ),* and a nonpliable calcified valve who are at high risk for surgery in the absence of left atrial thrombus or moderate to severe MR.	IIa
4. Asymptomatic patients, moderate or severe MS (mitral valve area $\leq 1.5$ cm <sup>2</sup> ),* and valve morphology favorable for percutaneous balloon valvotomy who have new onset of atrial fibrillation in the absence of left atrial thrombus or moderate to severe MR.	IIb

Indication	Class
5. Patients in NYHA functional Class III-IV, moderate or severe MS (mitral valve area $\leq 1.5$ cm <sup>2</sup> ), and a nonpliable calcified valve who are low-risk candidates for surgery.	IIb
6. Patients with mild MS.	III

\*The committee recognizes that there may be variability in the measurement of mitral valve area and that the mean transmitral gradient, pulmonary artery wedge pressure, and pulmonary artery pressure at rest or during exercise should also be taken into consideration.

**Recommendations for Mitral Valve Repair for Mitral Stenosis**

Indication	Class
1. Patients with NYHA functional Class III-IV symptoms, moderate or severe MS (mitral valve area $\leq 1.5$ cm <sup>2</sup> ),* and valve morphology favorable for repair if percutaneous mitral balloon valvotomy is not available.	I
2. Patients with NYHA functional Class III-IV symptoms, moderate or severe MS (mitral valve area $\leq 1.5$ cm <sup>2</sup> ),* and valve morphology favorable for repair if a left atrial thrombus is present despite anticoagulation.	I
3. Patients with NYHA functional Class III-IV symptoms, moderate or severe MS (mitral valve area $\leq 1.5$ cm <sup>2</sup> ),* and a nonpliable or calcified valve with the decision to proceed with either repair or replacement made at the time of the operation.	I
4. Patients in NYHA functional Class I, moderate or severe MS (mitral valve area $\leq 1.5$ cm <sup>2</sup> ),* and valve morphology favorable for repair who have had recurrent episodes of embolic events on adequate anticoagulation.	IIb
5. Patients with NYHA functional Class I-IV symptoms and mild MS.	III

\*The committee recognizes that there may be a variability in the measurement of mitral valve area and that the mean transmitral gradient, pulmonary artery wedge pressure, and pulmonary artery pressure at rest or during exercise should also be considered.

**Indications for Mitral Valve Replacement**

Mitral valve replacement (MVR) is an accepted surgical procedure for patients with severe MS who are not candidates for surgical commissurotomy or percutaneous mitral valvotomy. The risk of MVR is dependent on multiple factors, including functional status, age, LV function, cardiac output, concomitant medical problems, and concomitant CAD. In the young, healthy person, MVR can be performed with a risk of <5%. However, in the older patient with concomitant medical problems or pulmonary hypertension at systemic levels, the risk of MVR may be 10% to 20%.

If there is significant calcification, fibrosis, and subvalvular fusion of the mitral valve apparatus, commissurotomy or percutaneous balloon valvotomy is less likely to be successful, and MVR will be necessary. Given the risk of MVR and the potential long-term complications of a prosthetic valve, there are stricter indications for mitral valve operation in these patients with calcified fibrotic valves. For the patient with NYHA functional Class III symptoms due to severe MS or combined MS/MR, MVR results in excellent symptomatic improvement. Postpone-

ment of surgery until the patient reaches the functional Class IV symptomatic state should be avoided because operative mortality is high and long-term outcome suboptimal. However, if the patient presents in NYHA functional Class IV heart failure, surgery should not be denied because the outlook without surgical intervention is grave. It is controversial whether asymptomatic or mildly symptomatic patients with severe MS (valve area  $<1 \text{ cm}^2$ ) and severe pulmonary hypertension (pulmonary artery systolic pressure  $>60$  to  $80 \text{ mm Hg}$ ) should undergo MVR to prevent right ventricular failure, but surgery is generally recommended in such patients. It is recognized that patients with such severe pulmonary hypertension are rarely asymptomatic.

#### Recommendations for Mitral Valve Replacement for Mitral Stenosis

Indication	Class
1. Patients with moderate or severe MS (mitral valve area $\leq 1.5 \text{ cm}^2$ )* and NYHA functional Class III-IV symptoms who are not considered candidates for percutaneous balloon valvotomy or mitral valve repair.	I
2. Patients with severe MS (mitral valve area $\leq 1 \text{ cm}^2$ )* and severe pulmonary hypertension (pulmonary artery systolic pressure $>60$ to $80 \text{ mm Hg}$ ) with NYHA functional Class I-II symptoms who are not considered candidates for percutaneous balloon valvotomy or mitral valve repair.	IIa

\*The committee recognizes that there may be a variability in the measurement of mitral valve area and that the mean transmitral gradient, pulmonary artery wedge pressure, and pulmonary artery pressure should also be considered.

#### Management of Patients After Valvotomy or Commissurotomy

Recurrent symptoms after successful surgical commissurotomy have been reported to occur in as many as 60% of patients after 9 years, but recurrent stenosis accounts for symptoms in  $<20\%$ . In patients with adequate initial results, progressive MR and development of other valvular or coronary problems are more frequently responsible for recurrent symptoms. Thus, in patients presenting with symptoms late after commissurotomy, a comprehensive evaluation is required to look for other causes of the symptoms. Patients undergoing percutaneous mitral valvotomy have a higher incidence of recurrent symptoms at 1- to 2-year follow-up if there was an unfavorable mitral valve morphology due to either an initial inadequate result or restenosis.

The management of patients after successful percutaneous balloon valvotomy or surgical commissurotomy is similar to that of the asymptomatic patient with MS. A baseline echocardiogram should be performed after the procedure to assess hemodynamics as well as to exclude significant complications such as MR, LV dysfunction, or atrial septal defect (in the case of percutaneous valvotomy). The echocardiogram should be performed  $\geq 72$  hours after the procedure because acute changes in atrial and ventricular compliance immediately after the procedure affect the reliability of the half-time method in calculating valve area. Patients with severe MR or a large atrial septal defect should be considered for early

operation. However, the majority of small left-to-right shunts at the atrial level will close spontaneously over the course of 6 months. In patients with a history of atrial fibrillation, warfarin should be restarted 1 to 2 days after the procedure.

Repeat percutaneous balloon valvotomy can be performed in the patient who has restenosis after either a prior surgical commissurotomy or balloon valvotomy. The results of these procedures are less satisfactory than the overall results of initial valvotomy because there is usually more valve deformity, calcification, and fibrosis than with the initial procedure. MVR should be considered in those patients with recurrent severe symptoms and severe deformity of the mitral apparatus.

#### D. Mitral Valve Prolapse

MVP is the most common form of valvular heart disease and occurs in 2% to 6% of the population. MVP often occurs as a clinical entity with little or no MR but is also the most common cause of significant MR in the United States.

Primary and secondary MVP must be distinguished from normal variants by cardiac auscultation and/or echocardiography; these variations can result in an incorrect diagnosis of MVP, particularly in patients with hyperkinetic hearts or dehydration. Other auscultatory findings may be misinterpreted as midsystolic clicks or late systolic murmurs. Patients with mild to moderate billowing of 1 or more nonthickened leaflets toward the left atrium with the leaflet coaptation point on the LV side of the mitral annulus and minimal or no MR by Doppler echocardiography are probably normal. Unfortunately, many such patients are overdiagnosed as having the MVP syndrome.

#### Natural History

In most patient studies, the MVP syndrome is associated with a benign prognosis. The age-adjusted survival rate of both men and women with MVP is similar to that of individuals without this common clinical entity. The gradual progression of MR in patients with MVP may result in progressive dilatation of the left atrium and ventricle. Left atrial dilatation may result in atrial fibrillation, and moderate to severe MR may eventually result in LV dysfunction and development of congestive heart failure. Pulmonary hypertension may occur with associated right ventricular dysfunction. In some patients, after an initially prolonged asymptomatic interval, the entire process may enter an accelerated phase as a result of left atrial and LV dysfunction, atrial fibrillation, and in certain instances, ruptured mitral valve chordae.

Several long-term prognostic studies suggest that complications occur most commonly in patients with a mitral systolic murmur, thickened redundant mitral valve leaflets, and increased LV or left atrial size, especially in men  $>45$  years of age. Sudden death is a rare complication of MVP, occurring in  $<2\%$  of known cases during long-term follow-up, with annual mortality rates  $<1\%$  per year.

Infective endocarditis is a serious complication of MVP, which is the leading predisposing cardiovascular diagnosis in most series of patients reported with endocarditis. Because the absolute incidence of endocarditis is extremely low for the entire MVP population, there has been much controversy about the risk of endocarditis in MVP.



**Evaluation and Management of the Asymptomatic Patient**

The primary diagnostic evaluation of the patient with MVP is a careful *physical examination*. The principal cardiac auscultatory feature of this syndrome is the midsystolic click, which may vary considerably in intensity and timing according to LV loading conditions and contractility. Clicks result from sudden tensing of the mitral valve apparatus as the leaflets prolapse into the left atrium during systole. The midsystolic click(s) is frequently followed by a late systolic murmur, usually medium- to high-pitched and loudest at the cardiac apex. Dynamic auscultation is often useful for establishing the clinical diagnosis of the MVP syndrome. Changes in LV end-diastolic volume result in changes in the timing of the midsystolic click(s) and murmur. When end-diastolic volume is decreased (as with standing), the critical volume is achieved earlier in systole, and the click-murmur complex occurs shortly after the first heart sound. By contrast, any maneuver that augments the volume of blood in the ventricle (eg, squatting), reduces myocardial contractility, or increases LV afterload, lengthens the time from onset of systole to initiation of MVP, and the systolic click and/or murmur move toward the second heart sound.

*2-D and Doppler echocardiography* is the most useful non-invasive test for defining MVP. The M-mode echocardiographic definition of MVP includes  $\geq 2$ -mm posterior displacement of 1 or both leaflets or holosystolic posterior "hammocking"  $> 3$  mm. On 2-D echocardiography, systolic displacement of 1 or both mitral leaflets in the parasternal long-axis view, particularly when they coapt on the atrial side of the annular plane, indicates a high likelihood of MVP. There is disagreement about the reliability of echocardiographic diagnosis of MVP when observed in only the apical 4-chamber view. The diagnosis of MVP is even more certain when leaflet thickness is  $> 5$  mm. Leaflet redundancy is often associated with an enlarged mitral annulus and elongated chordae tendineae. On Doppler echocardiography, the presence or absence of MR is an important consideration, and MVP is more likely when MR is detected as a high-velocity eccentric jet in late systole.

At present, there is no consensus on the 2-D echocardiographic criteria for MVP. Because echocardiography is a tomographic cross-sectional technique, no single view should be considered diagnostic. The parasternal long-axis view permits visualization of the medial aspect of the anterior mitral leaflet and middle scallop of the posterior leaflet. If the findings of prolapse are localized to the lateral scallop in the posterior leaflet, they would be best visualized by the apical 4-chamber view. All available echocardiographic views should be used, with the provision that billowing of the anterior leaflet alone in the 4-chamber apical view is not evidence of prolapse; however, displacement of the posterior leaflet or coaptation point in any view, including the apical view, suggests the diagnosis of prolapse. The echocardiographic criteria for MVP should include structural changes, such as leaflet thickening, redundancy, annular dilatation, and chordal elongation.

Patients with echocardiographic evidence for MVP but no evidence of thickened/redundant leaflets or definite MR are more difficult to classify. If such patients have clinical auscultatory findings of MVP, the echocardiogram usually confirms the diagnosis.

**Recommendations for Echocardiography in Mitral Valve Prolapse\***

Indication	Class
1. <b>Diagnosis, assessment of hemodynamic severity of MR, leaflet morphology, and ventricular compensation in patients with physical signs of MVP.</b>	I
2. <b>To exclude MVP in patients who have been given the diagnosis when there is no clinical evidence to support the diagnosis.</b>	I
3. <b>To exclude MVP in patients with first-degree relatives with known myxomatous valve disease.</b>	IIa
4. <b>Risk stratification in patients with physical signs of MVP or known MVP.</b>	IIa
5. <b>To exclude MVP in patients in the absence of physical findings suggestive of MVP or a positive family history.</b>	III
6. <b>Routine repetition of echocardiography in patients with MVP with mild or no regurgitation and no changes in clinical signs or symptoms.</b>	III

\*From the ACC/AHA Guidelines for the Clinical Application of Echocardiography.<sup>2</sup>

Although there is controversy concerning the need for echocardiography in patients with classic auscultatory findings of MVP, the usefulness of echocardiography for risk stratification in patients with MVP has been demonstrated in  $\geq 6$  published studies. All patients with MVP should have an initial echocardiogram. Serial echocardiograms are not usually necessary in the asymptomatic patient with MVP unless there are clinical indications of severe or worsening MR.

Reassurance is a major part of the *management* of patients with MVP, most of whom are asymptomatic or have no cardiac symptoms and lack a high-risk profile. These patients with mild or no symptoms and findings of milder forms of prolapse should be reassured of the benign prognosis. A normal lifestyle and regular exercise are encouraged.

Antibiotic prophylaxis for prevention of infective endocarditis during procedures associated with bacteremia is recommended for most patients with a definite diagnosis of MVP, as indicated in section II.B. There has been some disagreement about whether patients with an isolated systolic click and no systolic murmur should undergo endocarditis prophylaxis. Patients with only a systolic click who have echocardiographic evidence of a higher-risk profile for endocarditis, such as leaflet thickening, elongated chordae, left atrial enlargement, or LV dilatation, should receive endocarditis prophylaxis.

**Recommendations for Antibiotic Endocarditis Prophylaxis for Patients With Mitral Valve Prolapse Undergoing Procedures Associated With Bacteremia\***

Indication	Class
1. <b>Patients with characteristic systolic click-murmur complex.</b>	I
2. <b>Patients with isolated systolic click and echocardiographic evidence of MVP and MR.</b>	I
3. <b>Patients with isolated systolic click, echocardiographic evidence of high-risk MVP.</b>	IIa
4. <b>Patients with isolated systolic click and equivocal or no evidence of MVP.</b>	III

\*These procedures are defined in the American Heart Association guidelines for prevention of endocarditis<sup>5</sup> and in the full-text version of these guidelines.

**Evaluation and Management of the Symptomatic Patient**

Patients with MVP and palpitations associated with mild tachyarrhythmias or increased adrenergic symptoms and those with chest pain, anxiety, or fatigue often respond to therapy with  $\beta$ -blockers. However, in many cases, the cessation of stimulants such as caffeine, alcohol, and cigarettes may be sufficient to control symptoms. In patients with recurrent palpitations, continuous or event-activated ambulatory ECG recordings may reveal whether arrhythmias are the cause of symptoms and indicate appropriate treatment of existing arrhythmias. The indications for electrophysiological testing are similar to those in the general population (eg, aborted sudden death, recurrent syncope of unknown cause, and symptomatic or sustained ventricular tachycardia).

Cardiac catheterization is not required for the diagnosis of MVP. It is helpful in evaluating associated conditions (eg, CAD and atrial septal defect) and may be needed to assess the hemodynamic effects of severe MR (as well as coronary artery anatomy) before consideration for valve repair or replacement.

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

**Recommendations for Aspirin and Oral Anticoagulants in Mitral Valve Prolapse**

Indication	Class
1. Aspirin therapy for cerebral transient ischemic attacks.	I
2. Warfarin therapy for patients aged $\geq 65$ years in atrial fibrillation with hypertension, MR murmur, or history of heart failure.	I
3. Aspirin therapy for patients aged <65 years in atrial fibrillation with no history of MR, hypertension, or heart failure.	I
4. Warfarin therapy for poststroke patients.	I
5. Warfarin therapy for transient ischemic attacks despite aspirin therapy.	IIa
6. Aspirin therapy for poststroke patients with contraindications to anticoagulants.	IIa
7. Aspirin therapy for patients in sinus rhythm with echocardiographic evidence of high-risk MVP.	IIb

Asymptomatic patients with MVP and no significant MR can be clinically evaluated every 3 to 5 years. Serial echocardiography is not necessary in most of these patients and is performed only if there is development of symptoms consis-

tent with cardiovascular disease and a change in physical findings suggesting development of significant MR, and in patients with high-risk characteristics observed on the initial echocardiogram. Patients with high-risk characteristics, including those with moderate to severe MR, should receive a follow-up once a year.

Patients with severe MR with symptoms and/or impaired LV systolic function require cardiac catheterization and evaluation for mitral valve surgery. The thickened, redundant mitral valve can often be repaired rather than replaced with lower operative mortality and excellent short- and long-term results, as discussed in section III.E.

**Surgical Considerations**

Management of MVP may require valve surgery, particularly for those who develop a flail mitral leaflet as a result of rupture of chordae tendineae or their marked elongation. Most such valves can be successfully repaired by surgeons experienced in mitral valve repair, especially when the posterior leaflet of the mitral valve is predominantly affected. Symptoms of heart failure, severity of MR, the presence or absence of atrial fibrillation, LV systolic function, LV end-diastolic and end-systolic volumes, and pulmonary artery pressure (at rest and during exercise) all influence the decision to recommend mitral valve surgery. Recommendations for surgery in patients with MVP and MR are the same as those with other forms of nonischemic severe MR, as indicated in section III.E.4.

**E. Mitral Regurgitation****1. Acute Severe Mitral Regurgitation**

In acute severe MR, acute volume overload increases LV preload, allowing for a modest increase in total LV stroke volume. However, forward stroke volume and cardiac output are reduced, and the regurgitant volume results in pulmonary congestion. In acute severe MR, the hemodynamic overload often cannot be tolerated, and mitral valve repair or replacement must often be performed urgently.

**Diagnosis**

The patient with acute severe MR is almost always symptomatic. Physical examination of the precordium may be misleading because a normal-sized left ventricle does not produce a hyperdynamic apical impulse. The systolic murmur of MR, which may or may not be holosystolic, and a third heart sound may be the only abnormal physical findings present. A fourth heart sound is common. Transthoracic echocardiography may demonstrate the disruption of the mitral valve and help provide semiquantitative information about lesion severity. However, transthoracic echocardiography may underestimate lesion severity by inadequate imaging of the color flow jet. Because transesophageal echocardiography can more accurately assess the color flow jet, transesophageal imaging should be performed if mitral valve morphology and regurgitant severity are still in question after transthoracic echocardiography. Transesophageal echocardiography is also helpful in demonstrating the anatomic cause of MR and directing successful surgical repair.

If ischemia is not the cause of MR and there is no reason to suspect CAD, mitral valve repair can usually be performed

without cardiac catheterization. However, if CAD is suspected or there are risk factors for CAD, coronary arteriography is necessary before surgery.

#### Medical Therapy

In acute severe MR, the goal of nonsurgical therapy is to diminish the amount of MR, in turn increasing forward output and reducing pulmonary congestion. In the normotensive patient, administration of nitroprusside may effectively accomplish all 3 goals. Nitroprusside alone should not be administered to patients with hypotension, but combination therapy with an inotropic agent (such as dobutamine) and nitroprusside is of benefit in some patients. In such patients, aortic balloon counterpulsation increases forward output and mean arterial pressure while diminishing regurgitant volume and LV filling pressure and can be used to stabilize hemodynamics while preparing for surgery. If infective endocarditis is the cause of acute MR, identification and treatment of the infectious organism are essential.

#### 2. Chronic Mitral Regurgitation

In chronic severe MR, the increase in LV end-diastolic volume permits an increase in total stroke volume, allowing for restoration of forward cardiac output. Augmented preload and reduced or normal afterload (provided by unloading of the left ventricle into the left atrium) facilitate LV ejection. At the same time, the increase in LV and left atrial size allows accommodation of the regurgitant volume at a lower filling pressure. In this phase of compensated MR, the patient may be entirely asymptomatic, even during vigorous exercise.

The duration of the compensated phase of MR varies but may last for many years. However, the prolonged burden of volume overload may eventually result in LV dysfunction. In this phase, contractile dysfunction impairs ejection, and end-systolic volume increases. There may be further LV dilatation and increased LV filling pressure. These hemodynamic events result in reduced forward output and pulmonary congestion. However, the still favorable loading conditions often maintain ejection fraction in the low normal range (0.50 to 0.60) despite the presence of significant muscle dysfunction. Correction of MR should occur before advanced LV decompensation.

#### Diagnosis

In evaluating the patient with chronic MR, a careful history is invaluable. A well-established estimation of baseline exercise tolerance is important in gauging the subtle onset of symptoms at subsequent evaluations. Physical examination should demonstrate displacement of the LV apical impulse, which indicates that MR is severe and chronic, producing cardiac enlargement. A third heart sound is usually present and does not necessarily indicate heart failure. An ECG and a chest x-ray are useful in establishing rhythm and heart size, respectively. An initial echocardiogram, including Doppler interrogation of the mitral valve, is indispensable in the management of MR. The echocardiogram provides a baseline estimation of LV and left atrial volume, an estimation of LV ejection fraction, and approximation of the severity of regurgitation. Changes from these baseline values are subsequently used to guide the timing of mitral valve surgery. In addition, the echocardiogram can often disclose the anatomic cause of

the patient's condition. In the presence of even mild TR, interrogation of the tricuspid valve yields an estimate of pulmonary artery pressure.

In some patients, Doppler studies show that MR worsens with exercise, possibly reconciling exercise-induced symptoms with resting echocardiograms that show only mild or moderate regurgitation.

#### Serial Testing

Asymptomatic patients with mild MR and no evidence of LV enlargement or dysfunction or pulmonary hypertension can be followed up on a yearly basis with instructions to alert the physician if symptoms develop in the interim. Yearly echocardiography is not necessary unless there is clinical evidence that regurgitation has worsened. In patients with moderate MR, clinical evaluations should be performed annually, and echocardiography is not necessary more than once a year.

Asymptomatic patients with severe MR should be followed up with a history, physical examination, and echocardiography every 6 to 12 months to assess symptoms or transition to asymptomatic LV dysfunction. Serial chest x-rays and ECGs are of less value but are helpful in selected patients. Most patients develop symptoms before developing LV dysfunction. Exercise stress testing may be used to add objective evidence of symptoms and changes in exercise tolerance. Exercise testing is especially important if a good history of the patient's exercise capacity cannot be obtained.

Several studies have indicated that preoperative ejection fraction is an important predictor of postoperative survival in patients with chronic MR. The loading conditions of MR facilitate ejection and increase ejection fraction, and the ejection fraction in a patient with MR with normal LV function is usually  $\geq 0.60$ . Consistent with this concept, postoperative survival is reduced in patients with a preoperative ejection fraction  $< 0.60$  compared with patients with higher ejection fractions.

Alternatively or in concert, echocardiographic LV end-systolic dimension (or volume) can be used in the timing of mitral valve surgery. End-systolic dimension, which may be less load dependent than ejection fraction, should be  $< 45$  mm before surgery to ensure normal postoperative LV function. If patients become symptomatic, they should undergo mitral valve surgery even if LV function is normal.

#### Recommendations for Transthoracic Echocardiography in Mitral Regurgitation

Indication	Class
1. For baseline evaluation to quantify severity of MR and LV function in any patient suspected of having MR.	I
2. For delineation of mechanism of MR.	I
3. For annual or semiannual surveillance of LV function (estimated by ejection fraction and end-systolic dimension) in asymptomatic severe MR.	I
4. To establish cardiac status after a change in symptoms.	I
5. For evaluation after MVR or mitral valve repair to establish baseline status.	I
6. Routine follow-up evaluation of mild MR with normal LV size and systolic function.	III

**Recommendations for Transesophageal Echocardiography in Mitral Regurgitation**

Indication	Class
1. Intraoperative transesophageal echocardiography to establish the anatomic basis for MR and to guide repair.	I
2. For evaluation of MR patients in whom transthoracic echocardiography provides nondiagnostic images regarding severity of MR, mechanism of MR, and/or status of LV function.	I
3. In routine follow-up or surveillance of patients with native valve MR.	III

*Medical Therapy*

For the asymptomatic patient with chronic MR, there is no generally accepted medical therapy. Although intuitively the use of vasodilators may appear to be logical for the same reasons that they are effective in acute MR and chronic AR, there are no large long-term studies to indicate that they are beneficial. Furthermore, because MR with normal ejection fraction is a disease in which afterload is not increased, drugs that reduce afterload might produce a physiological state of chronic low afterload for which there is very little experience. Thus, in the absence of systemic hypertension, there is no known indication for the use of vasodilating drugs in asymptomatic patients with preserved LV function.

In patients with MR who develop symptoms but have preserved LV function, surgery is the most appropriate therapy. If atrial fibrillation develops, heart rate should be controlled with digitalis, rate-lowering calcium channel blockers,  $\beta$ -blockers, or, rarely, amiodarone. Although the risk of embolism with the combination of MR and atrial fibrillation may be less than that of MS and atrial fibrillation, INR should be maintained between 2 and 3 in patients with MR who develop atrial fibrillation.

*Indications for Cardiac Catheterization*

Cardiac catheterization, with or without exercise, is necessary when there is a discrepancy between clinical and noninvasive findings. Catheterization is also performed when surgery is contemplated and there is uncertainty about the severity of MR after noninvasive testing or when there is a need to assess extent and severity of CAD before surgery. In patients with MR who have risk factors for CAD (advanced age, hypercholesterolemia, hypertension, etc) or when there is suspicion that MR is ischemic in etiology (either because of known myocardial infarction or suspected ischemia), coronary angiography should be performed before surgery. For cases in which no reasonable suspicion of CAD exists, coronary angiography can be avoided.

Obviously, patients should not undergo valve surgery unless the valve lesion is severe. In cases of chronic MR, noninvasive imaging should demonstrate anatomic disruption of the valve or its apparatus, and color flow Doppler should indicate severe MR. Although the standard semiquantitative approach to determining severity of MR from ventriculography has its own limitations, ventriculography does provide an additional method to assess LV dilatation and function and to gauge severity of MR. Exercise hemodynamics and quantitative angiography may provide additional information that is helpful for decision making. During the catheterization procedure, *a right-heart catheterization should be performed* if severity of MR is uncertain.

**Recommendations for Coronary Angiography in Mitral Regurgitation**

Indication	Class
1. When mitral valve surgery is contemplated in patients with angina or previous myocardial infarction.	I
2. When mitral valve surgery is contemplated in patients with $\geq 1$ risk factor for CAD (see section VIII.B.).	I
3. When ischemia is suspected as an etiologic factor in MR.	I
4. To confirm noninvasive tests in patients not suspected of having CAD.	IIb
5. When mitral valve surgery is contemplated in patients aged <35 years and there is no clinical suspicion of CAD.	III

**Recommendations for Left Ventriculography and Hemodynamic Measurements in Mitral Regurgitation**

Indication	Class
1. When noninvasive tests are inconclusive regarding the severity of MR, LV function, or the need for surgery.	I
2. When there is a discrepancy between clinical and noninvasive findings regarding severity of MR.	I
3. In patients in whom valve surgery is not contemplated.	III

*Indications for Surgery*

Three different mitral valve operations are used to correct MR: mitral valve repair, MVR with preservation of part or all of the mitral apparatus, and MVR with removal of the mitral apparatus. In most cases, mitral valve repair is the operation of choice when the valve is suitable for repair and appropriate surgical skill and expertise are available. This procedure preserves the patient's native valve without a prosthesis, avoiding the risk of long-term anticoagulation (except in patients in atrial fibrillation) or prosthetic valve failure late after surgery. In addition, preservation of the mitral apparatus leads to better postoperative LV function and survival than in cases when the apparatus is removed. However, mitral valve repair is technically more demanding than MVR, may require longer extracorporeal circulation time, and may occasionally fail.

The advantage of MVR with preservation of the chordal apparatus is that this operation ensures postoperative mitral valve competence, preserves LV function, and enhances postoperative survival compared with MVR, in which the apparatus is disrupted. Its disadvantage is the use of a prosthetic valve, with the risks of deterioration in biological valves or the need for anticoagulation in mechanical valves.

MVR in which the mitral valve apparatus is destroyed should almost never be performed. It should be reserved for those circumstances in which the native valve and apparatus are so distorted by the preoperative pathology (eg, rheumatic disease) that the mitral apparatus cannot be saved.

Many factors are useful in the preoperative prediction of success of mitral valve repair. This prediction is based on the surgeon's skill and experience in performing repair and on the location and type of mitral valve disease that caused MR. Nonrheumatic posterior leaflet prolapse due to degenerative mitral valve disease or a ruptured chorda tendineae can usually be repaired. Involvement of the anterior leaflet diminishes the likelihood of repair, and consequently the skill

and experience of the surgeon are probably the most important determinants of whether the operation is eventually performed. In general, rheumatic and ischemic involvement of the mitral valve and calcification of the mitral valve leaflets or annulus diminish the likelihood of repair even in experienced hands.

**1. Symptomatic Patients With Normal Left Ventricular Function.** Patients with severe MR and symptoms of congestive heart failure despite normal LV function on echocardiography (ejection fraction  $>0.60$  and end-systolic dimension  $<45$  mm) require surgery. The feasibility of mitral valve repair is dependent on several factors, including valve anatomy and surgical expertise. Successful surgical repair improves symptoms, preserves LV function, and avoids problems associated with prosthetic valves. When repair is not feasible, MVR with chordal preservation should relieve symptoms and maintain LV function.

**2. Asymptomatic or Symptomatic Patients With Left Ventricular Dysfunction.** The timing of surgery for asymptomatic patients was once controversial, but most now agree that mitral valve surgery is appropriate once the echocardiographic indicators of LV dysfunction have appeared. These include LV ejection fraction  $\leq 0.60$  and/or LV end-systolic dimension  $\geq 45$  mm. Although some would recommend a slightly lower threshold ejection fraction (0.55), it must be emphasized that, unlike timing of AVR for AR, LV ejection fraction should not be allowed to fall into the low normal range in patients with chronic MR. The data regarding postoperative survival are much stronger with LV ejection fraction than end-systolic dimension, whereas both ejection fraction and end-systolic dimension strongly influence postoperative LV function and heart failure. Mitral valve surgery should also be recommended for symptomatic patients with evidence of LV systolic dysfunction (ejection fraction  $\leq 0.60$ , end-systolic dimension  $\geq 45$  mm). Determining the surgical candidacy of the symptomatic patient with MR and far-advanced LV dysfunction is a common clinical dilemma. If mitral valve repair appears likely, surgery should still be contemplated, provided ejection fraction is  $\geq 0.30$ . Even though such a patient is likely to have persistent LV dysfunction, surgery is likely to improve symptoms and prevent further deterioration of LV function.

**3. Asymptomatic Patients With Normal Left Ventricular Function.** Repair of a severely regurgitant valve may be contemplated in an asymptomatic patient with normal LV function to preserve LV size and function and prevent the sequelae of chronic MR. Although there are no data with which to recommend this approach to all patients, the committee recognizes that some experienced centers are moving in this direction when there is a high likelihood of successful repair. This approach is often recommended in hemodynamically stable patients with newly acquired severe MR, as might occur with ruptured chordae. Surgery is also recommended in asymptomatic patients with chronic MR with recent onset of episodic or chronic atrial fibrillation in whom there is a high likelihood of successful valve repair (see below).

**4. Atrial Fibrillation.** Atrial fibrillation is a common, potentially morbid arrhythmia associated with MR. Preoperative atrial fibrillation is an independent predictor of reduced long-term survival after mitral valve surgery for chronic MR. The persistence of atrial fibrillation after mitral valve surgery partially nullifies an advantage of mitral repair by requiring anticoagulation. Predictors of persistent atrial fibrillation after successful valve surgery are the presence of atrial fibrillation for  $>1$  year and left atrial size  $>50$  mm. In 1 study, an even shorter duration of preoperative atrial fibrillation (3 months) was a predictor of persistent atrial fibrillation after mitral valve repair. Although patients who develop atrial fibrillation usually manifest other symptomatic or functional changes that would warrant mitral valve repair or replacement, many clinicians consider the onset of episodic or chronic atrial fibrillation to be an indication in and of itself for surgery.

#### Recommendations for Mitral Valve Surgery in Nonischemic Severe Mitral Regurgitation

Indication	Class
1. Acute symptomatic MR in which repair is likely.	I
2. Patients with NYHA functional Class II, III, or IV symptoms with normal LV function defined as ejection fraction $>0.60$ and end-systolic dimension $<45$ mm.	I
3. Symptomatic or asymptomatic patients with mild LV dysfunction, ejection fraction 0.50 to 0.60, and end-systolic dimension 45 to 50 mm.	I
4. Symptomatic or asymptomatic patients with moderate LV dysfunction, ejection fraction 0.30 to 0.50, and/or end-systolic dimension 50 to 55 mm.	I
5. Asymptomatic patients with preserved LV function and atrial fibrillation.	Ila
6. Asymptomatic patients with preserved LV function and pulmonary hypertension (pulmonary artery systolic pressure $>50$ mm Hg at rest or $>60$ mm Hg with exercise).	Ila
7. Asymptomatic patients with ejection fraction 0.50 to 0.60 and end-systolic dimension $<45$ mm and asymptomatic patients with ejection fraction $>0.60$ and end-systolic dimension 45 to 55 mm.	Ila
8. Patients with severe LV dysfunction (ejection fraction $<0.30$ and/or end-systolic dimension $>55$ mm) in whom chordal preservation is highly likely.	Ila
9. Asymptomatic patients with chronic MR with preserved LV function in whom mitral valve repair is highly likely.	Ilb
10. Patients with MVP and preserved LV function who have recurrent ventricular arrhythmias despite medical therapy.	Ilb
11. Asymptomatic patients with preserved LV function in whom significant doubt about the feasibility of repair exists.	III

#### 3. Ischemic Mitral Regurgitation

The outlook for the patient with ischemic MR is substantially worse than that for regurgitation from other causes, as ischemic MR is usually caused by LV dysfunction and/or papillary muscle dysfunction. On the other hand, coronary artery bypass graft surgery may improve LV function and reduce ischemic MR, and in many patients with transient

severe MR due to ischemia, myocardial revascularization can eliminate episodes of severe MR.

Hypotension and pulmonary edema often occur in severe MR secondary to acute myocardial infarction. Treatment is aimed at hemodynamic stabilization, usually with insertion of an intra-aortic balloon pump. Occasionally, revascularization of the coronary artery supplying an ischemic papillary muscle can lead to improvement in mitral valve competence. However, such improvement is rare, and correction of acute severe ischemic MR usually requires valve surgery. Unlike nonischemic MR, in which mitral repair is clearly the operation of choice, the best operation for ischemic MR is controversial.

## F. Multiple Valve Disease

Remarkably few data exist to objectively guide management of mixed valve disease. Each case must be considered individually and management based on understanding the potential derangements in hemodynamics and LV function and the probable benefit of medical versus surgical therapy. The committee has developed no specific recommendations for treatment of multiple valve disease. Specific valve lesions are discussed in the full text of these guidelines.

## G. Tricuspid Valve Disease

Tricuspid valve dysfunction can occur with normal or abnormal valves. Normal tricuspid valves develop regurgitation with elevation of right ventricular systolic and/or diastolic pressure, right ventricular cavity enlargement, and tricuspid annular dilatation. Right ventricular systolic hypertension occurs in MS, pulmonic valve stenosis, and the various causes of pulmonary hypertension. Right ventricular diastolic hypertension occurs in dilated cardiomyopathy and right ventricular failure of any cause.

### Diagnosis

The physical examination is the initial key to diagnosis of tricuspid valve disease. Echocardiography is valuable in assessing valve structure and motion, measuring annular size, and identifying other cardiac abnormalities that might influence tricuspid valve function. Doppler echocardiography estimates severity of TR, right ventricular systolic pressure, and the tricuspid valve diastolic gradient. It should be pointed out that clinically insignificant TR is detected by color Doppler imaging in many normal persons. This is not an indication for either routine follow-up or prophylaxis against bacterial endocarditis. Thus, clinical correlation and judgment must accompany the echocardiographic results. Systolic pulmonary artery pressure estimation combined with information about annular circumference will further improve the accuracy of clinical assessment.

### Management

In patients with severe MS and pulmonary hypertension with resulting right ventricular dilatation and TR, relief of MS and the resulting decrease in pulmonary artery pressure may result in substantial diminution of the degree of TR. Although the timing of surgery for TR remains controversial, as do the surgical techniques, this controversy has diminished since the advent of 2-D and Doppler echocardiography for preoperative assessment. Intraoperative transesophageal Doppler

echocardiography allows refinement of annuloplasty techniques to optimize outcome.

Patients with severe TR of any cause have a poor long-term outcome because of right ventricular dysfunction and/or systemic venous congestion. Tricuspid valve and chordal reconstruction can be attempted in some cases of TR that are the result of endocarditis and trauma. In recent years, annuloplasty has become an established surgical approach to significant TR.

When the valve leaflets themselves are diseased, abnormal, or destroyed, valve replacement with a low-profile mechanical valve or bioprosthesis is often necessary. A biological prosthesis is preferred because of the high rate of thromboembolic complications with mechanical prostheses in the tricuspid position.

## Recommendations for Surgery for Tricuspid Regurgitation

Indication	Class
1. Annuloplasty for severe TR and pulmonary hypertension in patients with mitral valve disease requiring mitral valve surgery.	I
2. Valve replacement for severe TR secondary to diseased/abnormal tricuspid valve leaflets not amenable to annuloplasty or repair.	IIa
3. Valve replacement or annuloplasty for severe TR with mean pulmonary artery pressure <60 mm Hg when symptomatic.	IIa
4. Annuloplasty for mild TR in patients with pulmonary hypertension secondary to mitral valve disease requiring mitral valve surgery.	IIb
5. Valve replacement or annuloplasty for TR with pulmonary artery systolic pressure <60 mm Hg in the presence of a normal mitral valve, in asymptomatic patients, or in symptomatic patients who have not received a trial of diuretic therapy.	III

## H. Valvular Heart Disease Associated With Anorectic Drugs

In the summer of 1997, the association between anorexigens and valvular heart disease was reported in 24 patients receiving the drug combination of fenfluramine and phentermine; unusual valve morphology and associated regurgitation were identified in both left- and right-sided heart valves. The echocardiographic and histopathologic findings were similar to those described in patients with carcinoid or ergotamine-induced valvular heart disease. All 24 patients were symptomatic and had heart murmurs; thus, the frequency of valvular pathology in asymptomatic patients receiving the combination of fenfluramine-phentermine could not be determined. The FDA has reported 5 echocardiographic prevalence surveys in which 86 of 271 patients (32%) who received a combination of fenfluramine and phentermine for 6 to 24 months had evidence of significant AR and/or MR, as did 6 of 20 patients (30%) who received dexfenfluramine with or without phentermine.

In light of this information, fenfluramine and dexfenfluramine have been withdrawn from the market. The risk of valvular heart disease associated with exposure to fenfluramine or dexfenfluramine, alone or in combination with phentermine, has been addressed in recent peer-reviewed studies in which the prevalence of AR and/or MR in patients

exposed to these drugs varied widely. It does appear that the prevalence of significant valvular regurgitation may be related to the duration of exposure to the anorectic agents and that patients exposed for only brief periods of time have less risk of developing valvular regurgitation.

In addition to the uncertainties regarding the prevalence of valvular disease in patients receiving combination or single-drug therapy, the natural history of the valve disease during anorectic drug treatment and after drug withdrawal is unknown and awaits further clinical investigation. Thus, the risk of valvular heart disease relative to the benefit of weight reduction in patients with morbid obesity is unknown.

Considering these unknown variables, it is not possible to derive definitive diagnostic and treatment guidelines for patients who have received these anorectic drugs. Hence, clinical judgment is important. The US Department of Health and Human Services (DHHS), through the Centers for Disease Control and Prevention and the National Institutes of Health, has published interim recommendations.<sup>8</sup>

The Committee on Management of Patients With Valvular Heart Disease recommends that all patients with a history of use of fenfluramine or dexfenfluramine undergo a careful history and thorough cardiovascular physical examination. Physical examination should include auscultation with the patient in the upright position at end expiration to detect AR and in the left lateral decubitus position to detect MR. 2-D and Doppler echocardiography should be performed in those patients with symptoms, cardiac murmurs, or other signs of cardiac involvement (eg, widened pulse pressure or regurgitant *c* or *v* waves in the jugular venous pulse). Patients whose body habitus prevents adequate cardiac auscultation should also undergo 2-D and Doppler echocardiography. For example, mild AR may be difficult to detect on auscultation in an obese patient. Patients with clinical and echocardiographic evidence of valvular heart disease should then undergo treatment and/or further testing according to the recommendations developed for the specific valve lesions addressed earlier in these guidelines. Modification of these recommendations may be necessary as more information on the natural history of these specific valve lesions becomes available.

In light of the current evidence, echocardiographic screening of all patients with a history of fenfluramine or dexfenfluramine use, especially asymptomatic patients without murmurs or associated findings, is not recommended. However, because of possible progression of subclinical valvular disease, asymptomatic patients without murmurs should undergo repeat physical examinations in 6 to 8 months.

**Recommendations for Patients Who Have Used Anorectic Drugs\***

Indication	Class
1. Discontinuation of the anorectic drug(s).	I
2. Cardiac physical examination.	I
3. Echocardiography in patients with symptoms, heart murmurs, or associated physical findings.	I
4. Doppler echocardiography in patients for whom cardiac auscultation cannot be performed adequately because of body habitus.	I

Indication	Class
5. Repeat physical examination in 6 to 8 months for those without murmurs.	IIa
6. Echocardiography in all patients before dental procedures in the absence of symptoms, heart murmurs, or associated physical findings.	IIb
7. Echocardiography in all patients without heart murmurs.	III

\*Fenfluramine or dexfenfluramine or the combination of fenfluramine-phentermine or dexfenfluramine-phentermine.

**IV. Evaluation and Management of Infective Endocarditis**

**A. Antimicrobial Therapy**

Antimicrobial therapy in endocarditis is guided by identification of the causative organism. Eighty percent of endocarditis cases are due to streptococci and staphylococci. The majority of native valve endocarditis is caused by *Streptococcus viridans* (50%) and *Staphylococcus aureus* (20%). With prosthetic valve endocarditis, a wide spectrum of organisms can be responsible within the first year of operation. However, in "early" prosthetic valve endocarditis, usually defined as endocarditis during the first 2 months after surgery, *Staphylococcus epidermidis* is the frequent offending organism. Late-onset prosthetic valve endocarditis follows the profile of native valve endocarditis. *Enterococcus faecalis* and *Enterococcus faecium* account for 90% of enterococcal endocarditis, usually associated with malignancy or manipulation of the genitourinary or gastrointestinal tract. Gram-positive and gram-negative bacilli are relatively uncommon causes of endocarditis. In recent years, the HACEK group of organisms (*Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, and *Kingella* species) have become important causes of endocarditis. Fungi, especially *Candida*, are important causes of endocarditis in patients with prosthetic valves, compromised immune systems, and intravenous drug abuse. Recommended antimicrobial regimens for treatment of bacterial endocarditis have been published by the AHA<sup>9</sup> and are reproduced in the full-text version of these guidelines.

**B. Culture-Negative Endocarditis**

Culture-negative endocarditis most frequently (62%) results from prior antibiotic treatment before blood cultures were drawn. The other reasons for negative blood cultures are infections caused by *Candida*; *Aspergillus*; or fastidious, slow-growing organisms and noninfective endocarditis, such as Libman-Sacks endocarditis in patients with systemic lupus erythematosus. The recommended regimen for culture-negative presumed bacterial endocarditis is a 6-week course of intravenous vancomycin (15 mg/kg every 12 hours) plus intravenous or intramuscular gentamycin (1 mg/kg every 8 hours).

**C. Endocarditis in HIV Seropositive Patients**

Endocarditis in patients who are HIV seropositive usually occurs as a complication of drug injections or long-term indwelling central catheters. *S aureus* is the most frequent pathogen. Endocarditis-related mortality in patients with AIDS exceeds that of HIV-positive patients without AIDS.

Thus, it is recommended that endocarditis in patients with AIDS be treated with maximum-duration antibiotic regimens.

#### D. Indications for Echocardiography in Endocarditis

Echocardiography is useful for detection and characterization of the hemodynamic and pathological consequences of infection. These consequences include valvular vegetations; valvular regurgitation; ventricular dysfunction; and associated lesions such as abscesses, shunts, and ruptured chordae. The indications for transthoracic and transesophageal echocardiography are discussed in the ACC/AHA Guidelines for the Clinical Application of Echocardiography.<sup>2</sup> Transesophageal imaging is more sensitive for detecting vegetations than transthoracic imaging. Echocardiography may be useful in the case of culture-negative endocarditis or the diagnosis of a persistent bacteremia whose source remains unidentified after appropriate evaluation.

##### Recommendations for Echocardiography in Infective Endocarditis: Native Valves

Indication	Class
1. Detection and characterization of valvular lesions, their hemodynamic severity, and/or ventricular compensation.*	I
2. Detection of vegetations and characterization of lesions in patients with congenital heart disease in whom infective endocarditis is suspected.	I
3. Detection of associated abnormalities (eg, abscesses, shunts).*	I
4. Reevaluation studies in complex endocarditis (eg, virulent organism, severe hemodynamic lesion, aortic valve involvement, persistent fever or bacteremia, clinical change, or symptomatic deterioration).	I
5. Evaluation of patients with high clinical suspicion of culture-negative endocarditis.*	I
6. Evaluation of bacteremia without a known source.*	IIa
7. Risk stratification in established endocarditis.*	IIa
8. Routine reevaluation in uncomplicated endocarditis during antibiotic therapy.	IIb
9. Evaluation of fever and nonpathological murmur without evidence of bacteremia.	III

\*Transesophageal echocardiography may provide incremental value in addition to information obtained by transthoracic imaging.

From the ACC/AHA Guidelines for the Clinical Application of Echocardiography.<sup>2</sup>

##### Recommendations for Echocardiography in Infective Endocarditis: Prosthetic Valves

Indication	Class
1. Detection and characterization of valvular lesions, their hemodynamic severity, and/or ventricular compensation.*	I
2. Detection of associated abnormalities (eg, abscesses, shunts, etc).*	I
3. Reevaluation in complex endocarditis (eg, virulent organism, severe hemodynamic lesion, aortic valve involvement, persistent fever or bacteremia, clinical change, or symptomatic deterioration).	I

Indication	Class
4. Evaluation of suspected endocarditis and negative cultures.*	I
5. Evaluation of bacteremia without a known source.*	I
6. Evaluation of persistent fever without evidence of bacteremia or new murmur.*	IIa
7. Routine reevaluation in uncomplicated endocarditis during antibiotic therapy.*	IIb
8. Evaluation of transient fever without evidence of bacteremia or new murmur.	III

\*Transesophageal echocardiography may provide incremental value in addition to that obtained by transthoracic imaging.

From the ACC/AHA Guidelines for the Clinical Application of Echocardiography.<sup>2</sup>

#### E. Indications for Surgery in Patients With Active Infective Endocarditis

Surgery is indicated in patients with life-threatening congestive heart failure or cardiogenic shock due to surgically treatable valvular heart disease with or without established infective endocarditis if the patient's prospects for recovery are reasonable, with satisfactory quality of life after the operation. Surgery should not be delayed in the setting of acute infective endocarditis when congestive heart failure intervenes. Surgery is not indicated if complications (severe embolic cerebral damage) or comorbid conditions make the prospect of recovery remote.

The indications for surgery for infective endocarditis in patients with stable hemodynamics are less clear. Early consultation with a cardiovascular surgeon is recommended as soon as the diagnosis of aortic or mitral valve endocarditis is made so that the surgical team is aware of the patient who may suddenly need surgery. Surgery is recommended for patients with annular or aortic abscesses, infections resistant to antibiotic therapy, and fungal endocarditis.

When endocarditis develops in patients with prosthetic valves who are receiving warfarin anticoagulation, warfarin should be discontinued and replaced with heparin. This recommendation is less related to the possibility of hemorrhagic complications of endocarditis than the possibility of urgent surgery. If surgery is required, the effects of warfarin will have dissipated, and heparin can easily be reversed. Likewise, aspirin, if part of the medical regimen, should also be discontinued. If neurological symptoms develop, anticoagulation should be discontinued until an intracranial hemorrhagic event is excluded by MRI or computed tomographic scanning.

##### Recommendations for Surgery for Native Valve Endocarditis\*

Indication	Class
1. Acute AR or MR with heart failure.	I
2. Acute AR with tachycardia and early closure of the mitral valve.	I
3. Fungal endocarditis.	I
4. Evidence of annular or aortic abscess, sinus or aortic true or false aneurysm.	I



Indication	Class
5. Evidence of valve dysfunction and persistent infection after a prolonged period (7 to 10 days) of appropriate antibiotic therapy, as indicated by presence of fever, leukocytosis, and bacteremia, provided there are no noncardiac causes for infection.	I
6. Recurrent emboli after appropriate antibiotic therapy.	IIa
7. Infection with gram-negative organisms or organisms with a poor response to antibiotics in patients with evidence of valve dysfunction.	IIa
8. Mobile vegetations >10 mm.	IIb
9. Early infections of the mitral valve that can likely be repaired.	III
10. Persistent pyrexia and leukocytosis with negative blood cultures.	III

\*Criteria also apply to repaired mitral and aortic allograft or autograft valves. Endocarditis defined by clinical criteria with or without laboratory verification; there must be evidence that function of a cardiac valve is impaired.

#### Recommendations for Surgery for Prosthetic Valve Endocarditis\*

Indication	Class
1. Early prosthetic valve endocarditis (first 2 months or less after surgery).	I
2. Heart failure with prosthetic valve dysfunction.	I
3. Fungal endocarditis.	I
4. Staphylococcal endocarditis not responding to antibiotic therapy.	I
5. Evidence of paravalvular leak, annular or aortic abscess, sinus or aortic true or false aneurysm, fistula formation, or new-onset conduction disturbances.	I
6. Infection with gram-negative organisms or organisms with a poor response to antibiotics.	I
7. Persistent bacteremia after a prolonged course (7 to 10 days) of appropriate antibiotic therapy without noncardiac causes for bacteremia.	IIa
8. Recurrent peripheral embolus despite therapy.	IIa
9. Vegetation of any size on or near the prosthesis.	IIb

\*Criteria exclude repaired mitral valves or aortic allograft or autograft valves. Endocarditis is defined by clinical criteria with or without laboratory verification.

## V. Management of Valvular Disease in Pregnancy

### A. Physiological Changes of Pregnancy

The evaluation and management of valvular heart disease in the pregnant patient requires an understanding of the normal physiological changes associated with gestation, labor, delivery, and the early postpartum period. On average, there is a 50% increase in circulating blood volume during pregnancy, which is accompanied by a commensurate increase in cardiac output that usually peaks between the midportion of the second and third trimesters. The augmented cardiac output is caused by an increase in stroke volume, although there is also a smaller increase in heart rate, averaging 10 to 20 bpm. Because of the effects of uterine circulation and endogenous hormones, systemic vascular resistance falls with a dispropor-

tionately greater lowering of diastolic blood pressure and a wide pulse pressure. Inferior vena caval obstruction from a gravid uterus in the supine position can result in an abrupt decrease in cardiac preload, leading to hypotension with weakness and lightheadedness. These symptoms resolve quickly with a change in position.

There is a further abrupt increase in cardiac output during labor and delivery related in part to the associated anxiety and pain. Uterine contractions can lead to marked increases in both systolic and diastolic blood pressure. After delivery, there is an initial surge in preload related to the autotransfusion of uterine blood into the systemic circulation and to caval decompression.

Pregnancy is also associated with a hypercoagulable state, owing to relative decreases in protein S activity, stasis, and venous hypertension. Estrogens may interfere with collagen deposition within the media of the medium- and large-sized muscular arteries. Circulating elastase can break up the elastic lamellae and weaken the aortic media during pregnancy. Weakening of the vascular wall may in turn predispose to dissection with or without an underlying connective tissue disorder.

The increased blood volume and enhanced cardiac output associated with normal pregnancy can accentuate the murmurs associated with stenotic heart valve lesions (eg, MS, AS). On the other hand, murmurs of AR or MR may actually attenuate in the face of lowered systemic vascular resistance.

### B. Echocardiography

Normal pregnancy is accompanied by echocardiographic evidence of mild ventricular chamber enlargement. Pulmonic and tricuspid valvular regurgitation, as assessed by Doppler interrogation, is the rule rather than the exception. A large minority of women will demonstrate Doppler evidence of "physiological" MR in the absence of structural valve disease. Atrioventricular valve incompetence may be derived from the annular dilatation that accompanies ventricular enlargement. Appreciation of these echocardiographic and Doppler findings in normal individuals is an important foundation for noninvasive evaluation of subjects with suspected valvular disease. The use of ultrasound during pregnancy poses no risk to the mother or fetus.

### C. General Management Guidelines

Clinical experience has shown several cardiac conditions in which the physiological changes of pregnancy are poorly tolerated. Most experts would agree that pregnancy should be discouraged for some conditions, such as cyanotic heart disease, Eisenmenger syndrome, or severe pulmonary hypertension. Valvular heart lesions associated with increased maternal and fetal risk during pregnancy include severe AS with or without symptoms, MR or AR with NYHA functional Class III to IV symptoms, MS with NYHA functional Class II to IV symptoms, valve disease resulting in severe pulmonary hypertension (pulmonary pressure >75% of systemic pressures), valve disease with severe LV dysfunction (EF <0.40), mechanical prosthetic valves requiring anticoagulation, and AR in Marfan syndrome.

Individual counseling usually requires a multidisciplinary approach and should include information about contraception, maternal and fetal risks of pregnancy, and expected long-term outcomes. However, many patients with valvular heart disease can be successfully managed throughout pregnancy and during labor and delivery with conservative medical measures designed to optimize intravascular volume and systemic loading conditions.

Simple interventions such as bed rest and avoidance of the supine position should not be overlooked. Whenever possible, symptomatic or severe valvular lesions should be addressed and resolved before conception and pregnancy. Contemporaneous management with a dedicated obstetrical team accustomed to working with high-risk patients is encouraged.

## D. Specific Lesions

### 1. Mitral Stenosis

Young pregnant women with a previous history of acute rheumatic fever and carditis should continue to receive penicillin prophylaxis as indicated in the nonpregnant state. Patients with mild to moderate MS can almost always be managed with judicious use of diuretics and  $\beta$ -blockade. Care must be taken to avoid vigorous volume depletion to protect against uretero-placental hypoperfusion.  $\beta$ -Blockers are chiefly indicated to treat or prevent tachycardia to optimize diastolic filling.

Patients with severe MS who are symptomatic before conception will not predictably tolerate the hemodynamic burden of pregnancy and should be considered for percutaneous balloon mitral valvotomy before conception, provided the valve is anatomically suitable. Patients with severe MS who develop NYHA functional Class III-IV symptoms during pregnancy should undergo percutaneous balloon valvotomy.

Rarely, medical management of patients with MS does not prevent repetitive or persistent heart failure during pregnancy. However, there is now a near 10-year experience with balloon mitral valvotomy, with either very limited fluoroscopy (<1 to 2 minutes' exposure with both pelvic and abdominal shielding) or echocardiographic guidance. The reported results with mitral balloon valvotomy have been excellent, with few maternal and/or fetal complications. Percutaneous mitral balloon valvotomy should be performed only in experienced centers and only after aggressive medical measures have been exhausted. In developing countries, there is a long history of successful surgical closed commissurotomy for the pregnant woman.

### 2. Mitral Regurgitation

MVP is the most common cause of MR in pregnant women. The physical findings pertinent to MVP may be obscured or varied by the physiological changes of pregnancy, especially increased blood volume and reduced systemic vascular resistance. The associated MR can usually be managed medically, although on rare occasions, mitral valve surgery is required because of ruptured chordae and acute, severe worsening of the regurgitant lesion. When mitral valve surgery is required, repair is always preferred, as would be the case for any young

patient, but especially in relation to the desirability of avoiding the potential need for anticoagulation.

### 3. Aortic Stenosis

The most common cause of AS in pregnant women is congenital bicuspid disease. Patients with mild to moderate obstruction and normal LV systolic function can usually be managed conservatively through the entire pregnancy. Patients with more severe obstruction (pressure gradient >50 mm Hg) or symptoms should be advised to delay conception until relief of AS is obtained. There is an association between the presence of a bicuspid aortic valve and cystic medial necrosis, which may predispose to spontaneous aortic dissection, usually in the third trimester.

### 4. Aortic Regurgitation

Isolated AR, like MR, can usually be managed medically with a combination of diuretics and if necessary vasodilator therapy. Women with symptoms and/or signs of LV failure should be carefully monitored throughout labor and delivery with strict attention to volume status and blood pressure. As with MR, surgery during pregnancy should be contemplated only for the control of refractory Class III or IV symptoms. Consideration of LV size or systolic function in less symptomatic patients should not apply.

### 5. Pulmonary Valve Stenosis

Isolated pulmonic stenosis is rarely a significant impediment to a successful pregnancy. This lesion can be approached with percutaneous valvotomy under echocardiographic guidance when necessary.

### 6. Marfan Syndrome

Spontaneous aortic dissection and/or rupture are the most feared cardiovascular complications of Marfan syndrome associated with pregnancy. Dissection can occur at any point along the aorta but most commonly originates in the ascending portion. Enlargement of the aortic root >4.0 cm identifies a particularly high-risk group, although a normal dimension is by no means a guarantee against this catastrophic complication.

Any woman with Marfan syndrome who is contemplating pregnancy should have a screening transthoracic echocardiogram with careful assessment of aortic root dimensions. Enlargement  $\geq$  5.0 cm is considered an indication for elective repair before conception, usually with a composite valve-graft conduit and reimplantation of the coronary arteries. If aortic root enlargement (>4.0 cm) is first detected during pregnancy, some authorities recommend termination with prompt aortic repair, especially if serial echocardiographic studies demonstrate progressive dilatation over time. Dissection and rupture are most likely to occur during the third trimester or near the time of delivery. Special care must be taken to provide adequate analgesia to prevent wide surges in blood pressure during labor and delivery. Obstetrical techniques to shorten the second stage of labor are appropriate. General anesthesia and cesarean section may allow more optimal hemodynamic control. The use of prophylactic  $\beta$ -blockade throughout pregnancy is strongly recommended. Finally, it should be pointed out that patients with Marfan syndrome and no identifiable cardiovascular abnormalities on

examination or echocardiographic study can be safely shepherded through pregnancy and a normal vaginal delivery.

**E. Endocarditis Prophylaxis**

The Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the American Heart Association does not recommend routine antibiotic prophylaxis in patients with valvular heart disease undergoing uncomplicated vaginal delivery or cesarean section unless infection is suspected. Antibiotics are optional for high-risk patients with prosthetic heart valves, a previous history of endocarditis, complex congenital heart disease, or a surgically constructed systemic-pulmonary conduit. Many practitioners routinely provide antibiotics.

**F. Cardiac Valve Surgery**

Cardiac valve surgery is a difficult and complex undertaking in the pregnant patient. Even under ideal conditions, including the use of cardiopulmonary bypass techniques that promote high flow rates and warm perfusion temperatures, there is a high incidence of fetal distress, growth retardation, or wastage. If possible, it is always preferable to delay surgery until the fetus is viable and a cesarean section can be performed as part of a concomitant procedure. Surgery should be pursued only in the setting of medically refractory symptoms (pulmonary congestion), especially if a low output syndrome intervenes.

**G. Anticoagulation**

Pregnant patients with mechanical valve prostheses have an obligate need for anticoagulation. Unfortunately, significant problems remain, along with an impressive risk to both mother and fetus of either hemorrhage or thrombosis with the use of either warfarin or heparin.

**1. Warfarin**

Warfarin crosses the placenta and has been associated with an increased incidence of spontaneous abortion, fetal deformity, prematurity, and stillbirth. The true incidence of warfarin embryopathy has been difficult to ascertain from the reported case series and has ranged from <5% to 67%; an estimate of 4% to 10% seems reasonable, based on recent reports. The risk may be dose related and appears to be highest if exposure occurs during the 6th to 12th week of gestation. Fetal cerebral hemorrhage can complicate labor and delivery, especially if forceps evacuation is necessary.

**2. Heparin**

Heparin does not cross the placenta and is generally considered safer. However, its longer-term use is complicated by sterile abscesses, osteoporosis (albeit with a small risk of fracture), thrombocytopenia, and bleeding. Numerous reports attest to an unacceptable incidence of thromboembolic complications, including fatal valve thrombosis, in high-risk pregnant women managed with subcutaneous heparin (12% to 24%). These studies have several limitations, such as inclusion of a predominant population of women with older-generation and more

thrombogenic prostheses, inadequate heparin dosing, and/or lack of meticulous monitoring strategies. Unfortunately, the efficacy of adjusted-dose subcutaneous heparin has not been definitively established.

The choice of anticoagulant must be carefully considered and should consider the mother's preferences regarding the competing risks to her and the fetus. For many women, a 4% to 10% risk of warfarin embryopathy is unacceptable. These women may be unwilling to take warfarin at any time during the first trimester or throughout the entire pregnancy. However, implicit in their choice of heparin is the acceptance of increased risk of maternal hemorrhage or prosthetic valve thrombosis. Certainly, a full discussion of these issues is indicated before conception.

**Recommendations for Anticoagulation During Pregnancy: Weeks 1 Through 35 in Patients With Mechanical Prosthetic Valves**

Indication	Class
1. The decision whether to use heparin during the first trimester or to continue oral anticoagulation throughout pregnancy should be made after full discussion with the patient and her partner; if she chooses to change to heparin for the first trimester, she should be made aware that heparin is less safe for her, with a higher risk of both thrombosis and bleeding, and that any risk to the mother also jeopardizes the baby.*	I
2. High-risk women (a history of thromboembolism or an older-generation mechanical prosthesis in the mitral position) who choose <i>not</i> to take warfarin during the first trimester should receive continuous unfractionated heparin intravenously in a dose to prolong the midinterval (6 hours after dosing) aPTT to 2 to 3 times control. Transition to warfarin can occur thereafter.	I
3. In patients receiving warfarin, INR should be maintained between 2.0 and 3.0 with the lowest possible dose of warfarin, and low-dose aspirin should be added.	IIa
4. Women at low risk (no history of thromboembolism, newer low-profile prosthesis) may be managed with adjusted-dose subcutaneous heparin (17 500 to 20 000 U BID) to prolong the midinterval (6 hours after dosing) aPTT to 2 to 3 times control.	IIb

\*From the European Society of Cardiology Guidelines for Prevention of Thromboembolic Events in Valvular Heart Disease.

**Recommendations for Anticoagulation During Pregnancy: After the 36th Week in Patients With Mechanical Prosthetic Valves**

Indication	Class
1. Warfarin should be stopped no later than week 36 and heparin substituted in anticipation of labor.	IIa
2. If labor begins during treatment with warfarin, a cesarean section should be performed.	IIa
3. In the absence of significant bleeding, heparin can be resumed 4 to 6 hours after delivery and warfarin begun orally.	IIa

Low-molecular-weight heparins offer several potential advantages over unfractionated heparin, including greater bioavailability, ease of administration, lack of need for labora-

tory monitoring, and a lower incidence of thrombocytopenia and osteoporosis. Low-molecular-weight heparins do not cross the placenta. Although they have been used to treat deep venous thrombosis in pregnant patients, there are no data to guide their use in the management of patients with mechanical heart valves. Dipyridamole is not an acceptable alternative to aspirin because of its harmful effects on the fetus. Neither warfarin nor heparin is contraindicated in postpartum mothers who breast-feed.

## VI. Management of Valvular Heart Disease in Adolescents and Young Adults

Many patients with congenital heart disease have some valvular involvement. Frequently, it is part of a more complex congenital cardiac anomaly. The management of these complex diseases with multiple valve involvement is beyond the scope of these guidelines. Rather, this section concerns isolated valve involvement in which it is the primary anatomic abnormality in adolescents and young adults.

### A. Aortic Stenosis

Adolescents and young adults with isolated aortic valve stenosis almost always have congenital fusion of one or more commissures, resulting in a bicuspid or unicuspid valve. Although the prevalence of bicuspid and unicuspid valves may be as high as 2%, only 1 of 50 children born with these abnormalities will actually have significant obstruction or regurgitation by adolescence.

The rate of progression of AS during childhood and adolescence differs from that in the adult with acquired AS. One third of children manifest an increase in the transaortic gradient over a 4- to 8-year period. However, patients >12 years of age show very small increases. Those with higher initial gradients have a greater likelihood of progression.

Over the course of 20 years, only 20% of those with initial peak LV to peak aortic pressure gradients <25 mm Hg require any intervention. However, in those with an initial peak gradient >50 mm Hg, arrhythmias, sudden death, and other morbid events (including endocarditis, congestive heart failure, syncope, angina, myocardial infarction, stroke, and pacemaker insertion) occur at a rate of  $\approx$ 1.2% per year. Based on the experience of 370 patients followed up for  $\approx$ 8000 patient-years, the incidence of sudden death is  $\approx$ 0.3% per year. The severity of obstruction in those who died cannot be determined, and a higher-risk subgroup cannot be excluded.

#### Recommendations for Diagnostic Evaluation of the Adolescent or Young Adult With Aortic Stenosis\*

Indication	Class
1. ECG.*	I
2. Echo-Doppler study.*	I
3. Graded exercise test.†	Ila
4. Cardiac catheterization† for evaluation of gradient.	Ila
5. Chest x-ray.*	Ilb

Indication	Class
6. Coronary arteriography in the absence of history suggestive of concomitant CAD.	III

\*Yearly if echo-Doppler gradient >36 mm Hg (velocity  $\geq$ 3 m/s). Every 2 years if echo-Doppler gradient <36 mm Hg (peak velocity <3 m/s).

†If echo-Doppler gradient >36 mm Hg (velocity >3 m/s) and patient interested in athletic participation or if clinical findings and echo-Doppler are disparate.

Balloon valvotomy is an efficacious treatment option for children and adolescents with AS caused by fusion of commissures. Although balloon dilation has become standard in children and adolescents with AS, it is rarely recommended in older adults because even short-term palliation is uncommon. There are insufficient published data to establish an age cutoff. Until more information becomes available, recommendations for balloon valvotomy should be limited to adolescents and young adults in their early 20s, although some older young adults without heavily calcified valves may also benefit.

Because balloon valvotomy has resulted in good long-term palliation with little morbidity and little or no short- or intermediate-term mortality in children, adolescents, and young adults in their early 20s, the indications for intervention are considerably more liberal than those in older adults, for whom intervention usually involves valve replacement.

Children and young adults with Doppler gradients  $\geq$ 70 to 80 mm Hg (peak velocity >4.2 m/s), those who develop LV repolarization or ischemic changes on the ECG (T-wave inversion or ST depression) at rest or with exercise, and those with symptoms may be considered for cardiac catheterization and possible balloon dilation. The gradient should be confirmed hemodynamically before proceeding with dilation, and it is reasonable to perform valvotomy in patients with catheterization gradients >60 mm Hg. Patients with less severe gradients (50 to 70 mm Hg by Doppler echocardiography) who are interested in participating in vigorous athletics or those contemplating pregnancy are also commonly referred for balloon dilation. In most centers, balloon valvotomy has replaced surgical valvotomy, but the latter remains a reasonable alternative if skilled interventional cardiologists are not available.

#### Recommendations for Aortic Balloon Valvotomy in the Adolescent or Young Adult ( $\leq$ 21) With Normal Cardiac Output\*

Indication	Class
1. Symptoms of angina, syncope and dyspnea on exertion, with catheterization peak gradient $\geq$ 50 mm Hg.†	I
2. Catheterization peak gradient >60 mm Hg.	I
3. New-onset ischemic or repolarization changes on ECG at rest or with exercise (ST depression, T-wave inversion over left precordium) with a gradient >50 mm Hg.†	I
4. Catheterization peak gradient >50 mm Hg if patient wants to play competitive sports or desires to become pregnant.	Ila
5. Catheterization gradient <50 mm Hg without symptoms or ECG changes.	III

\*Adolescents and young adults almost invariably have normal or increased cardiac output. If cardiac index <2 L/min per m<sup>2</sup>, lower gradients should be used.

†If gradient <50 mm Hg, other causes of symptoms should be explored.

When balloon aortic valvotomy is ineffective or significant AR is present, valve replacement may be necessary. Replacement of the aortic valve with a pulmonary autograft, in which a pulmonary or aortic homograft replaces the native pulmonary valve, as first performed by Ross, has recently gained acceptance at some centers. Preliminary results indicate low surgical risk, with the majority of autograft valves performing well for  $\geq 1$  decade. This approach has the advantage of not requiring anticoagulation, an important issue for active adolescents and younger adults, including women contemplating pregnancy.

**B. Aortic Regurgitation**

The indications for surgery in adolescents and young adults with a bicuspid aortic valve with isolated AR or mixed aortic valve disease are at present similar to adults; ie, symptoms, LV dysfunction (ejection fraction  $< 0.50$ ), or greatly increased LV end-diastolic or end-systolic diameter, taking into account variations in body size. If the durability of pulmonary autograft and homograft valves in the right ventricular outflow tract is substantiated in long-term studies, the indications for autograft valve replacement are likely to become more liberal.

**Recommendations for Aortic Valve Surgery (Replacement With Mechanical Valve, Homograft, or Pulmonary Autograft) in the Adolescent or Young Adult With Chronic Aortic Regurgitation**

Indication	Class
1. Onset of symptoms.	I
2. Asymptomatic patients with LV systolic dysfunction (ejection fraction $< 0.50$ ) on serial studies 1 to 3 months apart.	I
3. Asymptomatic patients with progressive LV enlargement (end-diastolic dimension $> 4$ SD above normal).	I
4. Moderate AS (gradient $> 40$ mm Hg) (peak-to-peak gradient at cardiac catheterization).	IIb
5. Onset of ischemic or repolarization abnormalities (ST depression, T-wave inversion) over left precordium at rest.	IIb

**C. Mitral Regurgitation**

Isolated congenital MR is an extremely uncommon cardiac condition. The most common cause of MR in children is atrioventricular septal defects. MR can be associated with MVP in adolescents or young adults. The pathophysiology, diagnosis, and medical therapy of MR in adolescents is similar to that discussed for the adult (see section III.E.). When symptoms or deteriorating LV systolic function develop, surgery should be performed. Under most circumstances, it is possible to decrease regurgitation with a mitral annuloplasty. Occasionally, MVR with a mechanical or biological valve is necessary. When valve repair rather than MVR is likely, surgery for severe MR may be contemplated in the absence of heart failure or LV dysfunction.

**Recommendations for Mitral Valve Surgery in the Adolescent or Young Adult With Congenital Mitral Regurgitation With Severe MR**

Indication	Class
1. NYHA functional Class III or IV symptoms.	I
2. Asymptomatic patients with LV systolic dysfunction (ejection fraction $\leq 0.60$ ).	I
3. NYHA functional Class II symptoms with preserved LV systolic function if valve repair rather than replacement is likely.	IIa
4. Asymptomatic patients with preserved LV systolic function in whom valve replacement is highly likely.	IIb

**D. Mitral Stenosis**

In developed countries, virtually all MS in adolescents and young adults is congenital in origin. In the developing areas of the world, MS is more likely to result from rheumatic fever. Congenital MS may be associated with a wide variety of other congenital cardiac malformations of the left side of the heart, including coarctation of the aorta.

The clinical, ECG, and radiological features of congenital MS are similar to those of acquired MS in adults. The echocardiogram is beneficial for evaluating the mitral valve apparatus and papillary muscles and may provide considerable insight into the feasibility of successful valve repair. The information obtained from transthoracic imaging is usually sufficient, but in older children, adolescents, and young adults, a transesophageal echocardiogram is sometimes necessary.

**Recommendations for Mitral Valve Surgery in the Adolescent or Young Adult With Congenital Mitral Stenosis**

Indication	Class
1. Symptomatic patients (NYHA functional Class III or IV) and mean mitral valve gradient $> 10$ mm Hg on Doppler echocardiography.	I
2. Mildly symptomatic patients (NYHA functional Class II) and mean mitral valve gradient $> 10$ mm Hg on Doppler echocardiographic study.	IIa
3. Systolic pulmonary artery pressure 50 to 60 mm Hg with a mean mitral valve gradient $\geq 10$ mm Hg.	IIa
4. New-onset atrial fibrillation or multiple systemic emboli while receiving adequate anticoagulation.	IIb

The surgical management of congenital MS has improved considerably with the improved appreciation of the mechanism of mitral valve function and ability to visualize the valve afforded by transesophageal echocardiography. In those with a parachute mitral valve, creation of fenestrations among the fused chordae may increase effective orifice area and improve symptoms dramatically. MVR may occasionally be necessary but is especially problematic in those with a hypoplastic mitral annulus, who may require an annulus-enlarging operation. Balloon dilation of congenital MS was recently attempted, but its usefulness is unproved. This is one of the most difficult and dangerous therapeutic catheterization procedures and should be undertaken only in centers with operators who have established experience and skill in this interventional technique.

### E. Tricuspid Valve Disease

Acquired disease of the tricuspid valve is very uncommon in adolescents and young adults and is usually the result of trauma, bacterial endocarditis in intravenous drug abusers, and small ventricular septal defects. Most cases of tricuspid valve disease are congenital, with Ebstein's anomaly of the tricuspid valve being the most common.

There is variation in the severity of the valve leaflet abnormalities and TR. An interatrial communication, usually in the form of a patent foramen ovale, is present in most patients. If TR elevates right atrial pressure above left atrial pressure, right-to-left shunting can occur with resulting hypoxemia. One or more accessory conduction pathways are quite common, with a risk of paroxysmal atrial tachycardia of  $\approx 25\%$ .

Patients with Ebstein's anomaly may be asymptomatic with no cyanosis and no atrial arrhythmias. More commonly, they are cyanotic because of right-to-left shunting, which is associated with exercise intolerance. Right ventricular dysfunction may eventually lead to right-sided congestive heart failure frequently exacerbated by an atrial arrhythmia such as atrial tachycardia, atrial flutter, or atrial fibrillation.

#### Recommendations for Diagnostic Evaluation\* of Ebstein's Anomaly of the Tricuspid Valve in the Adolescent or Young Adult

Indication	Class
1. ECG.	I
2. Chest x-ray.	I
3. Echo-Doppler study.	I
4. Pulse oximetry at rest and/or during exercise.	Ila
5. Electrophysiological study if documented or suspected atrial arrhythmia.	Ila

\*Initial evaluation and every 1 to 3 years, depending upon severity.

The natural history of Ebstein's anomaly varies. In patients who present in the perinatal period, the 10-year actuarial survival is 61%. In a study that included more children who presented after the perinatal period, the probability of survival was 50% at 47 years of age. Predictors of poor outcome were NYHA functional Class III or IV symptoms, a cardiothoracic ratio  $>65\%$ , or atrial fibrillation. However, patients with Ebstein's anomaly who reach late adolescence and adulthood often have an excellent outcome.

The surgical management of Ebstein's anomaly remains challenging. For older children, adolescents, and young adults, tricuspid valve repair may be performed. Reconstruction of the valve is possible occasionally, especially when there is a mobile anterior leaflet not tethered to the ventricular septum.

Occasionally, the tricuspid valve is not reparable, and replacement with a bioprosthesis or a mechanical valve may be necessary. When present, atrial communications should be closed. If an accessory pathway is present, it should be mapped and obliterated either preoperatively in the electrophysiology laboratory or at the time of surgery.

#### Recommendations for Surgery in the Adolescent or Young Adult With Ebstein's Anomaly With Severe Tricuspid Regurgitation

Indication	Class
1. Congestive heart failure.	I
2. Deteriorating exercise capacity (NYHA functional Class III or IV).	I
3. Progressive cyanosis with arterial saturation $<80\%$ at rest or with exercise.	I
4. Progressive cardiac enlargement with cardiothoracic ratio $>60\%$ .	Ila
5. Systemic emboli despite adequate anticoagulation.	Ila
6. NYHA functional Class II symptoms with valve probably reparable.	Ila
7. Atrial fibrillation.	Ila
8. Deteriorating exercise tolerance (NYHA functional Class II).	Ila
9. Asymptomatic patients with increasing heart size.	Ilb
10. Asymptomatic patients with stable heart size.	III

### F. Pulmonic Stenosis

Because the pulmonary valve is the least likely valve to be affected by acquired heart disease, virtually all cases of pulmonary valve stenosis or regurgitation are congenital in origin. Most patients with stenosis have a conical or dome-shaped pulmonary valve formed by fusion of the valve leaflets, which project superiorly into the main pulmonary artery. Occasionally, the valve may be thickened and dysplastic, with stenosis caused by the inability of the valve leaflets to move sufficiently during ventricular systole.

Symptoms are unusual in children or adolescents with pulmonary valve stenosis, even when severe. Adults with long-standing severe obstruction may have dyspnea and fatigue secondary to an inability to increase cardiac output adequately with exercise. Exertional syncope or lightheadedness may occur, but sudden death is very unusual. Eventually, TR and right ventricular failure may occur.

At any age, if the foramen ovale is patent, right ventricular compliance may be reduced sufficiently to elevate right atrial pressure, allowing right-to-left shunting and cyanosis. This increases the risk of paradoxical emboli.

#### Recommendations for Initial Diagnostic Workup of Pulmonic Stenosis

Indication	Severity of Pulmonic Stenosis	
	Mild* Class	Moderate-Severe† Class
1. ECG.	I	I
2. Echo-Doppler study (transthoracic).	I	I
3. Chest x-ray.	Ila	Ila
4. Diagnostic cardiac catheterization.	III	Ilb‡

\*Right ventricular to pulmonary artery maximum instantaneous gradient  $<30$  mm Hg by Doppler echocardiography.

†Right ventricular to pulmonary artery gradient  $\geq 30$  mm Hg by Doppler echocardiography.

‡If catheterization gradient  $\geq 50$  mm Hg, balloon valvuloplasty should be performed (see recommendations for intervention).

### Clinical Course

The clinical course of children and young adults with pulmonary valve stenosis has been well described. The second Natural History Study of Congenital Heart Defects, reported in 1993, found that the probability of 25-year survival was 96%. Less than 20% of patients initially managed medically subsequently required a valvotomy, and only 4% of operated patients required a second operation. For patients with an initial transpulmonary gradient <25 mm Hg, 96% did not require surgery over a 25-year period.

Infective endocarditis is very uncommon, occurring with an incidence of 0.94 per 10 000 patient years.

Surgical relief of severe obstruction by valvotomy with a transventricular or transpulmonary artery approach predates the introduction of cardiopulmonary bypass. Balloon valvotomy has now become the procedure of choice for the typically domed, thickened valve in both children and adults virtually everywhere in the United States. Surgery is still required for the dysplastic valve often seen in Noonan syndrome. Although long-term follow-up of pulmonary balloon valvotomy is not yet available, early and midterm results (up to 10 years) suggest that the results will be similar to surgical valvotomy, ie, little or no recurrence over a 22- to 30-year period.

### Recommendations for Intervention in the Adolescent or Young Adult With Pulmonic Stenosis (Balloon Valvotomy or Surgery)

Indication	Class
1. Patients with exertional dyspnea, angina, syncope, or presyncope.	I
2. Asymptomatic patients with normal cardiac output (estimated clinically or determined by catheterization).	
a. Right ventricular to pulmonary artery peak gradient >50 mm Hg	I
b. Right ventricular to pulmonary artery peak gradient 40 to 49 mm Hg	IIa
c. Right ventricular to pulmonary artery peak gradient 30 to 39 mm Hg	IIb
d. Right ventricular to pulmonary artery peak gradient <30 mm Hg	III

In those with severe or long-standing valvular obstruction, infundibular hypertrophy may cause secondary obstruction when the pulmonary valve is successfully dilated. This frequently regresses over time without treatment. Some have advocated transient pharmacological  $\beta$ -blockade, but there is insufficient information to determine whether this is effective or necessary.

### Recommendations for Follow-up Exams in Pulmonic Stenosis

Indication	Severity of Pulmonic Stenosis	
	Mild* Class	Moderate-Severe† Class
1. ECG.	I	I
2. Echo Doppler.	I	I
3. Chest x-ray.	IIb	IIa
4. Catheterization (for evaluation of gradient).	III	III

\*<29 mm Hg gradient; testing every 5 to 10 years.

†>30 mm Hg gradient; testing every 3 years (consideration should be given to balloon or surgical valvuloplasty).

### G. Pulmonary Regurgitation

Pulmonary valve regurgitation is an uncommon congenital lesion occasionally seen with what has been described as idiopathic dilation of the pulmonary artery. Mild pulmonary regurgitation may be a normal finding on Doppler echocardiography.

Pulmonary regurgitation is an almost unavoidable result of either surgical or balloon valvuloplasty of valvular pulmonic stenosis or surgical repair of tetralogy of Fallot. Among patients who undergo surgical valvotomy, 87% have pulmonary regurgitation by Doppler echocardiography, although it is audible in only 58%. Pulmonary regurgitation after successful repair of tetralogy of Fallot usually has no long-term clinical consequence. However, a small group with long-standing pulmonary regurgitation has developed right ventricular dilatation and systolic dysfunction, which can lead to inability to augment cardiac output with exercise and in some cases congestive heart failure. This group has also had a significant incidence of ventricular arrhythmias associated with late sudden death. Pulmonary valve replacement, usually with a homograft, has been performed, but follow-up data are too preliminary to develop recommendations at this time.

## VII. Management of Patients With Prosthetic Heart Valves

### A. Antibiotic Prophylaxis

#### 1. Infective Endocarditis

All patients with prosthetic valves need appropriate antibiotics for prophylaxis against infective endocarditis (section II.B.).

#### 2. Recurrence of Rheumatic Carditis

Patients with rheumatic heart disease continue to need antibiotics for prophylaxis against recurrence of rheumatic carditis (section II.B.).

### B. Antithrombotic Therapy

All patients with mechanical valves require warfarin therapy. The risk of embolism is greater with a valve in the mitral position (mechanical or biological) compared with a valve in the aortic position. With either type of prosthesis or valve location, the risk of emboli is probably higher in the first few days and months after valve insertion, before the valve is fully endothelialized.

#### 1. Mechanical Valves

For mechanical prostheses in the aortic position, INR should be maintained between 2.0 and 3.0 for bileaflet valves and Medtronic Hall valves and between 2.5 and 3.5 for other disk valves and Starr-Edwards valves; for prostheses in the mitral position, INR should be maintained between 2.5 and 3.5 for

all mechanical valves. There was a difference of opinion regarding the Starr-Edwards valve in the aortic position, with a minority opinion recommending maintaining INR between 2.0 and 3.0. The recommendation for higher INR values in the mitral position is based on the greater risk of thromboembolic complications with mechanical valves in the mitral position and the greater risk of bleeding at higher INRs. In patients with aortic mechanical prostheses who are at higher risk of thromboembolic complications (see below), INR should be maintained at 2.5 to 3.5 and the addition of aspirin considered. Some valves are thought to be more thrombogenic than others (particularly the tilting disk valves), and a case could be made for increasing INR to between 3 and 4.5; however, this is associated with a considerably increased risk of bleeding.

The addition of low-dose aspirin (80 to 100 mg/d) to warfarin therapy (INR 2.0 to 3.5) further decreases the risk of thromboembolism and decreases mortality due to other cardiovascular diseases. A slight increase in risk of bleeding with this combination should be kept in mind. The risk of gastrointestinal irritation and hemorrhage with aspirin is dose dependent over the range of 100 to 1000 mg/d, and the antiplatelet effects are independent of dose over this range. There are no data in patients with prosthetic heart valves who are taking warfarin and aspirin in doses of 100 to 325 mg/d. Doses of 500 to 1000 mg/d clearly increase risk of bleeding. The addition of aspirin (80 to 100 mg/d) to warfarin should be strongly considered unless there is a contraindication to the use of aspirin (ie, bleeding or aspirin intolerance). This combination is particularly appropriate for patients who have had an embolus while on warfarin therapy, those with known vascular disease, and/or those known to be particularly susceptible to hypercoagulability.

It is important to note that thromboembolic risk is increased early after insertion of the prosthetic valve. The use of heparin early after prosthetic valve replacement and before warfarin achieves therapeutic levels is controversial. In some patients, achievement of therapeutic INR can be delayed several days postoperatively because of mitigating complications.

## 2. Biological Valves

Because of an increased risk of thromboemboli in the first 3 months after implantation of a biological prosthetic valve, anticoagulation with warfarin is usually recommended, although in several centers, only aspirin is used for biological valves in the aortic position. Risk is particularly high in the first few days after surgery, and heparin should be started as soon as the risk of increased surgical bleeding is reduced. After 3 months, the biological valve can be treated like native valve disease, and warfarin can be discontinued in over two thirds of patients with biological valves. In the remaining patients with associated risk factors for thromboembolism, such as atrial fibrillation, previous thromboembolism, or a hypercoagulable condition, lifelong warfarin therapy is indicated to achieve an INR of 2.0 to 3.0. Many would also recommend continuing anticoagulation in patients with severe LV dysfunction (ejection fraction <0.30).

## Recommendations for Antithrombotic Therapy in Patients With Prosthetic Heart Valves

Indication		Class
1. First 3 months after valve replacement:	Warfarin, INR 2.5 to 3.5	I
2. $\geq 3$ months after valve replacement:		
A. Mechanical valve		
AVR and no risk factor*		
Bileaflet valve or Medtronic Hall valve	Warfarin, INR 2 to 3	I
Other disk valves or Starr-Edwards valve	Warfarin, INR 2.5 to 3.5	I
AVR plus risk factor*	Warfarin, INR 2.5 to 3.5	I
MVR	Warfarin, INR 2.5 to 3.5	I
B. Bioprosthesis		
AVR plus no risk factor*	Aspirin, 80–100 mg/d	I
AVR plus risk factor*	Warfarin, INR 2 to 3	I
MVR plus no risk factor*	Aspirin, 80–100 mg/d	I
MVR plus risk factor*	Warfarin, INR 2.5 to 3.5	I
3. Addition of aspirin, 80 to 100 mg once daily if not on aspirin.		IIa
4. Warfarin, INR 3.5 to 4.5 in high-risk patients when aspirin cannot be used.		IIa
5. Warfarin, INR 2.0 to 3.0 in patients with Starr-Edwards AVR and no risk factor.		IIb
6. Mechanical valve, no warfarin therapy.		III
7. Mechanical valve, aspirin therapy only.		III
8. Bioprosthesis, no warfarin and no aspirin therapy.		III

\*Risk factors: Atrial fibrillation, LV dysfunction, previous thromboembolism, and hypercoagulable condition.

## 3. Embolic Events During Adequate Antithrombotic Therapy

In the patient who has a definite embolic episode(s) while receiving adequate antithrombotic therapy, antithrombotic therapy should be increased as follows:

- Warfarin, INR 2 to 3: warfarin dose increased to achieve INR of 2.5 to 3.5
- Warfarin, INR 2.5 to 3.5: warfarin dose may need to be increased to achieve INR of 3.5 to 4.5
- Not on aspirin: aspirin 80 to 100 mg/d should be initiated
- Warfarin plus aspirin 80 to 100 mg/d dose may also need to be increased to 325 mg/d if the higher dose of warfarin is not achieving the desired clinical result
- Aspirin alone: aspirin dose may need to be increased to 325 mg/d and/or warfarin added to achieve an INR of 2 to 3

## 4. Excessive Anticoagulation

In most patients with INR above the therapeutic range, excessive anticoagulation can be managed by withholding warfarin and following the level of anticoagulation with serial INR determinations. Excessive anticoagulation (INR >5) greatly increases the risk of hemorrhage. However, rapid decreases in INR that lead to INR falling below the therapeutic level increase the risk of thromboembolism. Patients with prosthetic heart valves with INR in the range of 5 to 10 who are not bleeding can be managed by withholding warfarin and administering 2.5 mg of vitamin K<sub>1</sub> orally. INR should be determined after 24 hours and subsequently as



needed. Warfarin therapy is restarted and dose appropriately adjusted to ensure that INR is in the therapeutic range. In emergency situations, the use of fresh frozen plasma is preferable to high-dose vitamin K<sub>1</sub>, especially if given parenterally.

### **5. Antithrombotic Therapy in Patients Requiring Noncardiac Surgery/Dental Care**

The risk of increased bleeding during a procedure performed on a patient receiving antithrombotic therapy has to be weighed against the increased risk of thromboembolism caused by stopping the therapy. The risk of stopping warfarin can be estimated and is relatively slight if the drug is withheld for only a few days. When warfarin therapy is reinstated, there are theoretic concerns about a hypercoagulable state caused by suppression of protein C and protein S before the drug affects the thrombotic factors. Although these risks are only hypothetical, individuals at very high risk should be treated with heparin therapy until INR returns to the desired range.

Admission to the hospital or a delay in discharge to give heparin is usually unnecessary. Determining which patients are at very high risk of thrombosis and require heparin until warfarin can be reinstated may be difficult, and clinical judgment is required. Heparin can usually be reserved for those who have had a recent thrombosis or embolus (arbitrarily within 1 year), those with demonstrated thrombotic problems when previously off therapy, those with the Björk-Shiley valve, and those with  $\geq 3$  "risk factors." Risk factors are atrial fibrillation, previous thromboembolism, a hypercoagulable condition, and mechanical prosthesis; many would also include LV dysfunction (ejection fraction  $< 0.30$ ) as a risk factor. A lower threshold for recommending heparin should be considered in patients with mechanical valves in the mitral position, in whom a single risk factor would be sufficient evidence of high risk. Low-molecular-weight heparin is attractive as it is even more easily used outside the hospital; however, there are no data on patients with prosthetic heart valves, and low-molecular-weight heparins cannot be recommended at this time.

### **6. Antithrombotic Therapy in Patients Needing Cardiac Catheterization/Angiography**

In an emergent or semiemergent situation, cardiac catheterization can be performed with a patient taking warfarin but preferably the drug should be stopped  $\approx 72$  hours before the procedure so that INR is  $\leq 1.5$  (see above). The drug should be restarted as soon as the procedure is completed. If a patient has 1 or more risk factors that predispose to thromboembolism, heparin should be started when INR falls below 2.0 and continued when warfarin is restarted. After an overlap of 3 to 5 days, heparin may be discontinued when the desired INR is achieved.

### **7. Thrombosis of Prosthetic Heart Valves**

Prosthetic valve obstruction may be caused by thrombus formation, pannus ingrowth, or a combination of these. If the prosthesis is obstructed by pannus, thrombolytic therapy will be ineffective, and the valve needs to be replaced. Thrombolytic therapy for a prosthetic valve obstructed by thrombus is

associated with significant risks and is often ineffective. Thrombolytic therapy is ineffective in 16% to 18% of patients, and the rate of acute mortality is 6%. Risk of thromboembolism is 12%; stroke, 3% to 10%; major bleeding episodes, 5%; nondisabling bleeding, 14%; and recurrent thrombosis, 11%. Patients who have a large clot or evidence of valve obstruction and who are in NYHA functional Classes III or IV because of prosthetic thrombosis should undergo early/immediate reoperation. Thrombolytic therapy in such patients is reserved for those for whom surgical intervention carries high risk and those with contraindications to surgery. Streptokinase and urokinase are the most frequently used thrombolytic agents. The duration of thrombolytic therapy depends on resolution of pressure gradients and valve areas to near normal by Doppler echocardiography. Thrombolytic therapy should be stopped at 24 hours if there is no hemodynamic improvement or after 72 hours, even if hemodynamic recovery is incomplete. If thrombolytic therapy is successful, it should be followed with intravenous heparin until warfarin achieves an INR of 3 to 4 for aortic prosthetic valves and 3.5 to 4.5 for mitral prosthetic valves. If partially successful, thrombolytic therapy may be followed by a combination of subcutaneous heparin twice daily (to achieve aPTT of 55 to 80 seconds) plus warfarin (INR 2.5 to 3.5) for a 3-month period.

Patients with a "small clot" who are in NYHA functional Class I or II and those with LV dysfunction should have in-hospital, short-term intravenous heparin therapy. If this is unsuccessful, they may receive a trial of continuous infusion thrombolytic therapy over several days. If this is unsuccessful or there is an increased risk associated with thrombolytic therapy, they may need reoperation. An alternative to thrombolytic therapy in patients who remain hemodynamically stable is to convert intravenous heparin to combined therapy with subcutaneous heparin (twice daily to an aPTT of 55 to 80 seconds) and warfarin (INR 2.5 to 3.5) for 1 to 3 months on an outpatient basis to allow endogenous thrombolysis. If intravenous heparin, heparin/thrombolytic therapy, or heparin/warfarin is successful, warfarin doses should be increased so that INR is between 3.0 and 4.0 (around 3.5) for prosthetic aortic valves and 3.5 and 4.5 (around 4.0) for prosthetic mitral valves. These patients should also receive low-dose aspirin.

## **C. Follow-up Visits**

### **1. First Outpatient Postoperative Visit**

The workup on this visit should include an interval or complete history and physical examination, ECG, chest x-ray, 2-D and Doppler echocardiography, complete blood count, BUN/creatinine, electrolytes, lactate dehydroxygenase (LDH), and INR, if indicated. Echocardiography is the most useful noninvasive test. It provides information about prosthesis stenosis/regurgitation, valve area, assessment of other valve disease(s), pulmonary hypertension, atrial size, left and right ventricular hypertrophy, left and right ventricular size and function, and pericardial effusion/thickening. Echocardiography is an essential component of the first postoperative visit because it assesses the effects and results of surgery and

serves as a baseline for comparison should complications and/or deterioration occur later.

## 2. Follow-up Visits in Patients Without Complications

Patients who have undergone valve replacement are not cured but still have serious heart disease. They have exchanged native valve disease for prosthetic valve disease and must be followed with the same care as patients with native valvular disease.

The asymptomatic patient without complications needs to be seen only at 1-year intervals. The frequency with which 2-D and Doppler echocardiography should be performed routinely in patients without complications is uncertain, and there are no data on which to base this decision. The committee did not reach consensus on this issue. The majority recommended no further echocardiographic testing after the initial postoperative evaluation in patients with mechanical valves whose condition is stable and who have no symptoms or clinical evidence of LV dysfunction, prosthetic valve dysfunction, or dysfunction of other heart valves in keeping with the ACC/AHA Guidelines for the Clinical Application of Echocardiography.<sup>2</sup> The committee also failed to reach consensus about serial echocardiography in patients with bioprosthetic valves, who have an increasing risk of structural deterioration of the valve after 5 years in the mitral position and 8 years in the aortic position. A minority opinion recommended annual echocardiography, whereas the majority recommended detailed histories and cardiac physical examinations with echocardiography when dictated by clinical circumstances, such as a regurgitant murmur or a change in symptoms. Once regurgitation is detected, close follow-up with 2-D and Doppler echocardiography every 3 to 6 months is indicated. The committee agreed that echocardiography is indicated for any patient with a prosthetic heart valve whenever there is evidence of a new murmur, there are questions of prosthetic valve integrity and function, or there are concerns about ventricular function.

### Recommendations for Follow-up Strategy of Patients With Prosthetic Heart Valves

Indication	Class
1. History, physical exam, ECG, chest x-ray, echocardiogram, complete blood count, serum chemistries, and INR (if indicated) at first postoperative outpatient evaluation.*	I
2. Radionuclide angiography or MRI to assess LV function if result of echocardiography is unsatisfactory.	I
3. Routine follow-up visits at yearly intervals with earlier reevaluations for change in clinical status.	I
4. Routine serial echocardiograms at time of annual follow-up visit in absence of change in clinical status.	IIb
5. Routine serial fluoroscopy.	III

\*This evaluation should be performed 3 to 4 weeks after hospital discharge. In some settings, the outpatient echocardiogram may be difficult to obtain; if so, an inpatient echocardiogram may be obtained before hospital discharge.

## 3. Follow-up Visits in Patients With Complications

LV dysfunction and clinical heart failure after valve replacement may be the result of (1) preoperative LV dysfunction

that persists or improves only partially; (2) perioperative myocardial damage; (3) other valve disease that has progressed; (4) complications of prosthetic heart valves; and (5) associated heart disease, such as CAD and systemic hypertension.

Any patient with a prosthetic heart valve who does not improve after surgery or who later shows deterioration of functional capacity should undergo appropriate testing, including 2-D and Doppler echocardiography and, if necessary, transesophageal echocardiography and cardiac catheterization with angiography to determine the cause.

## D. Major Criteria for Valve Selection

In general, mitral valve repair is preferable to replacement, provided that it is feasible and the appropriate skill and experience are available to perform the procedure successfully.

The major advantages of a mechanical valve are an extremely low rate of structural deterioration and a better survival rate in patients <65 years old after AVR and for MVR in patients ≤50 years old after MVR. The major disadvantages are increased incidence of bleeding due to the need for antithrombotic therapy and cost and disadvantages of antithrombotic therapy.

The major advantage of a bioprosthesis (whether porcine or pericardial) is lack of need for antithrombotic therapy. In addition, the rate of structural valve deterioration in the aortic position in patients ≥65 years is lower than in patients <65, especially in the aortic position. In patients ≥65 years undergoing AVR with a porcine bioprosthesis, the rate of structural deterioration is <10% at 10 years. The major disadvantage is the increased rate of structural valve deterioration and hence the need for reoperation in patients <65 years, particularly in those ≤50 years. Pericardial bioprostheses may have a lower rate of structural valve deterioration than porcine bioprostheses in patients ≥65 years.

Pregnancy after valve replacement poses a difficult problem. The disadvantages of a mechanical valve are that the patient is at risk for complications of warfarin therapy that may affect the patient and/or fetus and complications of heparin therapy (see section V.G.). The disadvantage of a bioprosthesis is the relatively higher rate of early structural valve deterioration. The Ross procedure (pulmonary autograft) or an aortic valve homograft is associated with a lower rate of such complications in young women and does not require anticoagulation. These procedures are strongly recommended for women who wish to become pregnant, provided that the necessary surgical skill and experience in performing these procedures are available.

If the patient needs antithrombotic therapy for any reason, for example, atrial fibrillation or presence of a mechanical valve in another position, the major advantage of a biological valve is reduced substantially.

Biological valves have a much higher rate of structural deterioration when implanted in patients with renal failure, those on hemodialysis, and those with hypercalcemia. Adolescent patients who are still growing have a high risk for accelerated biological valve calcification.

### Recommendations for Valve Replacement With a Mechanical Prosthesis

Indication	Class
1. Patients with expected long life spans.	I
2. Patients with a mechanical prosthetic valve already in place in a different position than the valve to be replaced.	I
3. Patients in renal failure, on hemodialysis, or with hypercalcemia.	II
4. Patients requiring warfarin therapy because of risk factors* for thromboembolism.	IIa
5. Patients $\leq 65$ years for AVR and $\leq 70$ years for MVR.†	IIa
6. Valve rereplacement for thrombosed biological valve.	IIb
7. Patients who cannot or will not take warfarin therapy.	III

\*Risk factors: atrial fibrillation, severe LV dysfunction, previous thromboembolism, and hypercoagulable condition.

†The age at which patients may be considered for bioprosthetic valves is based on the major reduction in rate of structural valve deterioration after age 65 and the increased risk of bleeding in this age group.

### Recommendations for Valve Replacement With a Bioprosthesis

Indication	Class
1. Patients who cannot or will not take warfarin therapy.	I
2. Patients $\geq 65$ years* needing AVR who do not have risk factors for thromboembolism.†	I
3. Patients considered to have possible compliance problems with warfarin therapy.	IIa
4. Patients $> 70$ years* needing MVR who do not have risk factors for thromboembolism.†	IIa
5. Valve rereplacement for thrombosed mechanical valve.	IIb
6. Patients $< 65$ years.*	IIb
7. Patients in renal failure, on hemodialysis, or with hypercalcemia.	III
8. Adolescent patients who are still growing.	III

\*The age at which patients should be considered for bioprosthetic valves is based on the major reduction in rate of structural valve deterioration after age 65 and increased risk of bleeding in this age group.

†Risk factors: atrial fibrillation, severe LV dysfunction, previous thromboembolism, and hypercoagulable condition.

## VIII. Evaluation and Treatment of Coronary Artery Disease in Patients With Valvular Heart Disease

Many patients with valvular heart disease have concomitant CAD, but the data are limited regarding optimal strategies for diagnosis and treatment of CAD in such patients. Thus, management decisions are usually developed by blending information from the randomized studies of treatment of CAD and smaller published series of patients undergoing surgical treatment of valvular heart disease.

### A. Probability of Coronary Artery Disease in Patients With Valvular Heart Disease

Ischemic symptoms in patients with valvular heart disease may have multiple causes, such as LV chamber enlargement, increased wall stress or wall thickening with subendocardial ischemia, and right ventricular hypertrophy. In general, be-

cause angina is a poor marker of CAD in patients with AS, coronary arteriography is recommended in symptomatic patients before AVR, especially in men  $> 35$  years of age, premenopausal women  $> 35$  years of age with coronary risk factors, and postmenopausal women.

CAD is less prevalent in patients with AR and those with MS than in those with AS. Nonetheless, in symptomatic patients and/or those with LV dysfunction, preoperative coronary angiography is recommended in men  $> 35$  years old, premenopausal women  $> 35$  years old with coronary risk factors, and postmenopausal women.

The relation between MR and CAD is unique in that CAD is frequently the cause of this valve lesion. The management of these patients is discussed in section III.E.

### B. Diagnosis of Coronary Artery Disease

The resting ECG in patients with valvular heart disease frequently shows ST-segment changes due to LV hypertrophy, LV dilatation, or bundle branch block, which reduce the accuracy of the ECG at rest and during exercise for the diagnosis of concomitant CAD.

Similarly, resting or exercise-induced regional wall motion abnormalities are nonspecific markers for CAD in patients with underlying valvular heart disease who have LV hypertrophy and/or chamber dilatation, as are myocardial perfusion abnormalities induced by exercise or pharmacological stress. Thus, there are few indications for myocardial perfusion imaging with thallium 201 or technetium 99m perfusion agents in patients with severe valvular disease, and coronary arteriography remains the most appropriate method for definitive diagnosis of CAD. Noninvasive imaging is useful when CAD is suspected in patients with mild valve stenosis or regurgitation and normal LV cavity size and wall thickness.

### Recommendations for Coronary Angiography in Patients With Valvular Heart Disease

Indication	Class
1. Before valve surgery (including infective endocarditis) or mitral balloon commissurotomy in patients with: <ul style="list-style-type: none"> <li>• Chest pain</li> <li>• Other objective evidence of ischemia</li> <li>• Decreased LV systolic function</li> <li>• History of CAD</li> <li>• Coronary risk factors* (including advanced age)†</li> </ul>	I
2. Patients with apparently mild to moderate valvular heart disease but with <ul style="list-style-type: none"> <li>• Progressive (Class II or greater) angina</li> <li>• Objective evidence of ischemia</li> <li>• Decreased LV systolic function</li> <li>• Overt congestive heart failure</li> </ul>	I
3. Patients undergoing catheterization to confirm the severity of valve lesions before valve surgery without preexisting evidence of CAD, multiple coronary risk factors, or advanced age.†	IIb

Indication	Class
4. Young patients† undergoing nonemergent valve surgery when no further hemodynamic assessment by catheterization is deemed necessary and no coronary risk factors, no history of CAD, and no evidence of ischemia are present.	III
5. Asymptomatic patients with valvular heart disease when valve surgery or balloon commissurotomy is not being considered.	III
6. Patients having emergency valve surgery for acute valve regurgitation, aortic root disease, or infective endocarditis when there are no coronary risk factors, angina, objective evidence of ischemia, evidence of coronary embolization, LV systolic dysfunction, or age <35 years.	III

\*Patients undergoing mitral balloon valvotomy need not undergo coronary angiography based only on coronary risk factors.

†The age at which coronary angiography should be performed before valve surgery is difficult to define. The committee recommends coronary angiography in men  $\geq 35$  years of age, premenopausal women  $\geq 35$  years of age with coronary risk factors, and postmenopausal women.

### C. Treatment of Coronary Artery Disease at the Time of Aortic Valve Replacement

As noted previously,  $\geq 33\%$  of patients with AS undergoing AVR have concomitant CAD. More than 50% of patients >70 years old have CAD. Combined coronary artery bypass surgery has had little or no adverse effect on operative mortality. Moreover, combined coronary bypass grafting and AVR reduces the rates of perioperative myocardial infarction, operative mortality, and late mortality and morbidity, compared with patients with significant CAD who do not undergo revascularization at the time of AVR. Incomplete revascularization is associated with greater postoperative systolic dysfunction and reduced survival rates after surgery compared with patients who receive complete revascularization. For  $\geq 1$  decade, improved myocardial preservation techniques have been associated with reduced overall operative mortality, and it has become standard practice to bypass all significant coronary artery stenoses when possible in patients undergoing AVR. The committee recommends this approach.

### D. Aortic Valve Replacement in Patients Undergoing Coronary Artery Bypass Surgery

Patients undergoing coronary artery bypass surgery who have severe AS should undergo AVR at the time of revascularization. Decision making is less clear in patients with mild to moderate AS and CAD requiring coronary bypass surgery. Controversy persists regarding the indications for "prophylactic" AVR at the time of coronary bypass surgery in such patients. This decision should be made only after the severity of AS is carefully determined by Doppler echocardiography and cardiac catheterization.

It is difficult to predict whether a given patient with CAD and mild AS is likely to develop significant AS after revascularization. As noted previously (section III.A.), the natural history of mild AS is variable, with some patients manifesting a relatively rapid progression of AS, with a decrease in valve area of up to

0.3 cm<sup>2</sup> per year and an increase in pressure gradient of 15 to 19 mm Hg per year; however, the majority may show little or no change. The average rate of reduction in valve area is  $\approx 0.12$  cm<sup>2</sup> per year, but the rate of change in an individual patient is difficult to predict.

Although definitive data are not yet available, patients with intermediate aortic valve gradients (30 to 50 mm Hg mean gradient at catheterization or 3 to 4 m/s transvalvular velocity by Doppler echocardiography) who are undergoing coronary artery bypass surgery may warrant AVR at the time of revascularization, but this is controversial because there are limited data to indicate the wisdom of this general policy.

### Recommendations for Aortic Valve Replacement in Patients Undergoing Coronary Artery Bypass Surgery

Indication	Class
1. In patients undergoing CABG who have severe AS who meet the criteria for valve replacement (section III.A.).	I
2. In patients undergoing CABG who have moderate AS (mean gradient 30 to 50 mm Hg or Doppler velocity 3 to 4 m/s).	IIa
3. In patients undergoing CABG who have mild AS (mean gradient <30 mm Hg or Doppler velocity <3 m/s).	IIb

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