## ACC/AHA PRACTICE GUIDELINES—EXECUTIVE SUMMARY

# ACC/AHA 2006 Practice 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 (Writing Committee to Revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease)

*Developed in Collaboration With the Society of Cardiovascular Anesthesiologists*
*Endorsed by the Society for Cardiovascular Angiography and Interventions and*
*the Society of Thoracic Surgeons*

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## TABLE OF CONTENTS

## PREAMBLE

It is important that the medical profession play a significant role in critically evaluating the use of diagnostic procedures and therapies as they are introduced in the detection, management, or prevention of disease states. Rigorous and expert analysis of the available data documenting the absolute and relative benefits and risks of those procedures and therapies can produce helpful guidelines that improve the effectiveness of care, optimize patient outcomes, and favorably affect the overall cost of care by focusing resources on the most effective strategies.

The American College of Cardiology (ACC) and the American Heart Association (AHA) have jointly engaged in the production of such guidelines in the area of cardiovascular disease since 1980. This effort is directed by the ACC/AHA

Task Force on Practice Guidelines, whose charge is to develop, update, or revise practice guidelines for important cardiovascular diseases and procedures. Writing committees are charged with the task of performing an assessment of the evidence and acting as an independent group of authors to develop or update written recommendations for clinical practice.

Experts in the subject under consideration are selected from both organizations to examine subject-specific data and write guidelines. The process includes additional representatives from other medical practitioner and specialty groups where appropriate. Writing committees are specifically charged to perform a formal literature review, weigh the strength of evidence for or against a particular treatment or procedure, and include estimates of expected health outcomes where data exist. Patient-specific modifiers, co-morbidities, and issues of patient preference that might influence the choice of particular tests or therapies are considered, as well as frequency of follow-up. When available, information from studies on cost will be considered; however, review of data on efficacy and clinical outcomes will be the primary basis for preparing recommendation in these guidelines.

The ACC/AHA Task Force on Practice Guidelines makes every effort to avoid any actual, potential, or perceived conflicts of interest that might arise as a result of an outside relationship or personal interest of a member of the writing committee. Specifically, all members of the writing committee and peer reviewers of the document are asked to provide disclosure statements of all such relationships that might be perceived as real or potential conflicts of interest. Writing committee members are also strongly encouraged to declare a previous relationship with industry that might be perceived as relevant to guideline development. If a writing committee member develops a new relationship with industry during his or her tenure, he or she is required to notify guideline staff in writing. The continued participation of the writing committee member will be reviewed. These statements are reviewed by the parent task force, reported orally to all members of the writing panel at each meeting, and updated and reviewed by the writing committee as changes occur. Please refer to the methodology manual for ACC/AHA guideline writing committees for further description of the relationships with industry policy, available on ACC and AHA World Wide Web sites (http://www.acc.org/clinical/manual/manual_introltr.htm and http://circ.ahajournals.org/manual/). Relationships with industry pertinent to these guidelines are listed in Appendixes 1 and 2 of the full-text Guidelines for members of the writing committee and peer reviewers, respectively.

These practice guidelines are intended to assist healthcare providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, and prevention of specific diseases or conditions. These guidelines attempt to define practices that meet the needs of most patients in most circumstances. These guideline recommendations reflect a consensus of expert opinion after a thorough review of the available, current scientific evidence and are intended to improve patient care. If these guidelines are used as the basis for regulatory/payer decisions, the ultimate goal is quality of care and serving the patient's best interests. The ultimate judgment regarding care of a particular patient must be made by the healthcare provider and patient in light of all of the circumstances presented by that patient. There are circumstances in which deviations from these guidelines are appropriate.

The "ACC/AHA 2006 Practice Guidelines for the Management of Patients With Valvular Heart Disease" was approved for publication by the ACC Foundation (ACCF) board of trustees in May 2006 and the AHA Science Advisory and Coordinating Committee in May 2006. The executive summary and recommendations are published in the August 1, 2006 issue of the *Journal of the American College of Cardiology* and the August 1, 2006 issue of *Circulation*. The full-text guideline is e-published in the same issues of each journal and is posted on the World Wide Web sites of the ACC (www.acc.org) and the AHA (www.americanheart.org). The guidelines will be reviewed annually by the ACC/AHA Task Force on Practice Guidelines and will be considered current unless they are updated, revised, or sunsetted and withdrawn from distribution. Copies of the full text and the executive summary are available from both organizations.

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# I. INTRODUCTION

This guideline focuses primarily on valvular heart disease in the adult, with a separate section dealing with specific recommendations for valve disorders in adolescents and young adults. The diagnosis and management of infants and young children with congenital valvular abnormalities are significantly different from those of the adolescent or adult and are beyond the scope of these guidelines.

The committee emphasizes the fact that many factors ultimately determine the most appropriate treatment of individual patients with valvular heart disease within a given community. These 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 its recommendations are guidelines and not rigid requirements.

All of the recommendations in this guideline revision were converted from the tabular format used in the 1998 guideline to a listing of recommendations that has been written in full sentences to express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document, would still convey the full intent of the recommendation. It is hoped that this will increase the readers' comprehension of the guidelines. Also, the level of evidence, either A, B, or C, for each recommendation is now provided. See Figure 1 for further details on the classification and level of evidence schema.

## II. GENERAL PRINCIPLES

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

Cardiac auscultation remains the most widely used method of screening for valvular heart disease. The production of murmurs is due to 3 main factors: 1) high blood flow rate through normal or abnormal orifices, 2) forward flow through a narrowed or irregular orifice into a dilated vessel or chamber, and 3) backward or regurgitant flow through an incompetent valve.

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. Echocardiography is particularly useful in this regard, as discussed in the "ACC/AHA/ASE 2003 Guidelines for the Clinical Application of Echocardiography" (1). 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 souffles.

### 1. Electrocardiography and Chest Roentgenography

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 been obtained previously. The absence of ventricular hypertrophy, atrial enlargement, arrhythmias, conduction abnormalities, prior myocardial infarction, and evidence of active ischemia on the ECG provides useful negative information at a relatively low cost. Abnormal ECG findings in a patient with a heart murmur, such as ventricular hypertrophy or a prior infarction, should lead to a more extensive evaluation that includes echocardiography.

Chest roentgenograms often yield qualitative information on cardiac chamber size, pulmonary blood flow, pulmonary and systemic venous pressure, and cardiac calcification in patients with cardiac murmurs. When abnormal findings are present on chest X-ray, echocardiography should be performed.

### 2. Echocardiography

#### Class I

1. **Echocardiography is recommended for asymptomatic patients with diastolic murmurs, continuous murmurs, holosystolic murmurs, late systolic murmurs, murmurs associated with ejection clicks or murmurs that radiate to the neck or back.** *(Level of Evidence: C)*
2. **Echocardiography is recommended for patients with heart murmurs and symptoms or signs of heart failure, myocardial ischemia/infarction, syncope, thromboembolism, infective endocarditis, or other clinical evidence of structural heart disease.** *(Level of Evidence: C)*
3. **Echocardiography is recommended for asymptomatic patients who have grade 3 or louder midpeaking systolic murmurs.** *(Level of Evidence: C)*

#### Class IIa

1. **Echocardiography can be useful for the evaluation of asymptomatic patients with murmurs associated with other abnormal cardiac physical findings or murmurs associated with an abnormal ECG or chest X-ray.** *(Level of Evidence: C)*
2. **Echocardiography can be useful for patients whose symptoms and/or signs are likely noncardiac in origin but in whom a cardiac basis cannot be excluded by standard evaluation.** *(Level of Evidence: C)*

#### Class III

**Echocardiography is not recommended for patients who have a grade 2 or softer midsystolic murmur identified as innocent or functional by an experienced observer.** *(Level of Evidence: C)*

Echocardiography with color flow and spectral Doppler evaluation is an important noninvasive method for assessing the significance of cardiac murmurs. Information regarding valve morphology and function, chamber size, wall thickness, ventricular function, pulmonary and hepatic vein flow, and estimates of pulmonary artery pressures can be readily integrated.

Although echocardiography can provide important information, such testing is not necessary for all patients with cardiac murmurs and usually adds little but expense in the evaluation of asymptomatic younger patients with short

## "Size of Treatment Effect"

| | **Class I**<br><br>*Benefit >>> Risk*<br><br><br><br>Procedure/Treatment **SHOULD be** performed/administered | **Class IIa**<br><br>*Benefit >> Risk*<br>*Additional studies with focused objectives needed*<br><br>**IT IS REASONABLE to** perform procedure/administer treatment | **Class IIb**<br><br>*Benefit ≥ Risk*<br>*Additional studies with broad objectives needed; Additional registry data would be helpful*<br><br>Procedure/Treatmet **MAY BE CONSIDERED** | **Class III**<br><br>*Risk ≥ Benefit*<br>*No additional studies needed*<br><br><br>Procedure/Treatment should **NOT be** performed/administered **SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL** |
|---|---|---|---|---|
| **Level A**<br><br>*Multiple (3-5) population risk strata evaluated**<br><br>*General consistency of direction and magnitude of effect* | • Recommendation that procedure or treatment is useful/effective<br>• Sufficient evidence from multiple randomized trials or meta-analyses | • Recommendation in favor of treatment or procedure being useful/effective<br>• Some conflicting evidence from multiple randomized trials or meta-analyses | • Recommendation's usefulness/efficacy less well established<br>• Greater conflicting evidence from multiple randomized trials or meta-analyses | • Recommendation that procedure or treatment not useful/effective and may be harmful<br>• Sufficient evidence from multiple randomized trials or meta-analyses |
| **Level B**<br><br>*Limited (2-3) population risk strata evaluated** | • Recommendation that procedure or treatment is useful/effective<br>• Limited evidence from single randomized trial or non-randomized studies | • Recommendation in favor of treatment or procedure being useful/ effective<br>• Some conflicting evidence from single randomized trial or non-randomized studies | • Recommendation's usefulness/efficacy less well established<br>• Greater conflicting evidence from single randomized trial or non-randomized studies | • Recommendation that procedure or treatment not useful/effective and may be harmful<br>• Limited evidence from single randomized trial or non-randomized studies |
| **Level C**<br><br>*Very limited (1-2) population risk strata evaluated** | • Recommendation that procedure or treatment is useful/effective<br>• Only expert opinion, case studies, or standard-of-care | • Recommendation in favor of treatment or procedure being useful/ effective<br>• Only diverging expert opinion, case studies, or standard-of-care | • Recommendation's usefulness/efficacy less well established<br>• Only diverging expert opinion, case studies, or standard-of-care | • Recommendation that procedure or treatment not useful/effective and may be harmful<br>• Only expert opinion, case studies, or standard-of-care |
| **Suggested phrases for writing recommendations †** | should<br>is recommended<br>is indicated<br>is useful/effective/beneficial | is reasonable<br>can be useful/effective/ beneficial<br>is probably recommended or indicated | may/might be considered<br>may/might be reasonable<br>usefulness/effectiveness is unknown /unclear/uncertain or not well established | is not recommended<br>is not indicated<br>should not<br>is not useful/effective/beneficial<br>may be harmful |

**"Estimate of Certainty (Precision) of Treatment Effect"**

**Figure 1.** Applying classification of recommendations and level of evidence. *Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as gender, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective. †In 2003 the ACC/AHA Task Force on Practice Guidelines provided a list of suggested phrases to use when writing recommendations. All recommendations in this guideline have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines and will allow queries at the individual recommendation level.

grade 1 to 2 midsystolic murmurs and otherwise normal physical findings. At the other end of the spectrum are patients with heart murmurs for whom transthoracic echocardiography proves inadequate. Depending on the specific clinical circumstances, transesophageal echocardiography (TEE), cardiac magnetic resonance, or cardiac catheterization may be indicated for better characterization of the valvular lesion.

It is important to note that Doppler ultrasound devices are very sensitive and may detect trace or mild valvular regurgitation through structurally normal tricuspid and pulmonic valves in a large percentage of young, healthy subjects and through normal left-sided valves (particularly the mitral valve [MV]) in a variable but lower percentage of patients (2–6).

General recommendations for performing echocardiography in patients with heart murmurs are provided. Of course, individual exceptions to these indications may exist.

### 3. Cardiac Catheterization

Cardiac catheterization can provide important information about the presence and severity of valvular obstruction, valvular regurgitation, and intracardiac shunting. It is not necessary in most patients with cardiac murmurs and normal or diagnostic echocardiograms, but it provides additional information for some patients in whom there is a discrepancy between the echocardiographic and clinical findings. Indications for cardiac catheterization for hemodynamic assessment of specific valve lesions are given in Section III, "Specific Valve Lesions." Specific indications for coronary angiography to screen for the presence of coronary artery disease (CAD) are given in Section X-B.

### 4. Exercise Testing

Exercise testing can provide valuable information in patients with valvular heart disease, especially in those whose symptoms are difficult to assess. It can be combined with echocardiography, radionuclide angiography, and cardiac catheterization. It has a proven track record of safety, even among asymptomatic patients with severe aortic stenosis (AS). Exercise testing has generally been underutilized in this patient population and should constitute an important component of the evaluation process.

### 5. Approach to the Patient

The evaluation of the patient with a heart murmur may vary greatly depending on the timing of the murmur in the cardiac cycle, its location and radiation, and its response to various physiological maneuvers. Also of importance is the presence or absence of cardiac and noncardiac symptoms and other findings on physical examination that suggest the murmur is clinically significant.

Echocardiography is indicated for patients with diastolic or continuous heart murmurs not due to a cervical venous hum or a mammary souffle during pregnancy, for those with holosystolic or late systolic murmurs, for those with midsystolic murmurs of grade 3 or greater intensity, and for those with softer systolic murmurs in whom dynamic cardiac auscultation suggests a definite diagnosis (e.g., hypertrophic cardiomyopathy). Echocardiography is also indicated in certain patients with grade 1 or 2 midsystolic murmurs, including patients with symptoms or signs consistent with infective endocarditis, thromboembolism, heart failure, myocardial ischemia/infarction, or syncope.

It must be re-emphasized that trivial, minimal, or physiological valvular regurgitation, especially affecting the mitral, tricuspid, or pulmonic valves, is detected by color flow imaging techniques in many otherwise normal patients, including many patients who have no heart murmur at all (2,5,6). This observation must be considered when the results of echocardiography are used to guide decisions in asymptomatic patients in whom echocardiography was used to assess the significance of an isolated murmur.

Characteristics of innocent murmurs in asymptomatic adults that have no functional significance include the following:

- **grade 1 to 2 intensity at the left sternal border**
- **a systolic ejection pattern**
- **normal intensity and splitting of the second heart sound**
- **no other abnormal sounds or murmurs**
- **no evidence of ventricular hypertrophy or dilatation and the absence of increased murmur intensity with the Valsalva maneuver or with standing from a squatting position.**

Throughout these guidelines, treatment recommendations will often derive from specific echocardiographic measurements of left ventricular (LV) size and systolic function. Accuracy and reproducibility are critical, particularly when applied to surgical recommendations for asymptomatic patients with mitral regurgitation (MR) or aortic regurgitation (AR). Serial measurements over time, or reassessment with a different imaging technology (radionuclide ventriculography or cardiac magnetic resonance), are often helpful for counseling individual patients. Lastly, although handheld echocardiography can be used for screening purposes, it is important to note that its accuracy is highly dependent on the experience of the user. The precise role of handheld echocardiography for the assessment of patients with valvular heart disease has not been elucidated.

As valuable as echocardiography may be, the basic cardiovascular physical examination is still the most appropriate method of screening for cardiac disease and will establish many clinical diagnoses. Echocardiography should not replace the cardiovascular examination but can be useful in determining the cause and severity of valvular lesions, particularly in older and/or symptomatic patients.

### B. Valve Disease Severity Table

Classification of the severity of valve disease in adults is listed in Table 1. The classification for regurgitant lesions is adapted from the recommendations of the American Society of Echocardiog-raphy (7). For full recommendations of the American Society of Echocardiography, please refer to the original document. Subsequent sections of the current guidelines refer to the criteria in Table 1 to define severe valvular stenosis or regurgitation.

**Table 1.** Classification of the Severity of Valve Disease in Adults

**A. Left-Sided Valve Disease**

| | Aortic Stenosis | | |
|---|---|---|---|
| **Indicator** | **Mild** | **Moderate** | **Severe** |
| Jet velocity (m per second) | Less than 3.0 | 3.0–4.0 | Greater than 4.0 |
| Mean gradient (mm Hg)* | Less than 25 | 25–40 | Greater than 40 |
| Valve area (cm²) | Greater than 1.5 | 1.0–1.5 | Less than 1.0 |
| Valve area index (cm² per m²) | | | Less than 0.6 |

| | Mitral Stenosis | | |
|---|---|---|---|
| | **Mild** | **Moderate** | **Severe** |
| Mean gradient (mm Hg)* | Less than 5 | 5–10 | Greater than 10 |
| Pulmonary artery systolic pressure (mm Hg) | Less than 30 | 30–50 | Greater than 50 |
| Valve area (cm²) | Greater than 1.5 | 1.0–1.5 | Less than 1.0 |

| | Aortic Regurgitation | | |
|---|---|---|---|
| | **Mild** | **Moderate** | **Severe** |
| **Qualitative** | | | |
| Angiographic grade | 1+ | 2+ | 3–4+ |
| Color Doppler jet width | Central jet, width less than 25% of LVOT | Greater than mild but no signs of severe AR | Central jet, width greater than 65% LVOT |
| Doppler vena contracta width (cm) | Less than 0.3 | 0.3–0.6 | Greater than 0.6 |
| **Quantitative (cath or echo)** | | | |
| Regurgitant volume (ml per beat) | Less than 30 | 30–59 | Greater than or equal to 60 |
| Regurgitant fraction (%) | Less than 30 | 30–49 | Greater than or equal to 50 |
| Regurgitant orifice area (cm²) | Less than 0.10 | 0.10–0.29 | Greater than or equal to 0.30 |
| **Additional essential criteria** | | | |
| Left ventricular size | | | Increased |

| | Mitral Regurgitation | | |
|---|---|---|---|
| | **Mild** | **Moderate** | **Severe** |
| **Qualitative** | | | |
| Angiographic grade | 1+ | 2+ | 3–4+ |
| Color Doppler jet area | Small, central jet (less than 4 cm² or less than 20% LA area) | Signs of MR greater than mild present but no criteria for severe MR | Vena contracta width greater than 0.7 cm with large central MR jet (area greater than 40% of LA area) or with a wall-impinging jet of any size, swirling in LA |
| Doppler vena contracta width (cm) | Less than 0.3 | 0.3–0.69 | Greater than or equal to 0.70 |
| **Quantitative (cath or echo)** | | | |
| Regurgitant volume (ml per beat) | Less than 30 | 30–59 | Greater than or equal to 60 |
| Regurgitant fraction (%) | Less than 30 | 30–49 | Greater than or equal to 50 |
| Regurgitant orifice area (cm²) | Less than 0.20 | 0.2–0.39 | Greater than or equal to 0.40 |
| **Additional essential criteria** | | | |
| Left atrial size | | | Enlarged |
| Left ventricular size | | | Enlarged |

| **B. Right-Sided Valve Disease** | **Characteristic** |
|---|---|
| Severe tricuspid stenosis: | Valve area less than 1.0 cm² |
| Severe tricuspid regurgitation: | Vena contracta width greater than 0.7 cm and systolic flow reversal in hepatic veins |
| Severe pulmonic stenosis: | Jet velocity greater than 4 m per second or maximum gradient greater than 60 mm Hg |
| Severe pulmonic regurgitation: | Color jet fills outflow tract<br>Dense continuous wave Doppler signal with a steep deceleration slope |

*Valve gradients are flow dependent and when used as estimates of severity of valve stenosis should be assessed with knowledge of cardiac output or forward flow across the valve. Modified from the *Journal of the American Society of Echocardiography, 16*, Zoghbi WA, Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography, 777–802, Copyright 2003, with permission from American Society of Echocardiography (7). AR indicates aortic regurgitation; cath, catheterization; echo, echocardiography; LA, left atrial/atrium; LVOT, left ventricular outflow tract; and MR, mitral regurgitation.

### C. Endocarditis and Rheumatic Fever Prophylaxis

The following information is based on recommendations made by the AHA in 1997 (8). These recommendations are currently under revision and subject to change. Recommendations for prophylaxis against and treatment of nonvalvular cardiac device–related infections have been published previously (9).

### 1. Endocarditis Prophylaxis

#### Class I

**Prophylaxis against infective endocarditis is recommended for the following patients:**

- **Patients with prosthetic heart valves and patients with a history of infective endocarditis. *(Level of Evidence: C)***
- **Patients who have complex cyanotic congenital heart disease (e.g., single-ventricle states, transposition of the great arteries, tetralogy of Fallot). *(Level of Evidence: C)***
- **Patients with surgically constructed systemic-pulmonary shunts or conduits. *(Level of Evidence: C)***
- **Patients with congenital cardiac valve malformations, particularly those with bicuspid aortic valves, and patients with acquired valvular dysfunction (e.g., rheumatic heart disease). *(Level of Evidence: C)***
- **Patients who have undergone valve repair. *(Level of Evidence: C)***
- **Patients who have hypertrophic cardiomyopathy when there is latent or resting obstruction. *(Level of Evidence: C)***
- **Patients with MV prolapse (MVP) and auscultatory evidence of valvular regurgitation and/or thickened leaflets on echocardiography.\* *(Level of Evidence: C)***

#### Class III
**Prophylaxis against infective endocarditis is not recommended for the following patients:**

- **Patients with isolated secundum atrial septal defect. *(Level of Evidence: C)***
- **Patients 6 or more months after successful surgical or percutaneous repair of atrial septal defect, ventricular septal defect, or patent ductus arteriosus. *(Level of Evidence: C)***
- **Patients with MVP without MR or thickened leaflets on echocardiography.\* *(Level of Evidence: C)***
- **Patients with physiological, functional, or innocent heart murmurs, including patients with aortic valve sclerosis as defined by focal areas of increased echogenicity and thickening of the leaflets without restriction of motion and a peak velocity less than 2.0 m per second. *(Level of Evidence: C)***
- **Patients with echocardiographic evidence of physiologic MR in the absence of a murmur and with structurally normal valves. *(Level of Evidence: C)***

- **Patients with echocardiographic evidence of physiological tricuspid regurgitation (TR) and/or pulmonary regurgitation in the absence of a murmur and with structurally normal valves. *(Level of Evidence: C)***

*\*Patients with MVP without regurgitation require additional clinical judgment. Indications for antibiotic prophylaxis in MVP are discussed in Section III-E-2. Patients who do not have MR but who do have echocardiographic evidence of thickening and/or redundancy of the valve leaflets, and especially men 45 years of age or older, may be at increased risk for infective endocarditis (10). Additionally, approximately one third of patients with MVP without MR at rest may have exercise-induced MR (11). Some patients may exhibit MR at rest on one occasion and not on another. 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.*

### 2. Rheumatic Fever Prophylaxis

#### Class I

> **Patients who have had rheumatic fever with or without carditis (including patients with MS) should receive prophylaxis for recurrent rheumatic fever. *(Level of Evidence: B)***

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. The enhanced understanding of the causative organism, group A beta hemolytic streptococcus, has resulted in the development of kits that allow rapid detection of group A streptococci with specificity greater than 95% and more rapid identification of their presence in upper respiratory infection. Because the test has a low sensitivity, a negative test requires throat culture confirmation. Rheumatic fever prevention and treatment guidelines have been established previously by the AHA (12). Prompt recognition and treatment comprise primary rheumatic fever prevention.

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. Secondary prevention of rheumatic fever recurrence is thus of great importance. Continuous antimicrobial prophylaxis has been shown to be effective. Anyone who has had rheumatic fever with or without carditis, including patients with mitral stenosis (MS) should receive prophylaxis for recurrent rheumatic fever (12).

## III. SPECIFIC VALVE LESIONS

### A. Aortic Stenosis

The most common cause of AS in adults is calcification of a normal trileaflet or congenital bicuspid valve (13,14). Calcific AS is an active disease process characterized by lipid accumulation, inflammation, and calcification, with many similarities to atherosclerosis (15–19). Rheumatic AS due to fusion of the commissures with scarring and eventual calcification of the cusps is less common and is invariably accompanied by MV disease.

### 1. Grading the Degree of Stenosis

For these guidelines, we graded AS severity on the basis of a variety of hemodynamic and natural history data (Table 1) (7,20), using definitions of aortic jet velocity, mean pressure gradient, and valve area as follows:

- **Mild (area 1.5 cm$^2$, mean gradient less than 25 mm Hg, or jet velocity less than 3.0 m per second)**
- **Moderate (area 1.0 to 1.5 cm$^2$, mean gradient 25–40 mm Hg, or jet velocity 3.0–4.0 m per second)**
- **Severe (area less than 1.0 cm$^2$, mean gradient greater than 40 mm Hg or jet velocity greater than 4.0 m per second).**

When stenosis is severe and cardiac output is normal, the mean transvalvular pressure gradient is generally greater than 40 mm Hg. However, when cardiac output is low, severe stenosis may be present with a lower transvalvular gradient and velocity, as discussed below. 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 the primary determinant of the need for aortic valve replacement (AVR).

### 2. Natural History

The natural history of AS in the adult consists of a prolonged latent period during which morbidity and mortality are very low. The rate of progression of the stenotic lesion has been estimated in a variety of invasive and noninvasive studies (21). Once even moderate stenosis is present (jet velocity greater than 3.0 m per second; Table 1), the average rate of progression is an increase in jet velocity of 0.3 m per second per year, an increase in mean pressure gradient of 7 mm Hg per year, and a decrease in valve area of 0.1 cm$^2$ per year (22–27); however, there is marked individual variability in the rate of hemodynamic progression. Although it appears that the progression of AS can be more rapid in patients with degenerative calcific disease than in those with congenital or rheumatic disease (27–29), it is not possible to predict the rate of progression in an individual patient. For this reason, regular clinical follow-up

is mandatory in all patients with asymptomatic mild to moderate AS. In addition, progression to AS may occur in patients with aortic sclerosis, defined as valve thickening without obstruction to LV outflow (30).

Aortic sclerosis is present in approximately 25% of adults over 65 years of age and is associated with clinical factors such as age, sex, hypertension, smoking, serum low-density lipoprotein and lipoprotein(a) levels, and diabetes mellitus (31). Aortic sclerosis on echocardiography in subjects without known coronary disease is also associated with adverse clinical outcome, with an approximately 50% increased risk of myocardial infarction and cardiovascular death compared with subjects with a normal aortic valve (32–34). The mechanism of this association is unclear and is likely related to subclinical atherosclerosis, endothelial dysfunction, or systemic inflammation rather than valve hemodynamics.

Eventually, symptoms of angina, syncope, or heart failure develop after a long latent period, and the outlook changes dramatically. After the onset of symptoms, average survival is 2 to 3 years (35–39), with a high risk of sudden death. Thus, the development of symptoms identifies a critical point in the natural history of AS. It is important to emphasize that symptoms may be subtle and often are not elicited by the physician in taking a routine clinical history.

Sudden death is known to occur in patients with severe AS and, in older retrospective studies, has been reported to occur without prior symptoms (35,40–42). However, in prospective echocardiographic studies, sudden death in previously asymptomatic patients is rare (20,27,38,43–45), estimated at less than 1% per year when patients with known AS are followed up prospectively.

### 3. Management of the Asymptomatic Patient

Asymptomatic patients with AS have outcomes similar to age-matched normal adults; however, disease progression with symptom onset is common (20,27,38,43–47). Patients with asymptomatic AS require frequent monitoring for development of symptoms and progressive disease.

### a. Echocardiography (Imaging, Spectral, and Color Doppler) in Aortic Stenosis

### Class I

1. **Echocardiography is recommended for the diagnosis and assessment of AS severity. *(Level of Evidence: B)***
2. **Echocardiography is recommended in patients with AS for the assessment of LV wall thickness, size, and function. *(Level of Evidence: B)***
3. **Echocardiography is recommended for re-evaluation of patients with known AS and changing symptoms or signs. *(Level of Evidence: B)***
4. **Echocardiography is recommended for the assessment of changes in hemodynamic severity and LV function in patients with known AS during pregnancy. *(Level of Evidence: B)***

5. **Transthoracic echocardiography is recommended for re-evaluation of asymptomatic patients: every year for severe AS; every 1–2 years for moderate AS; and every 3–5 years for mild AS.** *(Level of Evidence: B)*

Echocardiography is indicated when there is a systolic murmur that is grade 3/6 or greater, when there is a single $S_2$, or if there are symptoms that might be due to AS. The 2-dimensional (2D) echocardiogram is valuable for evaluation of valve anatomy and function and to determine the LV response to pressure overload. In nearly all patients, the severity of the stenotic lesion can be defined with Doppler echocardiographic measurements of maximum jet velocity, mean transvalvular pressure gradient, and continuity equation valve area, as discussed in the "ACC/AHA/ASE 2004 Guidelines for the Clinical Application of Echocardiography" [1]. Doppler evaluation of AS severity requires attention to technical details, with the most common error being underestimation of disease severity due to a nonparallel intercept angle between the ultrasound beam and high-velocity jet through the narrowed valve. When measurement of LV outflow tract diameter is problematic, the ratio of outflow tract velocity to aortic jet velocity can be substituted for valve area, because this ratio is, in effect, indexed for body size. A ratio of 0.9 to 1.0 is normal, with a ratio less than 0.25 indicating severe stenosis. Echocardiography is also used to assess LV size and function, degree of hypertrophy, and presence of other associated valvular disease.

### b. Exercise Testing

**Class IIb**

> **Exercise testing in asymptomatic patients with AS may be considered to elicit exercise-induced symptoms and abnormal blood pressure responses.** *(Level of Evidence: B)*

**Class III**

> **Exercise testing should not be performed in symptomatic patients with AS.** *(Level of Evidence: B)*

Exercise testing in adults with AS has poor diagnostic accuracy for evaluation of concurrent CAD. Presumably, this is due to the presence of an abnormal baseline ECG, LV hypertrophy, and limited coronary flow reserve. Electrocardiographic ST depression during exercise occurs in 80% of adults with asymptomatic AS and has no known prognostic significance.

Exercise testing should not be performed in symptomatic patients because of the high risk of complications; however, in asymptomatic patients, exercise testing is relatively safe and may provide information that is not uncovered during the initial clinical evaluation (20,46–52). When the medical history is unclear, exercise testing can identify a limited exercise capacity, abnormal blood pressure responses, or even exercise-induced symptoms (46,47,52). An abnormal hemodynamic response (e.g., hypotension or failure to

increase blood pressure with exercise) in a patient with severe AS is considered a poor prognostic finding (46,53). Finally, in selected patients, the observations made during exercise may provide a basis for advice about physical activity. 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.

### c. Serial Evaluations

The frequency of follow-up visits to the physician depends on the severity of AS and on the presence of comorbid conditions. An essential component of each visit is patient education about the expected disease course and symptoms of AS. Patients should be advised to promptly report the development of any change in exercise tolerance, exertional chest discomfort, dyspnea, lightheadedness, or syncope.

Serial echocardiography is an important part of an integrated approach that includes a detailed history, physical examination, and, in some patients, a carefully monitored exercise test. Because the rate of progression varies considerably, clinicians often perform an annual echocardiogram on patients known to have moderate to severe AS. Serial echocardiograms are helpful to assess changes in stenosis severity, LV hypertrophy, and LV function. Therefore, in patients with severe AS, an echocardiogram every year may be appropriate. In patients with moderate AS, serial studies performed every 1 to 2 years are satisfactory, and in patients with mild AS, serial studies can be performed every 3 to 5 years. Echocardiograms should be performed more frequently if there is a change in signs or symptoms.

### d. Medical Therapy

Antibiotic prophylaxis is indicated in all patients with AS for prevention of infective endocarditis and, in those with rheumatic AS, for prevention of recurrent rheumatic fever. Patients with associated systemic arterial hypertension should be treated cautiously with appropriate antihypertensive agents. With these exceptions, there is no specific medical therapy for patients who have not yet developed symptoms. Patients who develop symptoms require surgery, not medical therapy.

There are no medical treatments proven to prevent or delay the disease process in the aortic valve leaflets; however, the association of AS with clinical factors similar to those associated with atherosclerosis and the mechanisms of disease at the tissue level (15–19,30–34,54–58) and small retrospective studies of the effect of lipid-lowering therapy (59–64) have led to the hypothesis that intervention may be possible to slow or prevent disease progression in the valve leaflet (56,65). Yet, a prospective, randomized, placebo-controlled trial in patients with calcific aortic valve disease failed to demonstrate a benefit of atorvastatin in reducing the progression of aortic valve stenosis over a 3-year period (66). It is

noteworthy that the patients in this study had high levels of aortic valve calcification by computed tomography and evidence of moderate to severe AS at baseline. Thus, further trials in patients with less severe aortic valve calcification, with longer follow-up periods, are needed. In the meanwhile, evaluation and modification of cardiac risk factors is important in patients with aortic valve disease to prevent concurrent CAD.

### e. Physical Activity and Exercise

Recommendations for physical activity are based on the clinical examination, with special emphasis on the hemodynamic severity of the stenotic lesion. Recommendations on participation in competitive sports have been published by the Task Force on Acquired Valvular Heart Disease of the 36th Bethesda Conference (67). Physical activity is not restricted in asymptomatic patients with mild AS; these patients can participate in competitive sports. Patients with moderate to severe AS should avoid competitive sports that involve high dynamic and static muscular demands. Other forms of exercise can be performed safely, but it is advisable to evaluate such patients with an exercise test before they begin an exercise or athletic program.

### 4. Indications for Cardiac Catheterization

#### Class I

1. **Coronary angiography is recommended before AVR in patients with AS at risk for CAD (see Section X-B). (Level of Evidence: B)**
2. **Cardiac catheterization for hemodynamic measurements is recommended for assessment of severity of AS in symptomatic patients when noninvasive tests are inconclusive or when there is a discrepancy between noninvasive tests and clinical findings regarding severity of AS. (Level of Evidence: C)**
3. **Coronary angiography is recommended before AVR in patients with AS for whom a pulmonary autograft (Ross procedure) is contemplated and if the origin of the coronary arteries was not identified by noninvasive technique. (Level of Evidence: C)**

#### Class III

1. **Cardiac catheterization for hemodynamic measurements is not recommended for the assessment of severity of AS before AVR when noninvasive tests are adequate and concordant with clinical findings. (Level of Evidence: C)**
2. **Cardiac catheterization for hemodynamic measurements is not recommended for the assessment of LV function and severity of AS in asymptomatic patients. (Level of Evidence: C)**

In preparation for AVR, coronary angiography is indicated in patients suspected of having CAD, as discussed in Section X-B. If the clinical and echocardiographic data are typical of severe isolated AS, coronary angiography may be

all that is needed before AVR. A complete left- and right-heart catheterization may be necessary to assess the hemodynamic severity of the AS if there is a discrepancy between clinical and echocardiographic data.

The pressure gradient across a stenotic valve is related to the valve orifice area and the transvalvular flow (68). Thus, in the presence of depressed cardiac output, relatively low pressure gradients may be obtained in patients with severe AS. On the other hand, during exercise or other high-flow states, significant pressure gradients can be measured in minimally stenotic valves. For these reasons, complete assessment of AS requires measurement of transvalvular flow, determination of the mean transvalvular pressure gradient, and calculation of the effective valve area. 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.

### 5. Low-Flow/Low-Gradient Aortic Stenosis

#### Class IIa

1. **Dobutamine stress echocardiography is reasonable to evaluate patients with low-flow/low-gradient AS and LV dysfunction. (Level of Evidence: B)**
2. **Cardiac catheterization for hemodynamic measurements with infusion of dobutamine can be useful for evaluation of patients with low-flow/low-gradient AS and LV dysfunction. (Level of Evidence: C)**

Patients with severe AS and low cardiac output often present with a relatively low transvalvular pressure gradient (i.e., mean gradient less than 30 mm Hg). Such patients can be difficult to distinguish from those with low cardiac output and only mild to moderate AS. In the latter group, primary contractile dysfunction is responsible for the decreased ejection fraction and low stroke volume; the problem is further complicated by reduced valve opening forces that contribute to limited valve mobility and apparent stenosis. 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. Alternate measures of AS severity have been proposed as being less flow dependent than gradients or valve area. These include valve resistance and stroke work loss. However, all of these measures are flow dependent, have not been shown to predict clinical outcome, and have not gained widespread clinical use (69).

In selected patients with low-flow/low-gradient AS and LV dysfunction, it may be useful to determine the transvalvular pressure gradient and to calculate valve area during a baseline state and again during exercise or low-dose pharmacological (i.e., dobutamine infusion) stress, with the goal of determining whether stenosis is severe or only moderate in severity (51,70–76). Such studies can be performed in either the echocardiography or the cardiac catheterization laboratory. If a dobutamine infusion produces an increment in stroke volume and an increase in valve area greater than 0.2 cm$^2$ and little change in gradient, it is likely that the

baseline evaluation overestimated the severity of stenosis. In contrast, patients with severe AS will have a fixed valve area with an increase in stroke volume and an increase in gradient. These patients are likely to respond favorably to surgery. Patients in whom stroke volume fails to increase with dobutamine (less than 20% increase) appear to have a very poor prognosis with either medical or surgical therapy (1,77).

Dobutamine stress testing in patients with AS should be performed only in centers with experience in pharmacological stress testing and with a cardiologist in attendance.

## 6. Indications for Aortic Valve Replacement

### Class I

1. **AVR is indicated for symptomatic patients with severe AS.\* *(Level of Evidence: B)***
2. **AVR is indicated for patients with severe AS\* undergoing coronary artery bypass graft surgery (CABG). *(Level of Evidence: C)***
3. **AVR is indicated for patients with severe AS\* undergoing surgery on the aorta or other heart valves. *(Level of Evidence: C)***
4. **AVR is recommended for patients with severe AS\* and LV systolic dysfunction (ejection fraction less than 0.50). *(Level of Evidence: C)***

### Class IIa

**AVR is reasonable for patients with moderate AS\* undergoing CABG or surgery on the aorta or other heart valves (see Section X-D). *(Level of Evidence: B)***

### Class IIb

1. **AVR may be considered for asymptomatic patients with severe AS\* and abnormal response to exercise (e.g., development of symptoms or asymptomatic hypotension). *(Level of Evidence: C)***
2. **AVR may be considered for adults with severe asymptomatic AS\* if there is a high likelihood of rapid progression (age, calcification, and CAD) or if surgery might be delayed at the time of symptom onset. *(Level of Evidence: C)***
3. **AVR may be considered in patients undergoing CABG who have mild AS\* when there is evidence, such as moderate to severe valve calcification, that progression may be rapid. *(Level of Evidence: C)***
4. **AVR may be considered for asymptomatic patients with extremely severe AS (aortic valve area less than 0.6 cm$^2$, mean gradient greater than 60 mm Hg, and jet velocity greater than 5.0 m per second) when the patient's expected operative mortality is 1.0% or less. *(Level of Evidence: C)***

### Class III

**AVR is not useful for the prevention of sudden death in asymptomatic patients with AS who have none of the findings listed under the Class IIa/IIb recommendations. *(Level of Evidence: B)***

**\*See Table 1 (7).**

In adults with severe, symptomatic, calcific AS, AVR is the only effective treatment. Younger patients with congenital or rheumatic AS may be candidates for valvotomy (see Section VI-A-2). Although there is some lack of agreement about the optimal timing of surgery in asymptomatic patients, it is possible to develop rational guidelines for most patients. A proposed management strategy for patients with severe AS is shown in Figure 2 (78). Particular consideration should be given to the natural history of asymptomatic patients and to operative risks and outcomes after surgery. See also Section VII-A.

#### a. Symptomatic Patients

In symptomatic patients with AS, AVR improves symptoms and improves survival (36,79–83). These salutary results of surgery are partly dependent on LV function. The depressed ejection fraction in many patients in this latter group is caused by excessive afterload (afterload mismatch) (84), and LV function improves after AVR in such patients. If LV dysfunction is not caused by afterload mismatch, survival is still improved, but improvement in LV function and resolution of symptoms might not be complete after AVR (79,82,85–87). Therefore, in the absence of serious comorbid conditions, AVR is indicated in virtually all symptomatic patients with severe AS. Because of the risk of sudden death, AVR should be performed promptly after the onset of symptoms. Age is not a contraindication to surgery, with several series showing outcomes similar to age-matched normal subjects in the very elderly. The operative risks can be estimated with readily available and well-validated online risk calculators from the Society of Thoracic Surgeons (www.sts.org), the European System for Cardiac Operative Risk Evaluation (www.euroscore.org) (88–90), and Ambler et al (91).

#### b. Asymptomatic Patients

Although AVR is associated with low perioperative morbidity and mortality in many centers, the average perioperative mortality in the Society of Thoracic Surgeons (STS) database is 3.0% to 4.0% for isolated AVR and 5.5% to 6.8% for AVR plus CABG (92,93). These rates are 33% higher in centers with low volume than in centers with the highest surgical volume (94). A review of Medicare data (95), involving 684 US hospitals and more than 142 000 patients, indicates that the average in-hospital mortality for AVR in patients over the age of 65 years is 8.8% (13.0% in low-volume centers and 6.0% in high-volume centers). In addition, despite improved longevity of current-generation bioprosthetic valves (96,97), AVR in young patients subjects them to the risks of structural valve deterioration of bioprostheses (96,98–102) and the appreciable morbidity and

## Severe Aortic Stenosis
Vmax greater than 4 m/s
AVA less than 1.0 cm$^2$
Mean gradient > 40 mm Hg
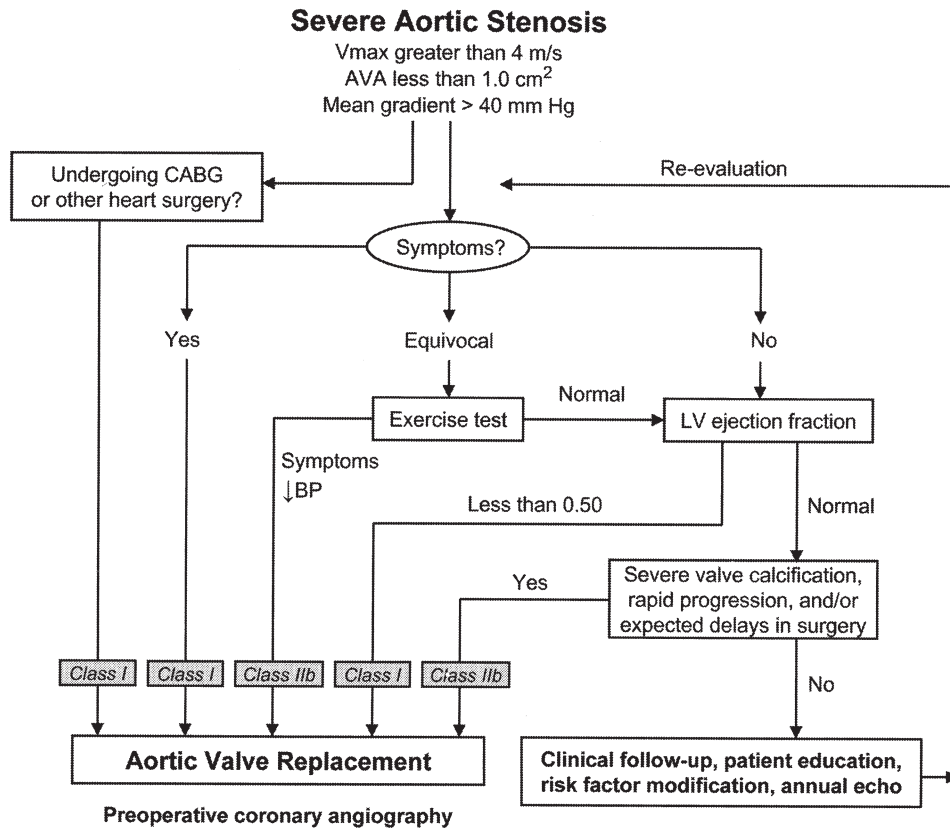


**Figure 2.** Management strategy for patients with severe aortic stenosis. Preoperative coronary angiography should be performed routinely as determined by age, symptoms, and coronary risk factors. Cardiac catheterization and angiography may also be helpful when there is discordance between clinical findings and echocardiography. Modified from CM Otto. Valvular aortic stenosis: disease severity and timing of intervention. J Am Coll Cardiol 2006;47:2141–51 (78). AVA indicates aortic valve area; BP, blood pressure; CABG, coronary artery bypass graft surgery; echo, echocardiography; LV, left ventricular; Vmax, maximal velocity across aortic valve by Doppler echocardiography.

mortality of mechanical valves (100,102–106). Thus, the combined risk of surgery in older patients and the late complications of a prosthesis in younger patients needs to be balanced against the possibility of preventing sudden death, which, as noted above, occurs at a rate of less than 1.0% per year.

Despite these considerations, some difference of opinion persists among clinicians regarding the indications for AVR in asymptomatic patients with severe AS, because the probability of remaining free of cardiac symptoms without surgery is less than 50% at 5 years (20,27,45). Studies suggest that patients at risk of rapid disease progression and impending symptom onset can be identified on the basis of clinical and echocardiographic parameters. The rate of hemodynamic progression is faster in patients with asymptomatic severe (27) or mild to moderate (29) AS when patient age is over 50 years and severe valve calcification or concurrent CAD is present. Adverse clinical outcomes are more likely in patients with a more rapid rate of hemodynamic progression, defined as an annual increase in aortic jet velocity greater than 0.3 m per second per year or a decrease in valve area greater than 0.1 cm$^2$ per year (20,27). The presence of LV hypertrophy by ECG and smaller aortic valve area by Doppler echocardiography predict the devel-

opment of symptoms (20,45). In addition, serum levels of B-type natriuretic peptide may provide important prognostic information (107). In situations in which there is delay between symptom onset and surgical intervention, patients are at high risk of adverse outcomes during the waiting period. These higher-risk patients might warrant more frequent echocardiography or earlier consideration of valve replacement.

### c. Patients Undergoing Coronary Artery Bypass or Other Cardiac Surgery

Patients with severe AS, with or without symptoms, who are undergoing CABG should undergo AVR at the time of the revascularization procedure. Similarly, patients with severe AS undergoing surgery on other valves (such as MV repair) or the aortic root should also undergo AVR as part of the surgical procedure. In patients with moderate AS, it is generally accepted practice to perform AVR at the time of CABG (108–112). However, there are no data to support a policy of AVR for mild AS at the time of CABG, with the exception of those patients with moderate to severe valvular calcification (29,108,109, 112–114). Recommendations for AVR at the time of CABG are discussed in Section X-D.

### 7. Aortic Balloon Valvotomy

#### Class IIb

1. **Aortic balloon valvotomy might be reasonable as a bridge to surgery in hemodynamically unstable adult patients with AS who are at high risk for AVR. _(Level of Evidence: C)_**
2. **Aortic balloon valvotomy might be reasonable for palliation in adult patients with AS in whom AVR cannot be performed because of serious comorbid conditions. _(Level of Evidence: C)_**

#### Class III

**Aortic balloon valvotomy is not recommended as an alternative to AVR in adult patients with AS; certain younger adults without valve calcification may be an exception (see Section VI-A-2). _(Level of Evidence: B)_**

Percutaneous balloon aortic valvotomy has an important role in treating adolescents and young adults with AS (see Section VI-A-2) but a very limited role in older adults. Immediate hemodynamic results include a moderate reduction in the transvalvular pressure gradient, but the postvalvotomy valve area rarely exceeds 1.0 cm$^2$. Although early symptomatic improvement often occurs, serious acute complications develop with a frequency greater than 10% (115–118), and restenosis and clinical deterioration occur within 6 to 12 months in most patients (116,119–122). Therefore, in adults with AS, balloon valvotomy is not a substitute for AVR (122–125).

The indications for palliative valvotomy in patients in whom AVR cannot be recommended because of serious comorbid conditions are even less well established. Most asymptomatic patients with severe AS who require urgent noncardiac surgery can undergo surgery at a reasonably low risk with monitoring of anesthesia and attention to fluid balance (126–130). Balloon aortic valvotomy is not recommended for these patients. If preoperative correction of AS is needed, they should be considered for AVR.

### 8. Medical Therapy for the Inoperable Patient

Comorbid conditions (e.g., malignancy) or, on occasion, patient preferences might preclude AVR for severe AS. Under such circumstances, there is no therapy that prolongs life, and only limited medical therapies are available to alleviate symptoms. Patients with evidence of pulmonary congestion can benefit from cautious treatment with digitalis, diuretics, and angiotensin-converting enzyme (ACE) inhibitors. In patients with acute pulmonary edema due to AS, nitroprusside infusion may be used to reduce congestion and improve LV performance. Such therapy should be performed in an intensive care unit under the guidance of invasive hemodynamic monitoring (131). Atrial fibrillation has an adverse effect on atrial pump function and ventricular rate; if prompt cardioversion is unsuccessful, pharmacological control of the ventricular rate is essential.

### 9. 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 (132), but the decision to proceed with such surgery depends on many factors, including the patient's wishes and expectations. Older patients with symptoms due to severe AS, normal coronary arteries, and preserved LV function can expect a better outcome than those with CAD or LV dysfunction (133). Deconditioned and debilitated patients often do not return to an active existence, and the presence of the other comorbid disorders could have a major impact on outcome.

In addition to the confounding effects of CAD and the potential for stroke, other considerations are peculiar to older patients. For example, a narrow LV outflow tract and a small aortic annulus sometimes present in elderly women could require enlargement of the annulus. Heavy calcification of the valve, annulus, and aortic root may require debridement. Likewise, excessive or inappropriate hypertrophy associated with AS can increase the risk of perioperative morbidity and mortality, and preoperative recognition of elderly patients with marked LV hypertrophy followed by appropriate perioperative management can reduce this risk substantially. There is no perfect method for weighing all of the relevant factors and identifying specifically high- and low-risk elderly patients, but this risk can be estimated well in individual patients (88–91,134).

### B. Aortic Regurgitation

#### 1. Acute Aortic Regurgitation

In acute severe 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. With an abrupt increase in end-diastolic volume, the ventricle operates on the steep portion of a normal diastolic pressure-volume relationship, and 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. Patients may also present with signs and symptoms of myocardial ischemia.

#### a. Diagnosis

Many of the characteristic physical findings of chronic AR are modified or absent when valvular regurgitation is acute, which can lead to underestimation of its severity. Echocardiography is indispensable in confirming the presence and severity of the valvular regurgitation, determining its cause, and determining whether there is rapid equilibration of

aortic and LV diastolic pressure. Evidence for rapid pressure equilibration includes a short AR diastolic half-time (less than 300 ms), a short mitral deceleration time (less than 150 ms), or premature closure of the MV.

Acute AR caused by aortic root dissection is a surgical emergency that requires particularly prompt identification and management. TEE is indicated when aortic dissection is suspected (135–137). In some settings, computed tomographic imaging or magnetic resonance imaging should be performed if this will lead to a more rapid diagnosis than can be achieved by TEE (135,136,138). Cardiac catheterization, aortography, and coronary angiography are rarely required, are associated with increased risk, and might delay urgent surgery unnecessarily (136,139–142). Angiography should be considered only when the diagnosis cannot be determined by noninvasive imaging and when patients have known CAD, especially those with previous CABG (see Section X-B).

### b. Treatment

Death due to pulmonary edema, ventricular arrhythmias, electromechanical dissociation, or circulatory collapse is common in acute severe AR, even with intensive medical management. Urgent 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 manage the patient temporarily before operation. Intra-aortic balloon counterpulsation is contraindicated. Although beta blockers are often used in treating aortic dissection, these agents should be used very cautiously, if at all, in the setting of acute AR because they will block the compensatory tachycardia. In patients with acute severe AR resulting from infective endocarditis, surgery should not be delayed, especially if there is hypotension, pulmonary edema, or evidence of low output.

### 2. Chronic Aortic Regurgitation

AR represents a condition of combined volume overload and pressure overload (143). 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. In many patients, however, the balance between afterload excess, preload reserve, and hypertrophy cannot be maintained indefinitely, and afterload mismatch (144) or depressed contractility ultimately results in a reduction in ejection fraction, first into the low-normal range and then below normal. Patients often develop dyspnea at this point in the natural history, and diminished coronary flow reserve may result in exertional angina. However, this transition may be much more insidious, and it is possible for patients to remain asymptomatic until severe LV dysfunction has developed.

For purposes of the subsequent discussion, patients with normal LV systolic function will be defined as those with normal LV ejection fraction at rest. It is recognized that other indices of LV function may not be "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 there is no single hemodynamic measurement that represents the absolute boundary between normal LV systolic function and LV systolic dysfunction.

LV systolic dysfunction (defined as an ejection fraction below normal at rest) is initially a reversible phenomenon related predominantly to afterload excess, and full recovery of LV size and function is possible with AVR (145–152). With time, 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 AR, in terms of recovery of LV function and improved survival, can no longer be achieved (150,153–159).

#### a. Natural History

##### Asymptomatic Patients With Normal Left Ventricular Function

The current recommendations are derived from 9 published series (160–169) involving a total of 593 asymptomatic patients with initially normal LV systolic function with a mean follow-up period of 6.6 years. The rate of progression to symptoms or LV systolic dysfunction averaged 4.3% per year. Sudden death occurred in 7 of the 593 patients, an average mortality rate of less than 0.2% per year. Seven of the 9 studies reported the rate of development of asymptomatic LV dysfunction, defined as an ejection fraction at rest below normal (161–165,167,168); 37 of a total of 535 patients developed depressed systolic function at rest without symptoms during a mean 5.9-year follow-up period, a rate of 1.2% per year.

Despite the low likelihood of patients developing asymptomatic LV dysfunction, it should also be emphasized that more than one fourth of patients who die or develop systolic dysfunction do so before the onset of warning symptoms (161–163,167). Thus, thorough questioning of patients regarding symptomatic status is not sufficient in the serial evaluation of asymptomatic patients, and quantitative evaluation of LV function is also indispensable.

##### Asymptomatic Patients With Depressed Systolic Function

The limited data in asymptomatic patients with depressed LV ejection fraction indicate that the majority develop symptoms that warrant AVR within 2 to 3 years (170–172). The average rate of symptom onset in such patients is greater than 25% per year.

##### Symptomatic Patients

There are no contemporary 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 emanating from the

presurgical era indicate that patients with dyspnea, angina, or overt heart failure have a poor outcome with mortality rates of greater than 10% per year in patients with angina pectoris and greater than 20% per year in those with heart failure (173–175). Similar poor outcomes have been reported in the current era in symptomatic patients who do not undergo AVR, even among those with preserved LV systolic function (166,176,177).

### b. Diagnosis and Initial Evaluation

#### Class I

1. **Echocardiography is indicated to confirm the presence and severity of acute or chronic AR. *(Level of Evidence: B)***
2. **Echocardiography is indicated for diagnosis and assessment of the cause of chronic AR (including valve morphology and aortic root size and morphology) and for assessment of LV hypertrophy, dimension (or volume), and systolic function. *(Level of Evidence: B)***
3. **Echocardiography is indicated in patients with an enlarged aortic root to assess regurgitation and the severity of aortic dilatation. *(Level of Evidence: B)***
4. **Echocardiography is indicated for the periodic re-evaluation of LV size and function in asymptomatic patients with severe AR. *(Level of Evidence: B)***
5. **Radionuclide angiography or magnetic resonance imaging is indicated for the initial and serial assessment of LV volume and function at rest in patients with AR and suboptimal echocardiograms. *(Level of Evidence: B)***
6. **Echocardiography is indicated to re-evaluate mild, moderate, or severe AR in patients with new or changing symptoms. *(Level of Evidence: B)***

#### Class IIa

1. **Exercise stress testing for chronic AR is reasonable for assessment of functional capacity and symptomatic response in patients with a history of equivocal symptoms. *(Level of Evidence: B)***
2. **Exercise stress testing for patients with chronic AR is reasonable for the evaluation of symptoms and functional capacity before participation in athletic activities. *(Level of Evidence: C)***
3. **Magnetic resonance imaging is reasonable for the estimation of AR severity in patients with unsatisfactory echocardiograms. *(Level of Evidence: B)***

#### Class IIb

**Exercise stress testing in patients with radionuclide angiography may be considered for assessment of LV function in asymptomatic or symptomatic patients with chronic AR. *(Level of Evidence: B)***

Echocardiography is indicated 1) to confirm the diagnosis of AR if there is an equivocal diagnosis based on physical examination; 2) to assess the cause of AR and to assess valve morphology; 3) to provide a semiquantitative estimate of the severity of AR; 4) to assess LV dimension, mass, and systolic function; and 5) to 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. In addition to semiquantitative assessment of the severity of AR by color flow jet area and width by Doppler echocardiography, quantitative measurement of regurgitant volume, regurgitant fraction, and regurgitant orifice area can be performed in experienced laboratories (Table 1). Indirect measures of severity of AR are helpful, using the rate of decline in regurgitant gradient measured by the slope of diastolic flow velocity, the degree of reversal in pulse wave velocity in the descending aorta, and the magnitude of LV outflow tract velocity (1,178,179).

For purposes of the subsequent discussion of management of patients with AR, severe AR is defined as clinical and Doppler evidence of severe regurgitation (Table 1) in addition to LV cavity dilatation. 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 (Fig. 3). If the echocardiogram is of insufficient quality to assess LV function, radionuclide angiography or cardiac magnetic resonance should be used in asymptomatic patients to measure LV ejection fraction at rest and to estimate LV volumes. In patients who are symptomatic on initial evaluation, it is reasonable to proceed directly to TEE or cardiac catheterization and angiography if the echocardiogram is of insufficient quality to assess LV function or severity of AR.

The exercise ejection fraction and the change in ejection fraction from rest to exercise are often abnormal, even in asymptomatic patients (160,162–164,67,172,180–186). However, the predictive nature of this response in asymptomatic patients with normal LV systolic function and without severe LV dilatation has not been fully demonstrated.

### c. Medical Therapy

#### Class I

**Vasodilator therapy is indicated for chronic therapy in patients with severe AR who have symptoms or LV dysfunction when surgery is not recommended because of additional cardiac or noncardiac factors. *(Level of Evidence: B)***

#### Class IIa

**Vasodilator therapy is reasonable for short-term therapy to improve the hemodynamic profile of patients with severe heart failure symptoms and severe LV**

**Chronic Severe Aortic Regurgitation**
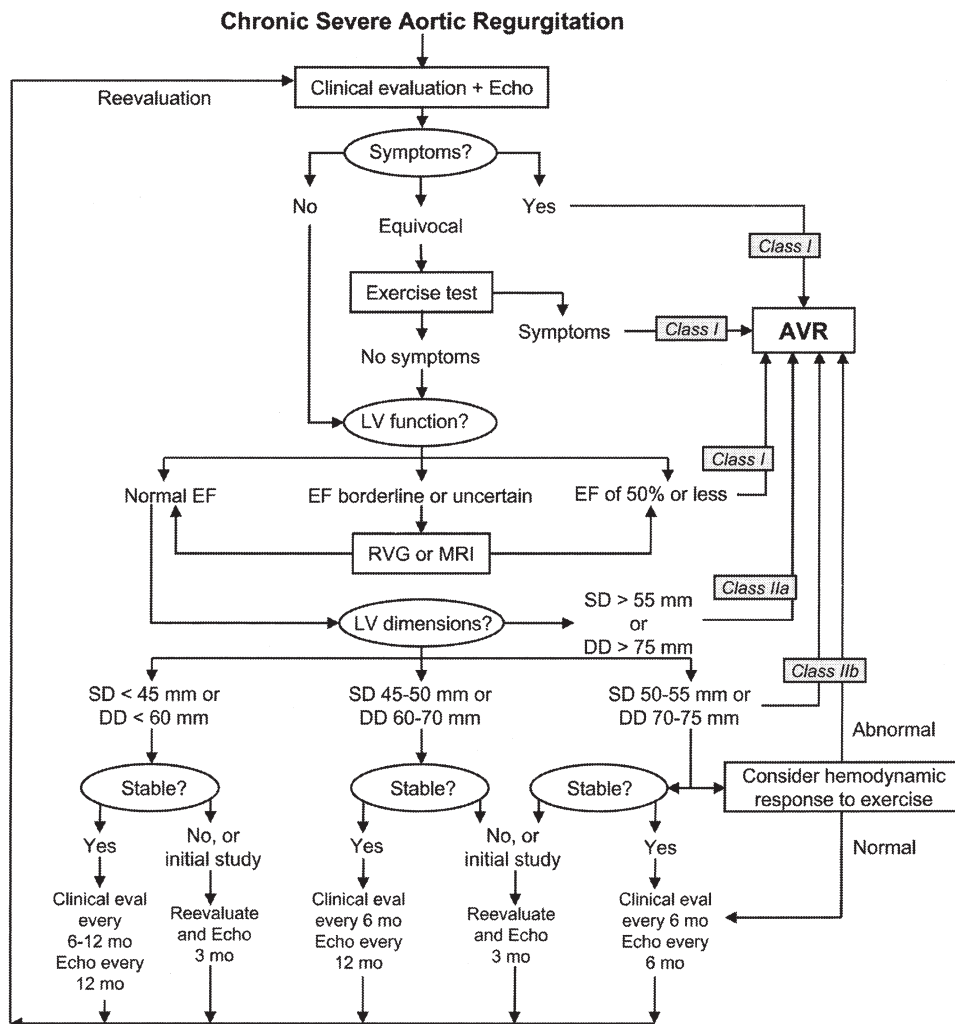


**Figure 3.** Management strategy for patients with chronic severe aortic regurgitation. Preoperative coronary angiography should be performed routinely as determined by age, symptoms, and coronary risk factors. Cardiac catheterization and angiography may also be helpful when there is discordance between clinical findings and echocardiography. "Stable" refers to stable echocardiographic measurements. In some centers, serial follow-up may be performed with radionuclide ventriculography (RVG) or magnetic resonance imaging (MRI) rather than echocardiography (Echo) to assess left ventricular (LV) volume and systolic function. AVR indicates aortic valve replacement; DD, end-diastolic dimension; EF, ejection fraction; eval, evaluation; SD, end-systolic dimension.

dysfunction before proceeding with AVR. *(Level of Evidence: C)*

**Class IIb**

Vasodilator therapy may be considered for long-term therapy in asymptomatic patients with severe AR who have LV dilatation but normal systolic function. *(Level of Evidence: B)*

**Class III**

1. Vasodilator therapy is not indicated for long-term therapy in asymptomatic patients with mild to moderate AR and normal LV systolic function. *(Level of Evidence: B)*
2. Vasodilator therapy is not indicated for long-term therapy in asymptomatic patients with LV systolic dysfunction who are otherwise candidates for AVR. *(Level of Evidence: C)*

3. Vasodilator therapy is not indicated for long-term therapy in symptomatic patients with either normal LV function or mild to moderate LV systolic dysfunction who are otherwise candidates for AVR. *(Level of Evidence: C)*

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. Reduced end-diastolic volume and increased ejection fraction have been observed in small numbers of patients receiving long-term oral therapy with hydralazine and nifedipine for periods of 1 to 2 years (187,188); with nifedipine, these effects are associated with a reduction in LV mass (164,188). Less consistent results have been reported with ACE inhibitors, depending on the degree of

reduction in arterial pressure and end-diastolic volume (189–191). Reduced blood pressure with enalapril and quinapril has been associated with decreases in end-diastolic volume and mass but no change in ejection fraction (190,191).

Whether vasodilator therapy can prolong the compensated phase of asymptomatic patients who have volume-loaded left ventricles but normal systolic function has been investigated in only 2 studies. The first compared long-acting nifedipine versus digoxin in a prospective randomized trial (164). Over a 6-year period, fewer patients randomized to nifedipine required AVR because of symptoms or development of LV dysfunction (ejection fraction less than 0.50). This study enrolled a relatively small number of patients (143 patients); there were relatively few end points (20 patients in the digoxin group and 6 in the nifedipine group underwent AVR); and there was no placebo control group. A second study compared placebo, long-acting nifedipine, and enalapril in 95 consecutive patients, who were followed for 7 years (169). Neither nifedipine nor enalapril reduced the development of symptoms or LV dysfunction warranting AVR compared with placebo. Moreover, neither drug significantly altered LV dimension, ejection fraction, or mass over the course of time compared with placebo. Thus, definitive recommendations regarding the indications for long-acting nifedipine or ACE inhibitors cannot be made at this time.

Vasodilator therapy is not recommended for asymptomatic patients with mild or moderate AR and normal LV function in the absence of systemic hypertension, because these patients have an excellent outcome with no therapy. In patients with severe AR, vasodilator therapy is not an alternative to surgery in asymptomatic patients with LV systolic dysfunction. Symptomatic patients should be considered surgical candidates rather than candidates for long-term medical therapy unless AVR is not recommended because of additional cardiac or noncardiac factors.

### d. Physical Activity and Exercise

Asymptomatic patients with normal LV systolic function may participate in all forms of normal daily physical activity, including mild forms of exercise and in some cases competitive athletics. Isometric exercise should be avoided. Recommendations regarding participation in competitive athletics were published by the Task Force on Acquired Valvular Heart Disease of the 36th Bethesda Conference (67). Before participation in athletics, exercise testing to at least the level of exercise required by the proposed activity is recommended so that the patient's tolerance for this degree of exercise can be evaluated. This does not necessarily evaluate the long-term effects of strenuous exercise, which are unknown.

### e. Serial Testing

In general, the stability and chronicity of the regurgitant lesion and the LV response to volume load need to 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 one of the indications for surgery, repeat physical examination and echocardiography should be performed within 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 re-evaluation and repeat noninvasive testing depends on the severity of the valvular regurgitation, the degree of LV dilatation, the level of systolic function, and whether previous serial studies have revealed progressive changes in LV size or function (Fig. 3).

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 greater than 60 mm) require more frequent and careful re-evaluation, with a history and physical examination every 6 months and echocardiography every 6 to 12 months, depending on the severity of dilatation and stability of measurements. If patients are stable, echocardiographic measurements are not required more frequently than every 12 months. In patients with more advanced LV dilatation (end-diastolic dimension greater than 70 mm or end-systolic dimension greater than 50 mm), for whom the risk of developing symptoms or LV dysfunction ranges between 10% and 20% per year (163,164), it is reasonable to perform serial echocardiograms as frequently as every 4 to 6 months. Serial chest X-rays and ECGs have less value but are helpful in selected patients.

Chronic AR may develop from disease processes that involve 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. This is discussed in Section III-B-3.

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 that suggest worsening regurgitation or progressive LV dilatation. Patients with echocardiographic evidence of progressive LV dilatation or declining systolic function have a greater likelihood of developing symptoms or LV dysfunction (163) and should have more frequent follow-up examinations (every 6 months) than those with stable LV function.

Serial exercise testing is also not recommended routinely in asymptomatic patients with preserved systolic function; however, exercise testing may be invaluable to assess functional capacity and symptomatic responses in patients with equivocal changes in symptomatic status. Serial exercise

imaging studies to assess LV functional reserve are not indicated in asymptomatic patients or those in whom symptoms develop.

### f. Indications for Cardiac Catheterization

**Class I**

1. **Cardiac catheterization with aortic root angiography and measurement of LV pressure is indicated for assessment of severity of regurgitation, LV function, or aortic root size when noninvasive tests are inconclusive or discordant with clinical findings in patients with AR.** *(Level of Evidence: B)*
2. **Coronary angiography is indicated before AVR in patients at risk for CAD.** *(Level of Evidence: C)*

**Class III**

1. **Cardiac catheterization with aortic root angiography and measurement of LV pressure is not indicated for assessment of LV function, aortic root size, or severity of regurgitation before AVR when noninvasive tests are adequate and concordant with clinical findings and coronary angiography is not needed.** *(Level of Evidence: C)*
2. **Cardiac catheterization with aortic root angiography and measurement of LV pressure is not indicated for assessment of LV function and severity of regurgitation in asymptomatic patients when noninvasive tests are adequate.** *(Level of Evidence: C)*

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 that persist despite physical examination and noninvasive testing, or unless AVR is contemplated and there is a need to assess coronary anatomy. The indications for coronary arteriography are discussed in Section X-B.

Hemodynamic and angiographic assessment of the 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 for determining the effect of AR on LV function or making decisions regarding medical or surgical therapy.

### g. Indications for Aortic Valve Replacement or Repair

The majority of patients with severe AR requiring surgery undergo valve replacement (see Section VII-A). However, in several surgical centers, there is increasing experience in performing aortic valve repair in selected patients. In the discussion that follows, the term "AVR" applies to both aortic valve replacement and aortic valve repair, with the understanding that aortic valve repair should be considered only in those surgical centers that have developed the appropriate technical expertise, gained experience in patient selection, and demonstrated outcomes equivalent to those of

valve replacement. The indications for valve replacement and repair do not differ.

In patients with pure, chronic AR, AVR should be considered only if AR is severe (Table 1). Patients with only mild AR are not candidates for AVR, and if such patients have symptoms or LV dysfunction, other causes should be considered, such as CAD, hypertension, or cardiomyopathic processes. The following discussion applies only to patients with pure, severe AR.

**Class I**

1. **AVR is indicated for symptomatic patients with severe AR irrespective of LV systolic function.** *(Level of Evidence: B)*
2. **AVR is indicated for asymptomatic patients with chronic severe AR and LV systolic dysfunction (ejection fraction 0.50 or less) at rest.** *(Level of Evidence: B)*
3. **AVR is indicated for patients with chronic severe AR while undergoing CABG or surgery on the aorta or other heart valves.** *(Level of Evidence: C)*

**Class IIa**

**AVR is reasonable for asymptomatic patients with severe AR with normal LV systolic function (ejection fraction greater than 0.50) but with severe LV dilatation (end-diastolic dimension greater than 75 mm or end-systolic dimension greater than 55 mm).\*** *(Level of Evidence: B)*

**Class IIb**

1. **AVR may be considered in patients with moderate AR while undergoing surgery on the ascending aorta.** *(Level of Evidence: C)*
2. **AVR may be considered in patients with moderate AR while undergoing CABG.** *(Level of Evidence: C)*
3. **AVR may be considered for asymptomatic patients with severe AR and normal LV systolic function at rest (ejection fraction greater than 0.50) when the degree of LV dilatation exceeds an end-diastolic dimension of 70 mm or end-systolic dimension of 50 mm, when there is evidence of progressive LV dilatation, declining exercise tolerance, or abnormal hemodynamic responses to exercise.\*** *(Level of Evidence: C)*

**Class III**

**AVR is not indicated for asymptomatic patients with mild, moderate, or severe AR and normal LV systolic function at rest (ejection fraction greater than 0.50) when the degree of dilatation is not moderate or severe (end-diastolic dimension less than 70 mm, end-systolic dimension less than 50 mm).\*** *(Level of Evidence: B)*

*\*Consider lower threshold values for patients of small stature of either gender.*

*Symptomatic Patients With Normal Left Ventricular Systolic Function*

AVR is indicated in patients with normal LV systolic function (ejection fraction greater than 0.50 at rest) who have symptoms. In selected patients, exercise testing may be valuable in determining symptomatic status. If the cause of these mild symptoms is uncertain and 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 if there is increasing LV chamber size or declining LV systolic function. Thus, even if patients have not achieved the threshold values of LV size and function recommended for surgery in asymptomatic patients, development of mild symptoms is an indication for AVR in a patient who is nearing these values.

*Symptomatic Patients With Left Ventricular Dysfunction*

Symptomatic patients with mild to moderate LV systolic dysfunction (ejection fraction 0.25 to 0.50) should undergo AVR. Patients with New York Heart Association (NYHA) functional class IV symptoms have worse postoperative survival rates and lower likelihood of recovery of systolic function than patients with less severe symptoms (151,153,155,157), but AVR will improve ventricular loading conditions and expedite subsequent management of LV dysfunction (192).

*Asymptomatic Patients*

AVR in asymptomatic patients remains a controversial topic, but it is generally agreed (144,193–199) that AVR is indicated in patients with LV systolic dysfunction. The committee recognizes that there may be variability in any given measurement of LV dimension or ejection fraction. Therefore, the committee recommends that 2 consecutive measurements be obtained before one proceeds with a decision to recommend surgery in the asymptomatic patient. These consecutive measurements could be obtained with the same test repeated in a short time period (such as a second echocardiogram after an initial echocardiogram) or with a separate, independent test (e.g., radionuclide ventriculography, magnetic resonance imaging, or contrast left ventriculography after an initial echocardiogram).

AVR is also recommended in patients with severe LV dilatation (end-diastolic dimension greater than 75 mm or end-systolic dimension greater than 55 mm), even if ejection fraction is normal. The relatively small number of asymptomatic patients with preserved ejection fraction despite severe increases in end-systolic and end-diastolic chamber size should be considered for surgery, because they appear to represent a high-risk group with an increased incidence of sudden death (163,200), and the results of valve replacement in such patients have thus far been excellent (201). In contrast, postoperative mortality is considerable once patients with severe LV dilatation develop symptoms

or LV systolic dysfunction (201). These data do not strongly support the use of extreme LV enlargement as an indication for AVR, unless cardiac symptoms or systolic dysfunction is present (202). However, the committee recommends surgery before the left ventricle achieves an extreme degree of dilatation and recommends AVR for patients with LV end-diastolic dimension greater than 75 mm.

Patients with severe AR in whom the degree of LV dilatation has not reached but is approaching these threshold values (e.g., LV end-diastolic dimension of 70 to 75 mm or end-systolic dimension of 50 to 55 mm) should be followed with frequent echocardiograms every 4 to 6 months, as noted previously (Fig. 3). In addition, AVR may be considered in such patients if there is evidence of declining exercise tolerance or abnormal hemodynamic responses to exercise, for example, an increase in pulmonary artery wedge pressure greater than 25 mm Hg with exercise.

Anthropometric normalization of LV end-diastolic dimension (or volume) should be considered, but unfortunately, there is lack of agreement as to whether or not normalization based on body surface area or body mass index is predictive of outcome (177,203). Normalization of end-diastolic dimension for body surface area tends to mask the diagnosis of LV enlargement, especially in patients who are overweight (204). The use of height and a consideration of gender are likely to be more appropriate than body surface area (205). LV dimensions alone may be misleading in small patients of either gender, and the threshold values of end-diastolic and end-systolic dimension recommended above for AVR in asymptomatic patients (75 and 55 mm, respectively) may need to be reduced in such patients. In such patients, it is particularly important that LV ejection fraction and not merely systolic dimension be monitored.

### 3. Concomitant Aortic Root Disease

In addition to causing acute AR, diseases of the proximal aorta may also contribute to chronic AR (206). In such patients, the valvular regurgitation may be less important in decision making than the primary disease of the aorta, such as Marfan syndrome, dissection, or chronic dilatation of the aortic root related to hypertension or a bicuspid aortic valve (see Section III-C). In general, AVR and aortic root reconstruction are indicated in patients with disease of the aortic root or proximal aorta and AR of any severity when the degree of dilatation of the aorta or aortic root reaches or exceeds 5.0 cm by echocardiography (207). However, some have recommended surgery at a lower level of dilatation (4.5 cm) or based on a rate of increase of 0.5 cm per year or greater in surgical centers with established expertise in repair of the aortic root and ascending aorta (208). Aortic root and ascending aorta dilation in patients with bicuspid aortic valves is discussed in greater detail in Section III-C.

### 4. Evaluation of Patients After Aortic Valve Replacement

After AVR, close follow-up is necessary during the early and long-term postoperative course to evaluate prosthetic valve function and assess LV function (see Section IX-B). 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 against which subsequent echocardiograms may be compared. Within the first few weeks of surgery, there is little change in LV systolic function, and ejection fraction may even deteriorate compared with preoperative values because of the reduced preload (209), even though ejection fraction may increase over the subsequent several months. Thus, persistent or more severe systolic dysfunction early after AVR is a poor predictor of subsequent improvement in LV function in patients with preoperative LV dysfunction. A better predictor of subsequent LV systolic function is the reduction in LV end-diastolic dimension, which declines significantly within the first week or 2 after AVR (151,210,211). This is an excellent marker of the functional success of valve replacement, because 80% of the overall reduction in end-diastolic dimension observed during the long-term postoperative course occurs within the first 10 to 14 days after AVR (151,210,211), and the magnitude of reduction in end-diastolic dimension after surgery correlates with the magnitude of increase in ejection fraction (151).

Patients with persistent LV dilatation on the initial postoperative echocardiogram should be treated as would any other patient with symptomatic or asymptomatic LV dysfunction, including treatment with ACE inhibitors and beta-adrenergic blocking agents. In such patients, repeat echocardiography to assess LV size and systolic function is warranted at the 6- and 12-month re-evaluations. If LV dysfunction persists beyond this time frame, repeat echocardiograms should be performed as clinically indicated.

### 5. Special Considerations in the Elderly

The vast majority of elderly patients with aortic valve disease have AS or combined AS and AR, and pure AR is uncommon (212). Patients older than 75 years are more likely to develop symptoms or LV dysfunction at earlier stages of LV dilatation, have more persistent LV dysfunction and heart failure symptoms after surgery, and have worse postoperative survival rates than their younger counterparts. Many such patients have concomitant CAD, which must be considered in the evaluation of symptoms, LV dysfunction, and indications for surgery.

### C. Bicuspid Aortic Valve With Dilated Ascending Aorta

### Class I

1. **Patients with known bicuspid aortic valves should undergo an initial transthoracic echocardiogram to assess the diameters of the aortic root and ascending aorta. *(Level of Evidence: B)***

2. **Cardiac magnetic resonance imaging or cardiac computed tomography is indicated in patients with bicuspid aortic valves when morphology of the aortic root or ascending aorta cannot be assessed accurately by echocardiography. *(Level of Evidence: C)***

3. **Patients with bicuspid aortic valves and dilatation of the aortic root or ascending aorta (diameter greater than 4.0 cm*) should undergo serial evaluation of aortic root/ascending aorta size and morphology by echocardiography, cardiac magnetic resonance, or computed tomography on a yearly basis. *(Level of Evidence: C)***

4. **Surgery to repair the aortic root or replace the ascending aorta is indicated in patients with bicuspid aortic valves if the diameter of the aortic root or ascending aorta is greater than 5.0 cm* or if the rate of increase in diameter is 0.5 cm per year or more. *(Level of Evidence: C)***

5. **In patients with bicuspid valves undergoing AVR because of severe AS or AR (see Sections III-A-6 and III-B-2-g), repair of the aortic root or replacement of the ascending aorta is indicated if the diameter of the aortic root or ascending aorta is greater than 4.5 cm.* *(Level of Evidence: C)***

### Class IIa

1. **It is reasonable to give beta-adrenergic blocking agents to patients with bicuspid valves and dilated aortic roots (diameter greater than 4.0 cm*) who are not candidates for surgical correction and who do not have moderate to severe AR. *(Level of Evidence: C)***

2. **Cardiac magnetic resonance imaging or cardiac computed tomography is reasonable in patients with bicuspid aortic valves when aortic root dilatation is detected by echocardiography to further quantify severity of dilatation and involvement of the ascending aorta. *(Level of Evidence: B)***

*Consider lower threshold values for patients of small stature of either gender.*

Many patients with bicuspid aortic valves have disorders of vascular connective tissue that involve loss of elastic tissue (213,214), which may result in dilatation of the aortic root or ascending aorta even in the absence of hemodynamically significant AS or AR (215–218). Aortic root or ascending aortic dilatation can progress with time in this condition, and the risk of aortic dissection is related to the severity of dilatation (214,219–221). Recommendations for athletic participation in patients with bicuspid valve disease and associated dilatation of the aortic root or ascending aorta from the 36th Bethesda Conference (67) are based on limited data but with the understanding that aortic dissection can occur in some patients with aortic root or ascending aorta diameters less than 50 mm (208,220,222). Therapy with beta-adrenergic blocking agents might be effective in

slowing the progression of aortic dilatation, but the available data have been developed in patients with Marfan syndrome (223) and not in patients with bicuspid aortic valves.

The dimensions of the aortic root and ascending aorta show considerable variability in normal populations. Regression formulas and nomograms have been developed for adolescents and adults that account for age and body surface area (224). An upper limit of 2.1 cm per $m^2$ has been established at the level of the aortic sinuses. Dilatation is considered an increase in diameter above the norm for age and body surface area, and an aneurysm has been defined as a 50% increase over the normal diameter (225).

In recommending elective surgery for this condition, a number of factors must be considered, including the patient's age, the relative size of the aorta and aortic root, the structure and function of the aortic valve, and the experience of the surgical team (208,214,221,222). Aortic valve–sparing operations are feasible in most patients with dilatation of the aortic root or ascending aorta who do not have significant AR or aortic valve calcification (226–228). Patients with bicuspid valves should undergo elective repair of the aortic root or replacement of the ascending aorta if the diameter of these structures exceeds 5.0 cm. Such surgery should be performed by a surgical team with established expertise in these procedures. Others have recommended a value of 2.5 cm per $m^2$ or greater as the indication for surgery (229). If patients with bicuspid valves and associated aortic root enlargement undergo AVR because of severe AS or AR (Sections III-A-6 and III-B-2-g), it is recommended that repair of the aortic root or replacement of the ascending aorta be performed if the diameter of these structures is greater than 4.5 cm (230).

### D. Mitral Stenosis

In patients with MS from rheumatic fever, the pathological process causes leaflet thickening and calcification, commissural fusion, chordal fusion, or a combination of these processes (231,232). The normal MV area is 4.0 to 5.0 $cm^2$. Narrowing of the valve area to less than 2.5 $cm^2$ typically occurs before the development of symptoms (68). With a reduction in valve area by the rheumatic process, blood can flow from the left atrium to the left ventricle only if propelled by a pressure gradient, and the transmitral gradient is the fundamental expression of MS (233). The resulting elevation of left atrial pressure is reflected back into the pulmonary venous circulation. Decreased pulmonary venous compliance that results in part from an increased pulmonary endothelin-1 spillover rate may also contribute to increased pulmonary venous pressure (234). Increased pressure and distension of the pulmonary veins and capillaries can lead to pulmonary edema as pulmonary venous pressure exceeds that of plasma oncotic pressure. In patients with chronic MV obstruction, however, even when it is severe and pulmonary venous pressure is very high, pulmonary edema may not occur owing to a marked decrease in pulmonary microvascular permeability. The pulmonary ar-

terioles may react with vasoconstriction, intimal hyperplasia, and medial hypertrophy, which lead to pulmonary arterial hypertension.

### 1. Natural History

An MV area greater than 1.5 $cm^2$ 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. From hydraulic considerations, at any given orifice size, the transmitral gradient is a function of the square of the transvalvular flow rate and is dependent on the diastolic filling period (68). 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. As the obstruction across the MV increases, decreasing effort tolerance occurs. As the severity of stenosis increases, cardiac output becomes subnormal at rest and fails to increase during exercise.

The natural history of patients with untreated MS has been defined from studies in the 1950s and 1960s (235–237). MS is a continuous, progressive, lifelong disease, usually consisting of a slow, stable course in the early years followed by a progressive acceleration later in life (235–238). Once symptoms develop, there is another period of almost a decade before symptoms become disabling (235). In the asymptomatic or minimally symptomatic patient, survival is greater than 80% at 10 years, with 60% of patients having no progression of symptoms, but once significant limiting symptoms occur, there is a dismal 0% to 15% 10-year survival rate (235–239). When severe pulmonary hypertension develops, mean survival drops to less than 3 years (240). The mortality rate of untreated patients with MS is due to progressive pulmonary and systemic congestion in 60% to 70%, systemic embolism in 20% to 30%, pulmonary embolism in 10%, and infection in 1% to 5% (231,237). In North America and Europe, this classic history of MS has been replaced by an even milder, delayed course with the decline in incidence of rheumatic fever (238,241). The mean age of presentation is now in the fifth to sixth decade (238,241); more than one third of patients undergoing valvotomy are older than 65 years (242). In some geographic areas, MS progresses more rapidly, presumably owing to either a more severe rheumatic insult or repeated episodes of rheumatic carditis due to new streptococcal infections, which results in severe symptomatic MS in the late teens and early 20s (238).

Although MS is best described as a disease continuum, and there is no single value that defines severity, for these guidelines, MS severity is based on a variety of hemodynamic and natural history data (Table 1) using mean gradient, pulmonary artery systolic pressure, and valve area as follows: mild (area greater than 1.5 $cm^2$, mean gradient less than 5 mm Hg, or pulmonary artery systolic pressure less than 30 mm Hg), moderate (area 1.0 to 1.5 $cm^2$, mean gradient 5 to 10 mm Hg, or pulmonary artery systolic

pressure 30 to 50 mm Hg), and severe (area less than 1.0 cm$^2$, mean gradient greater than 10 mm Hg, or pulmonary artery systolic pressure greater than 50 mm Hg).

## 2. Indications for Echocardiography in Mitral Stenosis

### Class I

1.  **Echocardiography should be performed in patients for the diagnosis of MS, assessment of hemodynamic severity (mean gradient, MV area, and pulmonary artery pressure), assessment of concomitant valvular lesions, and assessment of valve morphology (to determine suitability for percutaneous mitral balloon valvotomy). (Level of Evidence: B)**
2.  **Echocardiography should be performed for re-evaluation in patients with known MS and changing symptoms or signs. (Level of Evidence: B)**
3.  **Echocardiography should be performed for assessment of the hemodynamic response of the mean gradient and pulmonary artery pressure by exercise Doppler echocardiography in patients with MS when there is a discrepancy between resting Doppler echocardiographic findings, clinical findings, symptoms, and signs. (Level of Evidence: C)**
4.  **TEE in MS should be performed to assess the presence or absence of left atrial thrombus and to further evaluate the severity of MR in patients considered for percutaneous mitral balloon valvotomy. (Level of Evidence: C)**
5.  **TEE in MS should be performed to evaluate MV morphology and hemodynamics in patients when transthoracic echocardiography provides suboptimal data. (Level of Evidence: C)**

### Class IIa

**Echocardiography is reasonable in the re-evaluation of asymptomatic patients with MS and stable clinical findings to assess pulmonary artery pressure (for those with severe MS, every year; moderate MS, every 1 to 2 years; and mild MS, every 3 to 5 years). (Level of Evidence: C)**

### Class III

**TEE in the patient with MS is not indicated for routine evaluation of MV morphology and hemodynamics when complete transthoracic echocardiographic data are satisfactory. (Level of Evidence: C)**

The diagnostic tool of choice in the evaluation of a patient with MS is 2D and Doppler echocardiography. Echocardiography is able to identify restricted diastolic opening of the MV leaflets due to "doming" of the anterior leaflet and immobility of the posterior leaflet. Planimetry of the orifice area may be possible from the short-axis view. 2-D echocardiography can be used to assess the morphological appearance of the MV apparatus, including leaflet mobility and flexibility, leaflet thickness, leaflet calcification, subval-

vular fusion, and the appearance of commissures (243–245). These features may be important when one considers the timing and type of intervention to be performed. Patients with mobile noncalcified leaflets, no commissural calcification, and little subvalvular fusion may be candidates for either balloon catheter or surgical commissurotomy/valvotomy. There are several methods used to assess suitability for valvotomy, including a Wilkins score (246), an echocardiographic grouping (based on valve flexibility, subvalvular fusion, and leaflet calcification) (244), and the absence or presence of commisural calcium (245).

The mean transmitral gradient can be accurately and reproducibly measured from the continuous-wave Doppler signal across the MV with the modified Bernoulli equation (247,248). The MV area can be noninvasively derived from Doppler echocardiography with either the diastolic pressure half-time method (248–251) or the continuity equation (249). Doppler echocardiography may also be used to estimate pulmonary artery systolic pressure from the TR velocity signal (252) and to assess severity of concomitant MR or AR. Formal hemodynamic exercise testing can be done noninvasively with either a supine bicycle or upright treadmill with Doppler recordings of transmitral and tricuspid velocities to assess both the transmitral gradient and pulmonary artery systolic pressure at rest and with exercise (253–257). The criteria for assessment of the severity of MS are summarized in Table 1 and are applicable when the heart rate is between 60 and 90 bpm.

In the asymptomatic patient who has documented mild MS (valve area greater than 1.5 cm$^2$ and mean gradient less than 5 mm Hg), no further investigations are needed on the initial workup (Fig. 4). These patients usually remain stable for years. If there is more significant MS, a decision to proceed further should be based on the suitability of the patient for mitral valvotomy. In patients with pliable, noncalcified valves with no or little subvalvular fusion, no calcification in the commissures, and no left atrial thrombus, percutaneous mitral valvotomy can be performed with a low complication rate and may be indicated if symptoms develop. Because of the slowly progressive course of MS, patients may remain "asymptomatic" with severe stenosis merely by readjusting their lifestyles to a more sedentary level. Patients with moderate pulmonary hypertension at rest (pulmonary artery systolic pressure greater than 50 mm Hg) and pliable MV leaflets may be considered for percutaneous mitral valvotomy even if they deny having symptoms. In patients who lead a sedentary lifestyle, a hemodynamic exercise test with Doppler echocardiography is useful, as noted above. Objective limitation of exercise tolerance with a rise in transmitral gradient greater than 15 mm Hg and a rise in pulmonary artery systolic pressure greater than 60 mm Hg may be an indication for percutaneous valvotomy if the MV morphology is suitable. In asymptomatic patients with severe MS (valve area less than 1.0 cm$^2$) and severe pulmonary hypertension (pulmonary artery systolic pressure greater than 75% of systemic pressure either at rest or with exercise) who do
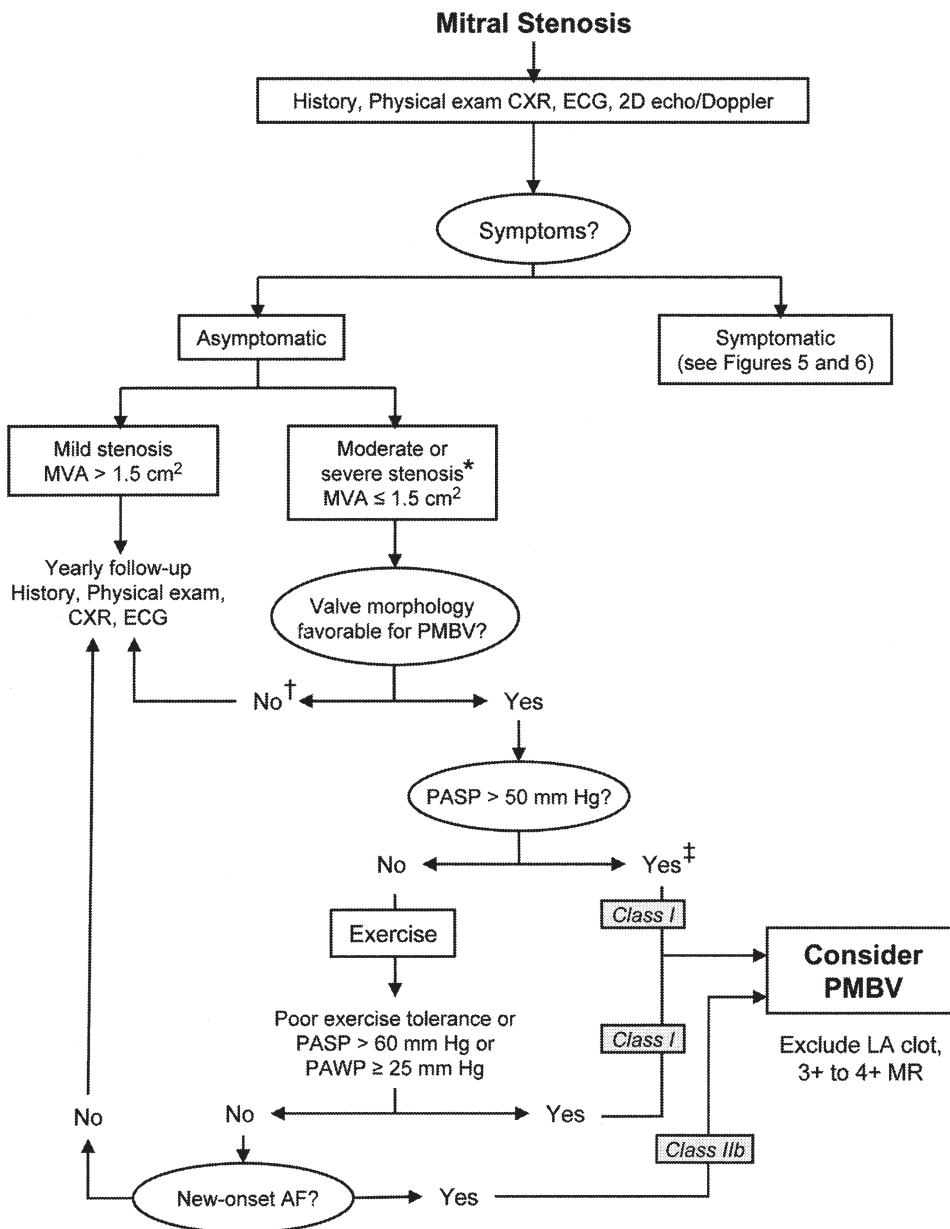
## Mitral Stenosis



**Figure 4.** Management strategy for patients with mitral stenosis. *The writing committee recognizes that there may be variability in the measurement of mitral valve area (MVA) and that the mean transmitral gradients, pulmonary artery wedge pressure (PAWP), and pulmonary artery systolic pressure (PASP) should also be taken into consideration. †There is controversy as to whether patients with severe mitral stenosis (MVA less than 1.0 cm²) and severe pulmonary hypertension (pulmonary artery pressure greater than 60 mm Hg) should undergo percutaneous mitral balloon valvotomy (PMBV) or mitral valve replacement to prevent right ventricular failure. ‡Assuming no other cause for pulmonary hypertension is present. AF indicates atrial fibrillation; CXR, chest X-ray; ECG, electrocardiogram; echo, echocardiography; LA, left atrial; MR, mitral regurgitation; 2D, 2-dimensional.

not have a valve morphology favorable for percutaneous mitral balloon valvotomy or surgical valve repair, it is controversial whether MV replacement should be performed to prevent right ventricular (RV) failure, but surgery is generally recommended in such patients.

### 3. Medical Therapy

#### a. Medical Therapy: General

Because rheumatic fever is the primary cause of MS, prophylaxis against rheumatic fever is recommended. Infective endocarditis is uncommon but does occur in isolated MS, and

appropriate endocarditis prophylaxis is also recommended. In patients with more than a mild degree of MS, counseling on avoidance of unusual physical stresses is advised. Agents with negative chronotropic properties, such as beta blockers or heart rate-regulating calcium channel blockers, may be of benefit in patients in sinus rhythm who have exertional symptoms if these symptoms occur with high heart rates. Salt restriction and intermittent administration of a diuretic are useful if there is evidence of pulmonary vascular congestion.

Although MS is a slowly progressive condition, acute pulmonary edema can occur suddenly in asymptomatic

patients with severe MS, especially with the onset of rapid atrial fibrillation, and this can be rapidly fatal. Thus, patients should be counseled to seek medical attention immediately if they experience a sudden marked increase in shortness of breath.

### b. Medical Therapy: Atrial Fibrillation

Thirty to forty percent of patients with symptomatic MS develop atrial fibrillation (235,236). There may be significant hemodynamic consequences that result from the acute development of atrial fibrillation, primarily from the rapid ventricular rate, which shortens the diastolic filling period and causes elevation of left atrial pressure. Atrial fibrillation occurs more commonly in older patients (235) 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 (237). 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, heart rate-regulating calcium channel blockers, or beta blockers should be used to control ventricular response. Intravenous or oral amiodarone can also be used when beta blockers or heart rate-regulating calcium channel blockers cannot be used. If there is hemodynamic instability, electrical cardioversion should be undertaken urgently, with intravenous heparin before, during, and after the procedure. In selected patients, chemical cardioversion may also be attempted. Patients who have been in atrial fibrillation longer than 24 to 48 hours without anticoagulation are at an increased risk for embolic events after cardioversion, but embolization may occur with less than 24 hours of atrial fibrillation. The decision to proceed with elective cardioversion is dependent on multiple factors, including duration of atrial fibrillation, hemodynamic response to the onset of atrial fibrillation, a documented history of prior episodes of atrial fibrillation, and a 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 longer than 24 to 48 hours and who has not been undergoing 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 more than 3 weeks, followed by elective cardioversion (258). The second is anticoagulation with heparin and TEE 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 (259). It is important to continue long-term anticoagulation after cardioversion.

Recurrent paroxysmal atrial fibrillation may be treated in selected patients with class IC antiarrhythmic drugs (in conjunction with a negative dromotropic agent) or class III antiarrhythmic drugs for maintenance of sinus rhythm. However, eventually, atrial fibrillation becomes resistant to prevention or cardioversion, and control of

ventricular response becomes the mainstay of therapy. Patients with either paroxysmal or sustained atrial fibrillation should be treated with long-term anticoagulation with warfarin to prevent embolic events. It is controversial whether percutaneous mitral valvotomy should be performed in patients with new-onset atrial fibrillation and moderate to severe MS who are otherwise asymptomatic.

### c. Medical Therapy: Prevention of Systemic Embolization

#### Class I

1. **Anticoagulation is indicated in patients with MS and atrial fibrillation (paroxysmal, persistent, or permanent).** *(Level of Evidence: B)*
2. **Anticoagulation is indicated in patients with MS and a prior embolic event, even in sinus rhythm.** *(Level of Evidence: B)*
3. **Anticoagulation is indicated in patients with MS with left atrial thrombus.** *(Level of Evidence: B)*

#### Class IIb

1. **Anticoagulation may be considered for asymptomatic patients with severe MS and left atrial dimension greater than or equal to 55 mm by echocardiography.\*** *(Level of Evidence: B)*
2. **Anticoagulation may be considered for patients with severe MS, an enlarged left atrium, and spontaneous contrast on echocardiography. *(Level of Evidence: C)***

*\*This recommendation is based on a grade C level of evidence given by the American College of Chest Physicians Fourth Consensus Conference on Antithrombotic Therapy (260).*

Systemic embolization may occur in 10% to 20% of patients with MS (235,236), with increasing risk related to age and atrial fibrillation (235,236,261). One third of embolic events occur within 1 month of the onset of atrial fibrillation, and two thirds occur within 1 year. An embolic event may thus be the initial manifestation of MS.

There are no randomized trials examining the efficacy of anticoagulation in preventing embolic events specifically in patients with MS, but retrospective studies have shown a 4- to 15-fold decrease in the incidence of embolic events with anticoagulation in these patients (262,263). Most studies involved patients who had 1 embolus before the onset of anticoagulation therapy. However, large randomized trials have demonstrated a significant reduction in embolic events by treatment with anticoagulation in patients with atrial fibrillation not associated with MS (264,265), and the subset of patients who benefited most from anticoagulation were those with the highest risk of embolic events. Patients with MS at the highest risk for future embolic events are those with prior embolic events and those with paroxysmal or persistent atrial fibrillation. 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 without atrial fibrillation or an embolic event who might be at higher risk for future embolic events (i.e., those with severe MS or an enlarged left atrium) should be considered for long-term warfarin therapy.

## 4. Recommendations Regarding Physical Activity and Exercise

In the majority of patients with MS, exertional symptoms are the limiting factor in terms of exercise tolerance. The 36th Bethesda Conference on Recommendations for Determining Eligibility for Competition in Athletes with Cardiovascular Abnormalities published guidelines for asymptomatic patients with MS who wish to engage in competitive athletics (67).

## 5. Serial Testing

In the asymptomatic patient, yearly re-evaluation is recommended (Fig. 4). At the time of the yearly evaluation, a history, physical examination, chest X-ray, and ECG should be obtained. An echocardiogram is not recommended yearly unless there is a change in clinical status or the patient has severe MS. Ambulatory ECG monitoring (Holter or event recorder) to detect paroxysmal atrial fibrillation is indicated in patients with palpitations.

## 6. Evaluation of the Symptomatic Patient

Patients who develop symptoms should undergo evaluation with a history, physical examination, ECG, chest X-ray, and echocardiogram (Figs. 5 and 6). 2-D and Doppler echocardiography is indicated to evaluate MV morphology, MV
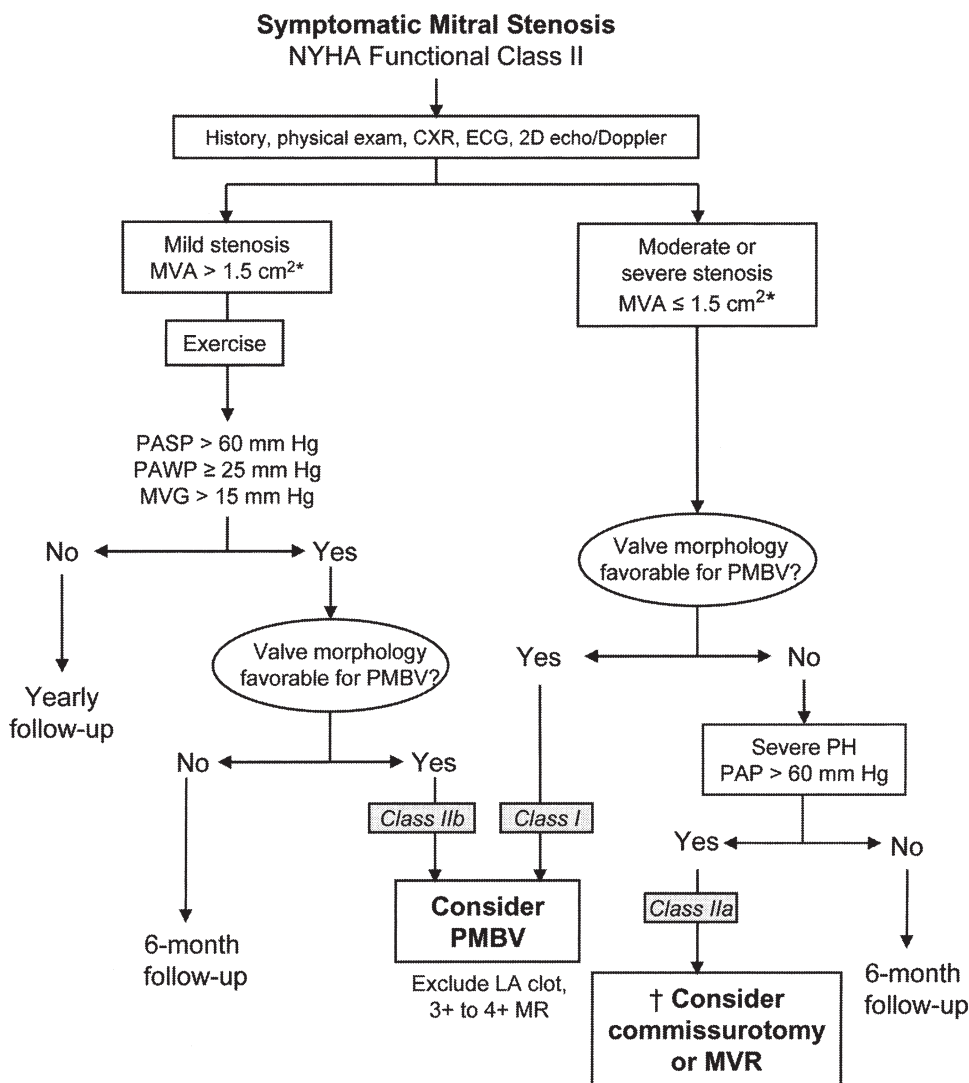


**Figure 5.** Management strategy for patients with mitral stenosis and mild symptoms. *The committee recognizes that there may be variability in the measurement of mitral valve area (MVA) and that the mean transmitral gradient, pulmonary artery wedge pressure (PAWP), and pulmonary artery systolic pressure (PASP) should also be taken into consideration. †There is controversy as to whether patients with severe mitral stenosis (MVA less than 1.0 cm²) and severe pulmonary hypertension (PH; PASP greater than 60 mm Hg) should undergo percutaneous mitral balloon valvotomy (PMBV) or mitral valve replacement (MVR) to prevent right ventricular failure. CXR indicates chest X-ray; ECG, electrocardiogram; echo, echocardiography; LA, left atrial; MR, mitral regurgitation; MVG, mean mitral valve pressure guidelines; NYHA, New York Heart Association; PAP, pulmonary artery pressure; 2D, 2-dimensional.
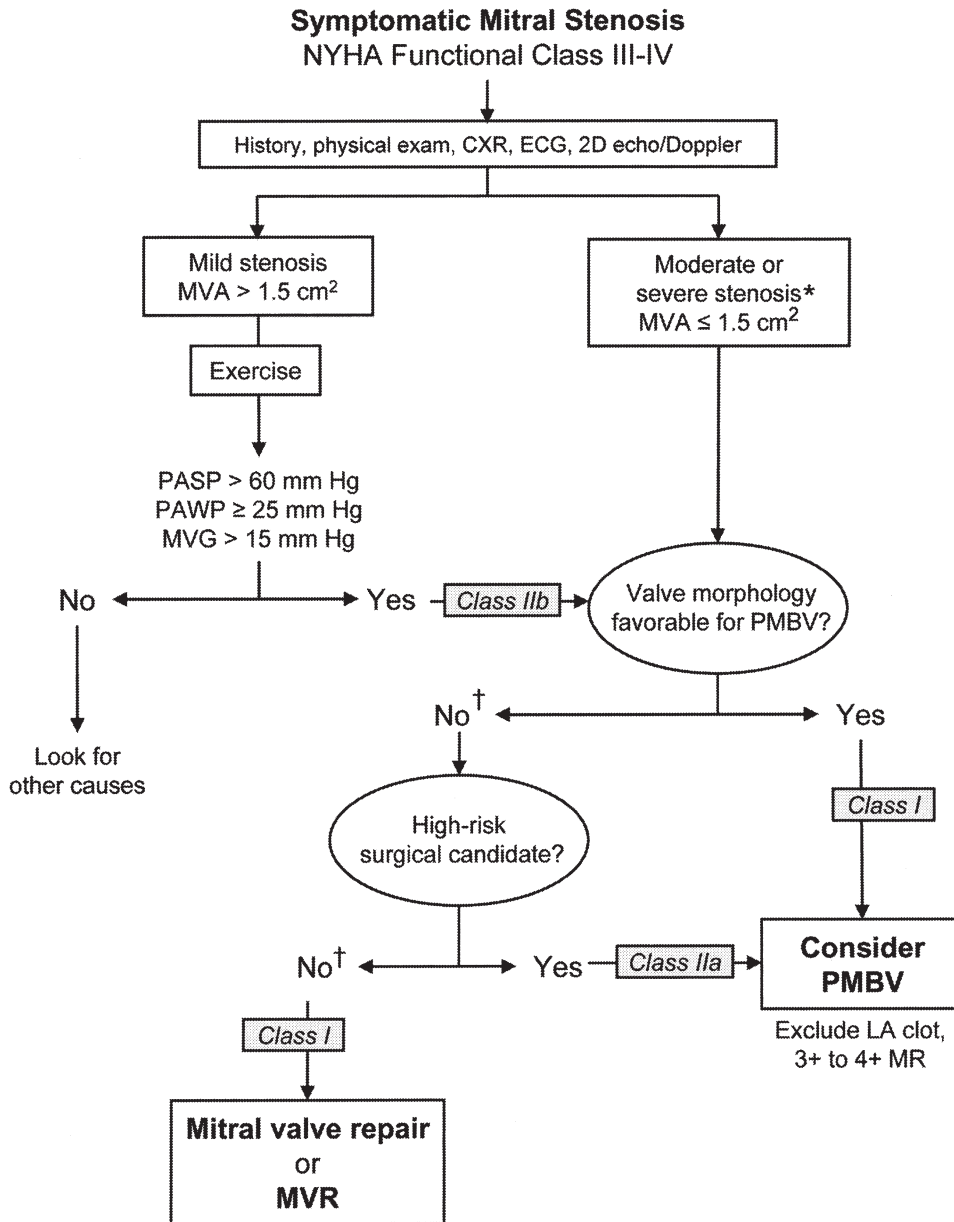
**Figure 6.** Management strategy for patients with mitral stenosis and moderate to severe symptoms. *The writing committee recognizes that there may be variability in the measurement of mitral valve area (MVA) and that the mean transmitral gradient, pulmonary artery wedge pressure (PAWP), and pulmonary artery systolic pressure (PASP) should also be taken into consideration. †It is controversial as to which patients with less favorable valve morphology should undergo percutaneous mitral balloon valvotomy (PMBV) rather than mitral valve surgery (see text). CXR, chest X-ray; ECG, electrocardiogram; echo, echocardiography; LA, left atrial; MR, mitral regurgitation; MVG, mean mitral valve pressure gradient; MVR, mitral valve replacement; NYHA, New York Heart Association; 2D, 2-dimensional.

hemodynamics, and pulmonary artery pressure. Patients with NYHA functional class II symptoms and moderate or severe MS (MV area less than or equal to 1.5 cm² or mean gradient greater than 5 mm Hg) may be considered for mitral balloon valvotomy if they have suitable MV morphology and no left atrial thrombi. Patients who have NYHA functional class III or IV symptoms and evidence of severe MS have a poor prognosis if left untreated and should be considered for intervention with either balloon valvotomy or surgery.

Formal exercise testing or dobutamine stress testing may be useful to differentiate symptoms due to 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 with either supine bicycle or upright exercise with Doppler recording of TR and transmitral velocities. Right- and left-heart catheterization with exercise may be helpful and occasionally necessary. Patients who are symptomatic with a significant elevation of pulmonary artery pressure (greater than 60 mm Hg), mean transmitral gradient (greater than 15 mm Hg), or pulmonary artery wedge pressure (greater than 25 mm Hg) during exercise

have hemodynamically significant MS and should be considered for further intervention.

### 7. Indications for Invasive Hemodynamic Evaluation

#### Class I

1. Cardiac catheterization for hemodynamic evaluation should be performed for assessment of severity of MS when noninvasive tests are inconclusive or when there is discrepancy between noninvasive tests and clinical findings regarding severity of MS. *(Level of Evidence: C)*
2. Catheterization for hemodynamic evaluation including left ventriculography (to evaluate severity of MR) for patients with MS is indicated when there is a discrepancy between the Doppler-derived mean gradient and valve area. *(Level of Evidence: C)*

#### Class IIa

1. Cardiac catheterization is reasonable to assess the hemodynamic response of pulmonary artery and left atrial pressures to exercise when clinical symptoms and resting hemodynamics are discordant. *(Level of Evidence: C)*
2. Cardiac catheterization is reasonable in patients with MS to assess the cause of severe pulmonary arterial hypertension when out of proportion to severity of MS as determined by noninvasive testing. *(Level of Evidence: C)*

#### Class III

Diagnostic cardiac catheterization is not recommended to assess the MV hemodynamics when 2D and Doppler echocardiographic data are concordant with clinical findings. *(Level of Evidence: C)*

With the advent of Doppler echocardiography, cardiac catheterization is no longer required for assessment of hemodynamics in the majority of patients with isolated MS. There is often overestimation of the transmitral gradient when catheterization is performed with pulmonary artery wedge pressure as a substitute for left atrial pressure, even after correction for phase delay. Thus, the transmitral gradient derived by Doppler echocardiography may be more accurate than that obtained by cardiac catheterization with pulmonary artery wedge pressure (266).

In most instances, Doppler measurements of transmitral gradient, valve area, and pulmonary pressure will 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-side 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 the severity of MR) is indicated when there is a discrepancy between the Doppler-derived mean gradient and valve area. If symptoms

appear to be out of proportion to noninvasive assessment of resting hemodynamics, right- and left-heart catheterization with exercise may be useful. Coronary angiography may be required in selected patients who may need intervention (see Section X-B).

### 8. Indications for Percutaneous Mitral Balloon Valvotomy

#### Class I

1. Percutaneous mitral balloon valvotomy is effective for symptomatic patients (NYHA functional class II, III, or IV), with moderate or severe MS* and valve morphology favorable for percutaneous mitral balloon valvotomy in the absence of left atrial thrombus or moderate to severe MR. *(Level of Evidence: A)*
2. Percutaneous mitral balloon valvotomy is effective for asymptomatic patients with moderate or severe MS* and valve morphology that is favorable for percutaneous mitral balloon valvotomy who have pulmonary hypertension (pulmonary artery systolic pressure greater than 50 mm Hg at rest or greater than 60 mm Hg with exercise) in the absence of left atrial thrombus or moderate to severe MR. *(Level of Evidence: C)*

#### Class IIa

Percutaneous mitral balloon valvotomy is reasonable for patients with moderate or severe MS* who have a nonpliable calcified valve, are in NYHA functional class III–IV, and are either not candidates for surgery or are at high risk for surgery. *(Level of Evidence: C)*

#### Class IIb

1. Percutaneous mitral balloon valvotomy may be considered for asymptomatic patients with moderate or severe MS* and valve morphology favorable for percutaneous mitral balloon valvotomy who have new onset of atrial fibrillation in the absence of left atrial thrombus or moderate to severe MR. *(Level of Evidence: C)*
2. Percutaneous mitral balloon valvotomy may be considered for symptomatic patients (NYHA functional class II, III, or IV) with MV area greater than 1.5 cm$^2$ if there is evidence of hemodynamically significant MS based on pulmonary artery systolic pressure greater than 60 mm Hg, pulmonary artery wedge pressure of 25 mm Hg or more, or mean MV gradient greater than 15 mm Hg during exercise. *(Level of Evidence: C)*
3. Percutaneous mitral balloon valvotomy may be considered as an alternative to surgery for patients with moderate or severe MS who have a nonpliable calcified valve and are in NYHA class III–IV. *(Level of Evidence: C)*

#### Class III

1. Percutaneous mitral balloon valvotomy is not indicated for patients with mild MS. *(Level of Evidence: C)*

2. **Percutaneous mitral balloon valvotomy should not be performed in patients with moderate to severe MR or left atrial thrombus. (Level of Evidence: C)**

*See Table 1 (7).*

The immediate results of percutaneous mitral valvotomy are similar to those of mitral commissurotomy (267–276). The mean valve area usually doubles (from 1.0 to 2.0 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 an MV area greater than 1.5 cm$^2$ and a decrease in left atrial pressure to less than 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.

Event-free survival after percutaneous balloon valvotomy (freedom from death, repeat valvotomy, or MV replacement) overall is 50% to 65% over 3 to 7 years, with an event-free survival of 80% to 90% in patients with favorable MV morphology (245,269,271–278). 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 (279–284). 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 (282,283) indicate more favorable hemodynamic and symptomatic results with percutaneous balloon valvotomy than with closed commissurotomy.

The immediate results, acute complications, and follow-up results of percutaneous balloon valvotomy are dependent on multiple factors. It is of utmost importance that this procedure be performed in centers with skilled and experienced operators. Other factors include age, NYHA functional class, stenosis severity, LV end-diastolic pressure, cardiac output, and pulmonary artery wedge pressure (269,271,272,276). The underlying MV morphology is the factor of greatest importance in determining outcome (243–246,269,272,273,276,277,285–288), and immediate postvalvotomy hemodynamics are predictive of long-term clinical outcome (271,273,276). 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.

Patients who are being considered for an intervention should undergo evaluation with a history, physical examination, and 2D and Doppler echocardiographic examination. The appearance and mobility of the MV apparatus and commissures should be evaluated by 2D echocardiography, and the transmitral gradient, MV area, and pulmonary artery pressure should be obtained from the Doppler examination. If there is a discrepancy between symptoms and hemodynamics, a formal hemodynamic exercise test may be performed.

Relative contraindications to percutaneous balloon valvotomy include the presence of a left atrial thrombus and significant (3+ to 4+) MR. Patients thought to be candidates for percutaneous mitral valvotomy should undergo TEE to rule out left atrial thrombus and to examine the severity of MR. Percutaneous mitral balloon valvotomy should be performed only by skilled operators at institutions with extensive experience in performing the technique (267,270). Thus, the decision to proceed with percutaneous balloon valvotomy or surgical commissurotomy is dependent on the experience of the operator and institution. Because of the less invasive nature of percutaneous balloon valvotomy compared with surgical intervention, appropriate patients without symptoms or those with NYHA functional class II symptoms may be considered for catheter-based therapy (Figs. 4 and 5).

### 9. Indications for Surgery for Mitral Stenosis

**Class I**

1. **MV surgery (repair if possible) is indicated in patients with symptomatic (NYHA functional class III–IV) moderate or severe MS\* when 1) percutaneous mitral balloon valvotomy is unavailable, 2) percutaneous mitral balloon valvotomy is contraindicated because of left atrial thrombus despite anticoagulation or because concomitant moderate to severe MR is present, or 3) the valve morphology is not favorable for percutaneous mitral balloon valvotomy in a patient with acceptable operative risk. (Level of Evidence: B)**

2. **Symptomatic patients with moderate to severe MS\* who also have moderate to severe MR should receive MV replacement, unless valve repair is possible at the time of surgery. (Level of Evidence: C)**

**Class IIa**

MV replacement is reasonable for patients with severe MS\* and severe pulmonary hypertension (pulmonary artery systolic pressure greater than 60 mm Hg) with NYHA functional class I–II symptoms who are not considered candidates for percutaneous mitral balloon valvotomy or surgical MV repair. (Level of Evidence: C)

**Class IIb**

MV repair may be considered for asymptomatic patients with moderate or severe MS\* who have had recurrent embolic events while receiving adequate anticoagulation and who have valve morphology favorable for repair. (Level of Evidence: C)

**Class III**

1. **MV repair for MS is not indicated for patients with mild MS. (Level of Evidence: C)**

2. **Closed commissurotomy should not be performed in patients undergoing MV repair; open commissurotomy is the preferred approach.** *(Level of Evidence: C)*

*\*See Table 1 (7).*

If there is significant calcification, fibrosis, and subvalvular fusion of the MV apparatus, commissurotomy or percutaneous balloon valvotomy is less likely to be successful, and MV replacement will be necessary. Given the risk of MV replacement and the potential long-term complications of a prosthetic valve, there are stricter indications for MV operation in these patients with calcified fibrotic valves. In the patient with NYHA functional class III symptoms due to severe MS or combined MS/MR, MV replacement results in excellent symptomatic improvement. Postponement of surgery until the patient reaches the functional class IV symptomatic state should be avoided, because operative mortality is high and the long-term outcome is 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 less than 1 cm$^2$) and severe pulmonary hypertension (pulmonary artery systolic pressure greater than 60 to 80 mm Hg) should undergo MV replacement to prevent RV failure, but surgery is generally recommended in such patients. It is recognized that patients with such severe pulmonary hypertension are rarely asymptomatic.

### 10. Management of Patients After Valvotomy or Commissurotomy

A baseline echocardiogram should be performed after the procedure to obtain a baseline measurement of postoperative hemodynamics and to exclude significant complications such as MR, LV dysfunction, or atrial septal defect (in the case of percutaneous valvotomy). This echocardiogram should be performed at least 72 h after the procedure, because acute changes in atrial and ventricular compliance immediately after the procedure affect the reliability of the half-time in calculation of valve area (249,250). Patients with severe MR or a large atrial septal defect should be considered for early surgery; however, the majority of small left-to-right shunts at the atrial level will close spontaneously over the course of 6 months.

Repeat percutaneous balloon valvotomy can be performed in the patient in whom there is restenosis after either a prior surgical commissurotomy or balloon valvotomy (289,290). The results of these procedures are adequate in many patients but may be less satisfactory than the overall results of initial valvotomy because there is usually more valve deformity, calcification, and fibrosis than with the initial procedure (286,290,291).

### E. Mitral Valve Prolapse

Utilizing current echocardiographic criteria for diagnosing MVP (valve prolapse of 2 mm or more above the mitral annulus in the long-axis parasternal view and other views (292), the prevalence of this entity is 1% to 2.5% of the population (293). MVP occurs as a clinical entity with or without thickening (5 mm or greater, measured during diastasis) and with or without MR.

The basic microscopic feature of primary MVP is marked proliferation of the spongiosa, the delicate myxomatous connective tissue between the atrialis (a thick layer of collagen and elastic tissue that forms the atrial aspect of the leaflet) and the fibrosa or ventricularis (dense layer of collagen that forms the basic support of the leaflet). Myxomatous proliferation of the acid mucopolysaccharide–containing spongiosa tissue causes focal interruption of the fibrosa. Secondary effects of the primary MVP syndrome include fibrosis of the surface of the MV leaflets, thinning and/or elongation of the chordae tendineae, and ventricular friction lesions.

#### 1. Natural History

The natural history of asymptomatic MVP is heterogeneous and can vary from benign with normal life expectancy to adverse with significant morbidity or mortality. The most frequent predictor of cardiovascular mortality is moderate to severe MR and, less frequently, an LV ejection fraction less than 0.50 (294). Echocardiographic evidence of thickened MV leaflets (5 mm or greater) is also a predictor of complications related to MVP (295–299). In most patients, MVP is associated with a benign prognosis (300,301), with an age-adjusted survival rate for both men and women similar to that of individuals without this entity (302).

In some patients, after an initially prolonged asymptomatic interval, the entire process may enter an accelerated phase as a result of left atrial and ventricular dysfunction and atrial fibrillation. In some instances, spontaneous rupture of MV chordae will occur. Infective endocarditis is a serious complication of MVP, which is the leading predisposing cardiovascular diagnosis in most series of patients reported with endocarditis. Several studies have indicated an increased likelihood of cerebrovascular accidents in patients under 45 years of age who have MVP beyond what would have been expected in a similar population without MVP (303).

Sudden death is a rare complication of MVP, occurring in fewer than 2% of known cases during long-term follow-up (296,303–309). Annual mortality rates are less than 1% per year.

#### 2. Evaluation and Management of the Asymptomatic Patient

**Class I**

**Echocardiography is indicated for the diagnosis of MVP and assessment of MR, leaflet morphology, and**

ventricular compensation in asymptomatic patients with physical signs of MVP. *(Level of Evidence: B)*

**Class IIa**

1. **Echocardiography can effectively exclude MVP in asymptomatic patients who have been diagnosed without clinical evidence to support the diagnosis.** *(Level of Evidence: C)*
2. **Echocardiography can be effective for risk stratification in asymptomatic patients with physical signs of MVP or known MVP.** *(Level of Evidence: C)*

**Class III**

1. **Echocardiography is not indicated to exclude MVP in asymptomatic patients with ill-defined symptoms in the absence of a constellation of clinical symptoms or physical findings suggestive of MVP or a positive family history.** *(Level of Evidence: B)*
2. **Routine repetition of echocardiography is not indicated for the asymptomatic patient who has MVP and no MR or MVP and mild MR with no changes in clinical signs or symptoms.** *(Level of Evidence: C)*

The primary diagnostic evaluation of the patient with MVP is the physical examination (307,310). However, MVP can be present in the absence of the classic auscultatory findings, and systolic clicks may be intermittent and variable.

2D and Doppler echocardiography is the most useful noninvasive tests for defining MVP. Valve prolapse of 2 mm or more above the mitral annulus in the long-axis parasternal view and other views, especially when the leaflet coaptation occurs on the atrial side of the annular plane, indicates a high likelihood of MVP. There is disagreement concerning the reliability of the echocardiographic appearance of anterior leaflet billowing when observed only in the apical 4-chamber view (297,311). Leaflet thickness of 5 mm or more indicates abnormal leaflet thickness, and its added presence makes MVP even more certain. Leaflet redundancy is often associated with an enlarged mitral annulus and elongated chordae tendineae (307). The absence or presence of MR is an important consideration, and MVP is more likely when MR is detected as a high-velocity eccentric jet in late systole (312).

Antibiotic prophylaxis, for the prevention of endocarditis during procedures associated with bacteremia, is recommended for most patients with a definite diagnosis of MVP, particularly if there is associated MR (313). The committee recommends that patients without MR who have leaflet thickening, elongated chordae, left atrial enlargement, or LV dilatation receive endocarditis prophylaxis (295–299,314) (see Section II-C-1).

**3. Evaluation and Management of the Symptomatic Patient**

**Class I**

1. **Aspirin therapy (75 to 325 mg per day) is recommended for symptomatic patients with MVP who experience cerebral transient ischemic attacks.** *(Level of Evidence: C)*
2. **In patients with MVP and atrial fibrillation, warfarin therapy is recommended for patients aged greater than 65 or those with hypertension, MR murmur, or a history of heart failure.** *(Level of Evidence: C)*
3. **Aspirin therapy (75 to 325 mg per day) is recommended for patients with MVP and atrial fibrillation who are less than 65 years old and have no history of MR, hypertension, or heart failure.** *(Level of Evidence: C)*
4. **In patients with MVP and a history of stroke, warfarin therapy is recommended for patients with MR, atrial fibrillation or left atrial thrombus.** *(Level of Evidence: C)*

**Class IIa**

1. **In patients with MVP and a history of stroke, who do not have MR, atrial fibrillation or left atrial thrombus, warfarin therapy is reasonable for patients with echocardiographic evidence of thickening (5 mm or greater) and/or redundancy of the valve leaflets.** *(Level of Evidence: C)*
2. **In patients with MVP and a history of stroke, aspirin therapy is reasonable for patients who do not have MR, atrial fibrillation, left atrial thrombus, or echocardiographic evidence of thickening (5mm or greater) or redundancy of the valve leaflets.** *(Level of Evidence: C)*
3. **Warfarin therapy is reasonable for patients with MVP with transient ischemic attacks despite aspirin therapy.** *(Level of Evidence: C)*
4. **Aspirin therapy (75 to 325 mg per day) can be beneficial for patients with MVP and a history of stroke who have contraindications to anticoagulants.** *(Level of Evidence: B)*

**Class IIb**

**Aspirin therapy (75 to 325 mg per day) may be considered for patients in sinus rhythm with echocardiographic evidence of high-risk MVP.** *(Level of Evidence: C)*

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 (315). In many cases, however, the cessation of stimulants such as caffeine, alcohol, and cigarettes may be sufficient to control symptoms.

Daily aspirin therapy (75 to 325 mg per day) is recommended for MVP patients with documented transient focal

neurological events who are in sinus rhythm with no atrial thrombi. Such patients also should avoid cigarettes and oral contraceptives. The American Stroke Association guidelines (315a) recommend aspirin for patients with MVP who have experienced an ischemic stroke (class IIa, level of evidence C), based on the evidence of efficacy of antiplatelet agents for general stroke patients. No randomized trials have addressed the efficacy of selected antithrombotic therapies for the specific subgroup of stroke patients with MVP. In the current guidelines, the committee recommends aspirin for those post-stroke patients with MVP who have no evidence of MR, atrial fibrillation, left artrial thrombus, or echocardiographic evidence of thickening (5mm or greater) or redundancy of the valve leaflets. However, long-term anticoagulation therapy with warfarin is recommended (class I) for post-stroke patients with MVP who have MR, atrial fibrillation, or left atrial thrombus. In the absence of these indications, warfarin is also recommended (class IIa) in post-stroke patients with MVP who have echocardiographic evidence of thickening (5 mm or greater) or redundancy of the valve leaflets and in MVP patients who experience recurrent transient ischemic attacks while taking aspirin. In each of these situations, the international normalized ratio (INR) should be maintained between 2.0 to 3.0).

In MVP patients with atrial fibrillation, warfarin therapy is indicated in patients aged greater than 65 years and in those with MR, hypertension, or a history of heart failure (INR 2.0 to 3.0). Aspirin therapy is satisfactory in patients with atrial fibrillation who are younger than 65 years old, have no MR, and have no history of hypertension or heart failure (316,317). Daily aspirin therapy is often recommended for patients with high-risk echocardiographic characteristics.

A normal lifestyle and regular exercise are encouraged for most patients with MVP, especially those who are asymptomatic (309,317). Restriction from competitive sports is recommended when moderate LV enlargement, LV dysfunction, uncontrolled tachyarrhythmias, long-QT interval, unexplained syncope, prior resuscitation from cardiac arrest, or aortic root enlargement is present individually or in combination (307).

Asymptomatic patients with MVP and no significant MR can be evaluated clinically every 3 to 5 years. Serial echocardiography is not necessary in most patients and is recommended only in patients who have high-risk characteristics on the initial echocardiogram and in those who develop symptoms consistent with cardiovascular disease or who have a change in physical findings that suggests development of significant MR. Patients who have high-risk characteristics, including those with moderate to severe MR, should be followed up once a year.

Patients with severe MR with symptoms or impaired LV systolic function require cardiac catheterization and evaluation for MV surgery (see Section III-F-3-b). The thickened, redundant MV can often be repaired rather than replaced, with a low operative mortality and excellent short- and long-term results (318,319).

## 4. Surgical Considerations

Management of MVP may require surgery, particularly in those patients who develop a flail leaflet due to rupture of chordae tendineae or their marked elongation. Most such valves can be repaired successfully by surgeons experienced in MV repair, especially when the posterior leaflet of the MV is predominantly affected. MV repair for MR due to MVP is associated with excellent long-term survival and remains superior to MV replacement beyond 10 years and up to 20 years after surgery (318,319). Anterior leaflet repair is associated with a higher risk for reoperation than posterior leaflet repair. As noted in Section III-F-3-b, cardiologists are strongly encouraged to refer patients who are candidates for complex MV repair to surgical centers experienced in performing MV repair. Residual MR is associated with a higher risk for reoperation (319). Recommendations for surgery in patients with MVP and MR are the same as for those with other forms of nonischemic severe MR (see Section VII-B-1-c).

### F. Mitral Regurgitation

#### 1. Acute Severe Mitral Regurgitation

##### a. Diagnosis

The patient with acute severe MR is almost always severely 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 may not be holosystolic and may even be absent. Transthoracic echocardiography may demonstrate the disruption of the MV and provide semiquantitative information on lesion severity; however, transthoracic echocardiography may underestimate lesion severity by inadequate imaging of the color flow jet, and TEE should be performed if MV morphology and regurgitant severity are still in question after transthoracic echocardiography. TEE is also helpful in demonstrating the anatomic cause of acute severe MR and directing successful surgical repair.

##### b. Medical Therapy

In acute severe MR, medical therapy has a limited role and is aimed primarily to stabilize hemodynamics in preparation for surgery. In the normotensive patient, nitroprusside may effectively diminish the amount of MR, which in turn increases forward output and reduces pulmonary congestion. In the hypotensive patient, nitroprusside should not be administered alone, 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 the patient while they are prepared for surgery. If infective endocarditis is the cause of acute MR, identification and treatment of the infectious organism are essential.

## 2. Chronic Asymptomatic Mitral Regurgitation

### a. Natural History

Patients with mild to moderate MR may remain asymptomatic with little or no hemodynamic compromise for many years; however, MR from a primary MV abnormality tends to progress over time with an increase in volume overload due to an increase in the effective orifice area. Progression of the MR is variable and is determined by progression of lesions or mitral annulus size (320).

The compensated phase of MR is variable but may last for many years, but 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 (321–323). Correction of MR should be performed before the advanced phases of LV decompensation.

Numerous studies indicate that patients with chronic severe MR have a high likelihood of developing symptoms or LV dysfunction over the course of 6 to 10 years (313,317,324,325). However, the incidence of sudden death in asymptomatic patients with normal LV function varies widely among these studies.

The natural history of severe MR due to a flail posterior leaflet has been documented (313). At 10 years, 90% of patients are dead or require MV operation. The mortality rate in patients with severe MR caused by flail leaflets is 6% to 7% per year. However, patients at risk of death are predominantly those with LV ejection fractions less than 0.60 or with NYHA functional class III–IV symptoms, and less so those who are asymptomatic and have normal LV function (313,326). Severe symptoms also predict a poor outcome after MV repair or replacement (326).

### b. Indications for Transthoracic Echocardiography

#### Class I

1. **Transthoracic echocardiography is indicated for baseline evaluation of LV size and function, RV and left atrial size, pulmonary artery pressure, and severity of MR (Table 1) in any patient suspected of having MR.** *(Level of Evidence: C)*
2. **Transthoracic echocardiography is indicated for delineation of the mechanism of MR.** *(Level of Evidence: B)*
3. **Transthoracic echocardiography is indicated for annual or semiannual surveillance of LV function (estimated by ejection fraction and end-systolic dimension) in asymptomatic patients with moderate to severe MR.** *(Level of Evidence: C)*

4. **Transthoracic echocardiography is indicated in patients with MR to evaluate the MV apparatus and LV function after a change in signs or symptoms.** *(Level of Evidence: C)*
5. **Transthoracic echocardiography is indicated to evaluate LV size and function and MV hemodynamics in the initial evaluation after MV replacement or MV repair.** *(Level of Evidence: C)*

#### Class IIa

**Exercise Doppler echocardiography is reasonable in asymptomatic patients with severe MR to assess exercise tolerance and the effects of exercise on pulmonary artery pressure and MR severity.** *(Level of Evidence: C)*

#### Class III

**Transthoracic echocardiography is not indicated for routine follow-up evaluation of asymptomatic patients with mild MR and normal LV size and systolic function.** *(Level of Evidence: C)*

An initial comprehensive 2D Doppler echocardiogram provides a baseline estimation of LV and left atrial size, an estimation of LV ejection fraction, and approximation of the severity of MR (1). Quantification of the severity of MR (Table 1) is strongly recommended (7,324,327,328). In the majority of patients, an estimate of pulmonary artery pressure can be obtained from the TR peak velocity. Changes from these baseline values are used subsequently to guide the timing of MV surgery.

The initial transthoracic echocardiogram should disclose the anatomic cause of the MR. A central color flow jet of MR with a structurally normal MV apparatus suggests the presence of functional MR, which may be due to annular dilatation from LV dilatation or tethering of the posterior leaflet because of regional LV dysfunction in patients with ischemic heart disease. An eccentric color flow jet of MR with abnormalities of the MV apparatus indicates organic MR. In patients with organic MR, the echocardiogram should assess the presence of calcium in the annulus or leaflets, the redundancy of the valve leaflets, and the MV leaflet involved (anterior leaflet, posterior leaflet, or bileaflet). These factors will help determine the feasibility of valve repair if surgery is contemplated. The system proposed by Carpentier (329) identifies the anatomic and physiologic characteristics of the valve that aid the surgeon in planning MV repair. The valve dysfunction is described on the basis of the motion of the free edge of the leaflet relative to the plane of the annulus: type I, normal; type II, increased, as in MVP; type IIIA, restricted during systole and diastole, and type IIIB, restricted during systole.

Multiple parameters from the Doppler examination should be used to diagnose severe MR (Table 1), including the color flow jet width and area, the intensity of the continuous-wave Doppler signal, the pulmonary venous flow contour, the peak early mitral inflow velocity, and quantitative measures of

effective orifice area and regurgitation volume (1). In addition, there should be enlargement of the left ventricle and left atrium in chronic severe MR. Abnormalities of the MV apparatus are often present if there is severe MR, but ischemic LV dysfunction may also result in severe MR. If a discrepancy is present, or if the patient has poor windows on transthoracic echocardiography, then further evaluation of the severity of MR is required, including cardiac catheterization, magnetic resonance imaging, or TEE.

### c. Indications for Transesophageal Echocardiography

**Class I**

1. **Preoperative or intraoperative TEE is indicated to establish the anatomic basis for severe MR in patients in whom surgery is recommended to assess feasibility of repair and to guide repair. *(Level of Evidence: B)***
2. **TEE is indicated for evaluation of MR patients in whom transthoracic echocardiography provides nondiagnostic information regarding severity of MR, mechanism of MR, and/or status of LV function. *(Level of Evidence: B)***

**Class IIa**

**Preoperative TEE is reasonable in asymptomatic patients with severe MR who are considered for surgery to assess feasibility of repair. *(Level of Evidence: C)***

**Class III**

**TEE is not indicated for routine follow-up or surveillance of asymptomatic patients with native valve MR. *(Level of Evidence: C)***

### d. Serial Testing

Asymptomatic patients with mild MR and no evidence of LV enlargement, LV dysfunction, or pulmonary hypertension can be followed 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 MR has worsened. In patients with moderate MR, clinical evaluation including echocardiography should be performed annually and sooner if symptoms occur.

In asymptomatic patients with severe MR, clinical evaluation and echocardiography should be performed every 6 to 12 months to assess symptoms or transition to asymptomatic LV dysfunction. Exercise stress testing may be used to add objective evidence regarding symptoms and changes in exercise tolerance. Exercise testing is especially important if a good history of the patient's exercise capacity cannot be obtained. Measurement of pulmonary artery pressure and assessment of severity of MR during exercise may be helpful.

Although interpretation of LV ejection fraction in patients with severe MR is difficult because the loading conditions facilitate ejection, several studies indicate that the preoperative ejection fraction is an important predictor of postoperative survival in patients with chronic MR (321,330–333). Ejection fraction in a patient with MR with normal LV function is usually greater than or equal to 0.60. Consistent with this concept, postoperative ventricular function is lower and survival is reduced in patients with a preoperative ejection fraction less than 0.60 compared with patients with higher ejection fractions (332,333).

Alternatively or in concert, LV end-systolic dimension (or volume), which may be less load dependent than ejection fraction, can be used in timing of MV surgery. End-systolic dimension should be less than 40 mm preoperatively to ensure normal postoperative LV function (333–336).

If patients become symptomatic, they should undergo MV surgery even if LV function appears to be normal.

### e. Guidelines for Physical Activity and Exercise

Recommendations regarding participation in competitive athletics were published by the Task Force on Acquired Valvular Heart Disease of the 36th Bethesda Conference (67). Asymptomatic patients with MR of any severity who are in sinus rhythm and who have normal LV and left atrial dimensions and normal pulmonary artery pressure may exercise without restriction (67). However, those with definite LV enlargement (greater than or equal to 60 mm), pulmonary hypertension, or any degree of LV systolic dysfunction at rest should not participate in any competitive sports.

### f. Medical Therapy

In asymptomatic patients with chronic MR, there is no generally accepted medical therapy. Although the use of vasodilators may appear to be logical for the same reasons that they are effective in acute MR, there are no large long-term studies to indicate that they are beneficial. Thus, in the absence of systemic hypertension, there is no known indication for the use of vasodilating drugs or ACE inhibitors in asymptomatic patients with MR and preserved LV function.

However, in patients with functional or ischemic MR (resulting from dilated or ischemic cardiomyopathy), there is reason to believe that preload reduction may be beneficial (337). If LV systolic dysfunction is present, primary treatment of the LV systolic dysfunction with drugs such as ACE inhibitors or beta blockers (particularly carvedilol) and biventricular pacing have all been shown to reduce the severity of functional MR (338–341).

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 rate-lowering calcium channel blockers, beta blockers, digoxin, or, rarely, amiodarone. In patients with severe MR and chronic atrial fibrillation, a Maze

procedure may be added to an MV repair (see Atrial Fibrillation in Section III-F-3-b), because this will reduce the risk of postoperative stroke. Patients with MR and atrial fibrillation should receive chronic anticoagulation, with the INR maintained at 2.0 to 3.0.

### g. Indications for Cardiac Catheterization

#### Class I

1. **Left ventriculography and hemodynamic measurements are indicated when noninvasive tests are inconclusive regarding severity of MR, LV function, or the need for surgery. (Level of Evidence: C)**
2. **Hemodynamic measurements are indicated when pulmonary artery pressure is out of proportion to the severity of MR as assessed by noninvasive testing. (Level of Evidence: C)**
3. **Left ventriculography and hemodynamic measurements are indicated when there is a discrepancy between clinical and noninvasive findings regarding severity of MR. (Level of Evidence: C)**
4. **Coronary angiography is indicated before MV repair or MV replacement in patients at risk for CAD. (Level of Evidence: C)**

#### Class III

**Left ventriculography and hemodynamic measurements are not indicated in patients with MR in whom valve surgery is not contemplated. (Level of Evidence: C)**

Cardiac catheterization, with or without exercise, is necessary when there is a discrepancy between clinical and noninvasive findings. Although the standard semiquantitative approach to determining the severity of MR from ventriculography has its own limitations (342), ventriculography does provide an additional method to assess LV dilatation and function and gauge the severity of MR. Exercise hemodynamics may provide additional information that is helpful in decision making. In patients who have risk factors for CAD (e.g., advanced age, hypercholesterolemia, or hypertension), or when there is a suspicion that MR is ischemic in origin (either because of known myocardial infarction or suspected ischemia), coronary angiography should be performed before surgery.

### 3. Indications for Surgery

### a. Types of Surgery

In most cases, MV 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 and therefore avoids the risk of chronic anticoagulation (except in patients in atrial fibrillation) or prosthetic valve failure late after surgery. Additionally, preservation of the mitral apparatus leads to better postoperative LV function and

survival than in cases in which the apparatus is disrupted (327,343–348). Valve morphology and surgical expertise are of critical importance for the success of MV repair (see below).

The reoperation rate after MV repair is similar to that after MV replacement (319). There is a 7% to 10% reoperation rate at 10 years in patients undergoing MV repair, usually for severe recurrent MR (319,349–352). Approximately 70% of the recurrent MR is thought to be due to the initial procedure and 30% to progressive valve disease (349).

If MV replacement is required, MV replacement with preservation of the chordal apparatus enhances postoperative mitral competence, preserves LV function, and increases postoperative survival compared with MV replacement in which the apparatus is disrupted (345,353–356). This latter form of MV replacement is never recommended and should only be performed in those circumstances in which the native valve and apparatus are so distorted by the preoperative pathology (rheumatic disease, for example) that the mitral apparatus cannot be spared. Artificial chordal reconstruction does extend the opportunities for repair in some such patients (357,358).

The advantages of MV repair make it applicable across the full spectrum of MR, including the 2 extremes of the spectrum. Valve repair might be possible in patients with far-advanced symptomatic MR and depressed LV function, because it preserves LV function at the preoperative level (347). At the other extreme, in the relatively asymptomatic patient with well-preserved LV function, repair of a severely regurgitant valve might be contemplated to avoid the onset of LV dysfunction from long-standing volume overload. However, failed MV repair that results in the need for a prosthetic valve in an asymptomatic patient would represent a clear complication of surgery. Hence, "prophylactic" surgery in an asymptomatic patient with MR and normal LV function requires a very high likelihood of successful repair.

### b. Indications for Mitral Valve Operation

#### Class I

1. **MV surgery is recommended for the symptomatic patient with acute severe MR.\* (Level of Evidence: B)**
2. **MV surgery is beneficial for patients with chronic severe MR\* and NYHA functional class II, III, or IV symptoms in the absence of severe LV dysfunction (severe LV dysfunction is defined as ejection fraction less than 0.30) and/or end-systolic dimension greater than 55 mm. (Level of Evidence: B)**
3. **MV surgery is beneficial for asymptomatic patients with chronic severe MR\* and mild to moderate LV dysfunction, ejection fraction 0.30 to 0.60, and/or end-systolic dimension greater than or equal to 40 mm. (Level of Evidence: B)**

4. **MV repair is recommended over MV replacement in the majority of patients with severe chronic MR\* who require surgery, and patients should be referred to surgical centers experienced in MV repair.** *(Level of Evidence: C)*

### Class IIa

1. **MV repair is reasonable in experienced surgical centers for asymptomatic patients with chronic severe MR\* with preserved LV function (ejection fraction greater than 0.60 and end-systolic dimension less than 40 mm) in whom the likelihood of successful repair without residual MR is greater than 90%.** *(Level of Evidence: B)*
2. **MV surgery is reasonable for asymptomatic patients with chronic severe MR,\* preserved LV function, and new onset of atrial fibrillation.** *(Level of Evidence: C)*
3. **MV surgery is reasonable for asymptomatic patients with chronic severe MR,\* preserved LV function, and pulmonary hypertension (pulmonary artery systolic pressure greater than 50 mm Hg at rest or greater than 60 mm Hg with exercise).** *(Level of Evidence: C)*
4. **MV surgery is reasonable for patients with chronic severe MR\* due to a primary abnormality of the mitral apparatus and NYHA functional class III–IV symptoms and severe LV dysfunction (ejection fraction less than 0.30 and/or end-systolic dimension greater than 55 mm) in whom MV repair is highly likely.** *(Level of Evidence: C)*

### Class IIb

**MV repair may be considered for patients with chronic severe secondary MR\* due to severe LV dysfunction (ejection fraction less than 0.30) who have persistent NYHA functional class III–IV symptoms despite optimal therapy for heart failure, including biventricular pacing.** *(Level of Evidence: C)*

### Class III

1. **MV surgery is not indicated for asymptomatic patients with MR and preserved LV function (ejection fraction greater than 0.60 and end-systolic dimension less than 40 mm) in whom significant doubt about the feasibility of repair exists.** *(Level of Evidence: C)*
2. **Isolated MV surgery is not indicated for patients with mild or moderate MR.** *(Level of Evidence: C)*

*\*See Table 1 (7).*

The prediction of successful MV repair is important in timing surgery. This prediction is based on the skill and experience of the surgeon in performing repair, on the cause of the MR, and on MV morphology. The skill and

experience of the surgeon are probably the most important determinants of the eventual success of MV repair.

The number of patients undergoing MV repair for MR has increased steadily over the past decade in the United States and Canada in relation to the number undergoing MV replacement. However, among isolated MV procedures reported in the STS National Cardiac Database from 1999 to 2000 (359), the frequency of repair was only 35.7% (3027 of a total of 8486 procedures), which suggests that MV repair is underutilized. Current data indicate that the frequency of MV repair is increasing yearly (93). The STS national database also indicates an operative mortality rate of less than 2% in patients undergoing isolated MV repair in 2004, which compares favorably to the more than 6% operative mortality rate for patients undergoing isolated MV replacement (93). In light of the beneficial effect of MV repair on survival and LV function, cardiologists are strongly encouraged to refer patients who are candidates for MV repair to surgical centers experienced in performing MV repair.

*Symptomatic Patients With Normal Left Ventricular Function*

Patients with symptoms of congestive heart failure despite normal LV systolic function (ejection fraction greater than 0.60 and end-systolic dimension less than 40 mm) require surgery. Surgery should be performed in patients with even mild symptoms and severe MR (Fig. 7), especially if it appears that MV repair rather than replacement can be performed.

*Asymptomatic and Symptomatic Patients with Left Ventricular Dysfunction*

The timing of surgery for asymptomatic patients is controversial, but most would now agree that MV surgery is indicated with the appearance of echocardiographic indicators of LV dysfunction. These include LV ejection fraction less than or equal to 0.60 and/or LV end-systolic dimension greater than or equal to 40 mm (Fig. 7). MV surgery should also be recommended for symptomatic patients with evidence of LV systolic dysfunction (ejection fraction less than or equal to 0.60 and/or end-systolic dimension greater than or equal to 40 mm).

Determining the surgical candidacy of the symptomatic patient with MR and far-advanced LV dysfunction is a common clinical dilemma. The question that often arises is whether the patient with MR with advanced LV dysfunction is no longer a candidate for surgery. Although it is difficult, one must distinguish primary cardiomyopathy with secondary "functional" MR from primary MR with secondary myocardial dysfunction. In the latter case, surgery should still be contemplated if MV repair appears likely (Fig. 7). In patients with severe LV dysfunction and significant functional MR, the modification of MV geometry by an "undersized" annular ring may be beneficial (360–365), although the impact on outcomes compared with aggressive medical therapy, including beta blockers and

**Chronic Severe Mitral Regurgitation**
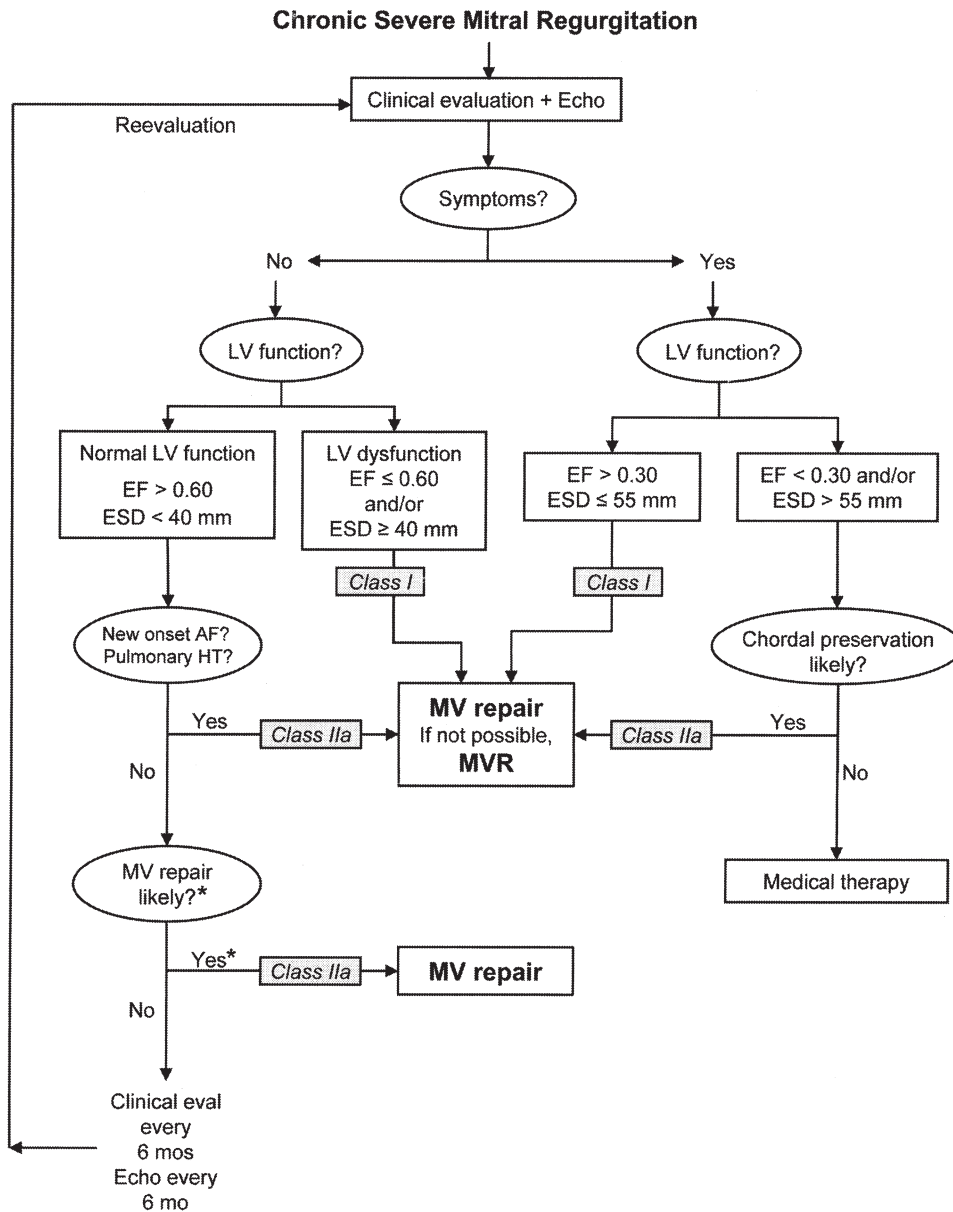


**Figure 7.** Management strategy for patients with chronic severe mitral regurgitation. *Mitral valve (MV) repair may be performed in asymptomatic patients with normal left ventricular (LV) function if performed by an experienced surgical team and if the likelihood of successful MV repair is greater than 90%. AF indicates atrial fibrillation; Echo, echocardiography; EF, ejection fraction; ESD, end-systolic dimension; eval, evaluation; HT, hypertension; MVR, mitral valve replacement.

cardiac resynchronization therapy (338–341), has not been studied in a prospective randomized trial.

*Asymptomatic Patients With Normal Left Ventricular Function*

As noted previously, repair of a severely regurgitant valve may be contemplated in an asymptomatic patient with severe MR and normal LV function to preserve LV size and function and prevent the sequelae of chronic severe MR (324). Although there are no randomized data with which to recommend this approach to all patients, the committee recognizes that some experienced centers are moving in this direction for patients for whom the likelihood of successful repair is high. Natural history studies indicate uniformly

that asymptomatic patients with severe MR and normal LV function have a high likelihood of developing symptoms and/or LV dysfunction that warrants surgery over the course of 6 to 10 years (313,317,324,325). Two recent studies have also addressed the risk of sudden death in asymptomatic patients with severe MR and normal LV function (324,325). In a long-term retrospective study in which severity of MR was quantified by Doppler echocardiography (324), 198 patients with an effective orifice area greater than 40 mm$^2$ had a 4% per year risk of cardiac death during a mean follow-up period of 2.7 years. However, in the second study of 132 patients followed up prospectively for 5 years, during which the indications for surgery were symptoms, development of

LV dysfunction (ejection fraction less than 0.60), LV dilatation (LV end-systolic dimension greater than 45 mm), atrial fibrillation, or pulmonary hypertension, there was only 1 cardiac death in an asymptomatic patient, but this patient had refused surgery which was indicated by development of LV dilatation (325).

MV repair is often recommended in hemodynamically stable patients with newly acquired severe MR, such as might occur with ruptured chordae. Surgery is also recommended in asymptomatic patients with chronic MR with recent onset of atrial fibrillation in whom there is a high likelihood of successful valve repair (see below).

Surgery for asymptomatic patients with severe MR and normal LV function should only be considered if there is a greater than 90% likelihood of successful valve repair in a center experienced in this procedure. As noted above, cardiologists are strongly encouraged to refer patients who are candidates for MV repair to surgical centers experienced in performing MV repair.

### Atrial Fibrillation

The development of atrial fibrillation is independently associated with a high risk of cardiac death or heart failure (366), and preoperative atrial fibrillation is an independent predictor of reduced long-term survival after MV surgery for chronic MR (333,366–368). Hence, many clinicians consider the recent onset of atrial fibrillation to be an indication in and of itself for surgery, if there is a high likelihood of valve repair (Fig. 7) (356,369). In patients presenting for MV operation with chronic atrial fibrillation, a concomitant Maze procedure may prevent future thromboembolic events by restoring normal sinus rhythm (370–376). The decision to proceed with a Maze procedure should be based on the age and health of the patient, as well as the surgical expertise, because this procedure may add to the morbidity of the operation.

### 4. Ischemic Mitral Regurgitation

The outlook for the patient with ischemic MR is substantially worse than that for regurgitation from other causes (377,378). A worse prognosis accrues from the fact that ischemic MR is usually caused by LV dysfunction resulting from myocardial infarction. Furthermore, the MV itself is usually anatomically normal, and MR is secondary to papillary muscle displacement and tethering of the mitral leaflet(s). The mechanism of MR in chronic ischemic disease is local LV remodeling (apical and posterior displacement of papillary muscles), which leads to excess valvular tenting and loss of systolic annular contraction (379–386). The indication for MV operation in the patient who undergoes CABG with mild to moderate MR is still unclear, but there are data to indicate benefit of MV repair in such patients (387–390). Patients with ischemic heart disease who have MR have a worse prognosis than those without MR (391–394). CABG alone may improve LV function and reduce ischemic MR in

selected patients (392,395), especially those with transient severe MR due to ischemia, in whom myocardial revascularization can eliminate episodes of severe MR. However, CABG alone is usually insufficient and leaves many patients with significant residual MR, and these patients would benefit from concomitant MV repair at the time of the CABG (386–390,396–405). Mitral annuloplasty alone with a downsized annuloplasty ring is often effective at relieving MR (400,401,404).

In severe MR secondary to acute myocardial infarction, hypotension and pulmonary edema often occur. Severe MR occurs in 6% to 7% of patients with cardiogenic shock (406). The cause of the MR should be established, because the MR may be due to a ruptured papillary muscle, papillary muscle displacement with leaflet tethering, or annular dilatation from severe LV dilatation. Those patients with an acute rupture of the papillary muscle should undergo surgery on an emergency basis, with either valve repair or MV replacement (407). In those patients with papillary muscle dysfunction, treatment should initially consist of hemodynamic stabilization, usually with insertion of an intra-aortic balloon pump. Surgery should be considered for those patients who do not improve with aggressive medical therapy. Correction of acute severe ischemic MR usually requires valve surgery in addition to revascularization. The best operation for ischemic MR is controversial (408,409), but MV repair with an annuloplasty ring is the best approach in most instances (387,390,396–405).

### 5. Evaluation of Patients After Mitral Valve Replacement or Repair

After MV surgery, follow-up is necessary to detect late surgical failure and assess LV function, as discussed in Section IX-B. For patients in whom a bioprosthesis has been inserted, the specter of eventual deterioration is always present and must be anticipated. If a mechanical valve has been inserted, anticoagulation is required, and chronic surveillance of prothrombin time and INR is necessary. After valve repair, follow-up to assess the effectiveness of the repair is indicated early, especially because most repair failures are detected soon after surgery.

### 6. Special Considerations in the Elderly

Operative mortality increases and survival is reduced in patients with MR older than 75 years of age, especially if MV replacement must be performed or if the patient has concomitant CAD or other valve lesions (92,95,327,410–413). Operative mortality in the elderly is low in experienced centers (414), but the overall operative mortality for MV replacement in this age group in the United States exceeds 14% (95,412,413) and is particularly high (greater than 20%) in low-volume centers (95). Although the risks are reduced if MV repair is performed rather than MV replacement, the majority of patients in this age group require concomitant CABG (413). The average operative risk for combined MV repair plus CABG in the United

States is 8% (93), which will undoubtedly be higher in the older population. These risks are worth taking in patients with significant symptoms. However, under most circumstances, asymptomatic patients or patients with mild symptoms should be treated medically.

## G. Multiple Valve Disease

Remarkably few data exist to objectively guide the management of mixed valve disease. The large number of combined hemodynamic disturbances (and their varied severity) yields a large number of potential combinations to consider, and few data exist for any specific category. Hence, each case must be considered individually, and management must be 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 in this section. Specific combined valve lesions are discussed in the full text of these guidelines.

## H. Tricuspid Valve Disease

### 1. Diagnosis

The physical examination is the initial key to diagnosis of tricuspid valve disease. Echocardiography is valuable in assessing tricuspid valve structure and motion, measuring annular size, and identifying other cardiac abnormalities that might influence tricuspid valve function. Doppler echocardiography provides estimation of the severity of TR (415), RV systolic pressure, and the tricuspid valve diastolic gradient. Because clinically insignificant TR is detected by color Doppler imaging in many normal persons, clinical correlation and judgment must accompany the echocardiographic results. Systolic pulmonary artery pressures greater than 55 mm Hg are likely to cause TR with anatomically normal tricuspid valves, whereas TR occurring with systolic pulmonary artery pressures less than 40 mm Hg is likely to reflect a structural abnormality of the valve apparatus. Systolic pulmonary artery pressure estimation combined with information about annular circumference will further improve the accuracy of clinical assessment.

### 2. Management

#### Class I

> Tricuspid valve repair is beneficial for severe TR in patients with MV disease requiring MV surgery. *(Level of Evidence: B)*

#### Class IIa

1. **Tricuspid valve replacement or annuloplasty is reasonable for severe primary TR when symptomatic.** *(Level of Evidence: C)*
2. **Tricuspid valve replacement is reasonable for severe TR secondary to diseased/abnormal tricuspid valve leaflets**

not amenable to annuloplasty or repair. *(Level of Evidence: C)*

#### Class IIb

> **Tricuspid annuloplasty may be considered for less than severe TR in patients undergoing MV surgery when there is pulmonary hypertension or tricuspid annular dilatation.** *(Level of Evidence: C)*

#### Class III

1. **Tricuspid valve replacement or annuloplasty is not indicated in asymptomatic patients with TR whose pulmonary artery systolic pressure is less than 60 mm Hg in the presence of a normal MV.** *(Level of Evidence: C)*
2. **Tricuspid valve replacement or annuloplasty is not indicated in patients with mild primary TR.** *(Level of Evidence: C)*

Surgery for TR commonly occurs at the time of MV surgery. TR associated with dilatation of the tricuspid annulus should be repaired (416,417) because tricuspid dilatation is an ongoing process that may progress to severe TR if left untreated. Patients with severe TR of any cause have a poor long-term outcome because of RV dysfunction and/or systemic venous congestion (418). Tricuspid valve and chordal reconstruction can be attempted in some cases of TR resulting from endocarditis and trauma (419–421). In recent years, annuloplasty has become an established surgical approach to significant TR (416,417,422–424).

When the valve leaflets themselves are diseased, abnormal, or destroyed, valve replacement with a low-profile mechanical valve or bioprosthesis is often necessary (425). A biological prosthesis is preferred because of the high rate of thromboembolic complications with mechanical prostheses in the tricuspid position.

## I. Drug-Related Valvular Heart Disease

In addition to the common causes of the valvular lesions described in the preceding sections, there are a number of uncommon causes related to systemic diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus, anti-phospholipid antibody syndrome, and ankylosing spondylitis), drugs (e.g., ergotamine, methysergide, anorexiant medications, and pergolide), and toxins. It is beyond the scope of these guidelines to discuss the specific pathology and natural history of valve disease stemming from each of these many causes. In general, the evaluation and management strategies for patients with valve disease related to these disorders are directed both toward the underlying systemic process when appropriate and to the diagnosis and treatment of the associated valvular disease according to the guidelines developed for each of the valve lesions, as described in Section III.

The sympathomimetic appetite-suppressant drug fenfluramine and its pure d-enantiomer, dexfenfluramine, were removed from the market in September 1997 after several

reports of unusual left-sided valvular heart disease (AR and MR) linked to these agents (426–430). To date, an excess prevalence of valvular heart disease has not been reported for sibutramine, a serotonin and norepinephrine reuptake inhibitor, or for phentermine when used as monotherapy for obesity (431,432). There are now several reports of a carcinoid-like valvulopathy in Parkinson's disease patients treated with pergolide, a dopamine-receptor agonist (433–435).

### J. Radiation Heart Disease

Mediastinal radiation may produce cardiac valve abnormalities that usually become evident at least 5 years after the radiation injury. The assessment and treatment of these patients can be difficult, in part because these valve lesions occur within a context of multiple cardiac and noncardiac abnormalities produced by radiation. Radiation-induced valvular lesions stem from calcification of valve leaflets and the fibrous skeleton of the heart. Mixed aortic valve disease with AS and AR is the most common lesion, but MR and TR may also occur.

Valve dysfunction is often part of a presenting picture of congestive heart failure and dyspnea, but the relative contributions of valve dysfunction and restrictive cardiomyopathy may be difficult to separate. In addition, recurrent pleural effusions are often prominent, and radiation-induced pulmonary dysfunction can occur. Thus, dyspnea is usually a multifactorial problem in these patients. For patients with radiation heart disease, surgery for any cardiac lesion should be approached with caution (436). Patients with this condition should be evaluated in centers with experience in its management (437).

## IV. EVALUATION AND MANAGEMENT OF INFECTIVE ENDOCARDITIS

### Class I

> Patients at risk for infective endocarditis who have unexplained fever for more than 48 h should have at least 2 sets of blood cultures obtained from different sites. *(Level of Evidence: B)*

### Class III

> Patients with known valve disease or a valve prosthesis should not receive antibiotics before blood cultures are obtained for unexplained fever. *(Level of Evidence: C)*

The diagnosis of infective endocarditis in a patient with a pathological murmur or a valvular prosthesis and unexplained fever lasting more than 72 h should include an assessment for vascular and immunologic phenomena, 3 to 5 sets of blood cultures, and a transthoracic echocardiogram. A definitive diagnosis may be made with positive blood cultures and/or characteristic echocardiographic findings. The role of echocardiography has emerged with visualiza-

tion of vegetation by transthoracic echocardiography in approximately 60% to 75% of patients and by TEE in more than 95% of patients (438). When the echocardiogram is technically inadequate, is nondiagnostic, or is negative for infective endocarditis, TEE should be obtained. The modified Duke criteria (439) define major and minor criteria for infective endocarditis.

### A. Antimicrobial Therapy

Antimicrobial therapy in endocarditis is guided by identification of the causative organism. The majority (80%) of cases of endocarditis are due to streptococcal and staphylococcal organisms. The latter species is also the most frequent organism in endocarditis resulting from intravenous drug abuse. Eighty percent of tricuspid valve infection is by *Staphylococcus aureus*. This organism is also a frequent cause of infective endocarditis in patients with insulin-dependent diabetes mellitus. 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 predominant offending organism. Late-onset prosthetic valve endocarditis follows the profile of native valve endocarditis, that is, *streptococci* (viridans) and *staphylococci*. *Enterococcus faecalis* and *E. faecium* account for 90% of enterococcal endocarditis, which is 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*) has become an important cause of endocarditis. These organisms cause large vegetations (greater than 1 cm), large-vessel embolism, and congestive heart failure. They should be considered along with fungal endocarditis when large vegetations are noted. Fungi, especially *Candida*, are important causes of endocarditis in patients with prosthetic valves, compromised immune systems, and intravenous drug abuse. The AHA recommendations for antimicrobial regimens were updated in 2005 (440), and complete treatment regimens are provided in that document which can be found at http://www.americanheart.org/presenter.jhtml?identifier=2158.

Culture-negative endocarditis most frequently (62%) results from prior antibiotic treatment before blood cultures are drawn. Other reasons for negative blood cultures include infections due to *Candida*; *Aspergillus*; other fastidious, slow-growing organisms such as Q-fever and Bartonella organisms; and noninfective endocarditis such as Libman-Sacks endocarditis in patients with systemic lupus erythematosus.

### B. Indications for Echocardiography in Suspected or Known Endocarditis

Echocardiography is useful for detection and characterization of the hemodynamic and pathological consequences

of infection, including valvular vegetations; valvular regurgitation; ventricular dysfunction; and associated lesions such as abscesses, shunts, and ruptured chordae. The indications for transthoracic and TEE are discussed in the "ACC/AHA/ASE 2004 Guidelines for the Clinical Application of Echocardiography" (1) and the 2005 AHA endocarditis guidelines (440). Transesophageal imaging is more sensitive in detecting vegetations than transthoracic imaging (438,440,441), particularly in patients with prosthetic valves, and in determining the presence and severity of important complications such as abscesses and perforations. In patients with prosthetic valves, it is reasonable to proceed directly to TEE as the first-line diagnostic test when endocarditis is suspected. Echocardiography can be useful in the case of culture-negative endocarditis (442) or the diagnosis of a persistent bacteremia the source of which remains unidentified after appropriate evaluation (1).

### 1. Transthoracic Echocardiography in Endocarditis

**Class I**

1. **Transthoracic echocardiography to detect valvular vegetations with or without positive blood cultures is recommended for the diagnosis of infective endocarditis. *(Level of Evidence: B)***
2. **Transthoracic echocardiography is recommended to characterize the hemodynamic severity of valvular lesions in known infective endocarditis. *(Level of Evidence: B)***
3. **Transthoracic echocardiography is recommended for assessment of complications of infective endocarditis (e.g., abscesses, perforation, and shunts). *(Level of Evidence: B)***
4. **Transthoracic echocardiography is recommended for reassessment of high-risk patients (e.g., those with a virulent organism, clinical deterioration, persistent or recurrent fever, new murmur, or persistent bacteremia). *(Level of Evidence: C)***

**Class IIa**

**Transthoracic echocardiography is reasonable to diagnose infective endocarditis of a prosthetic valve in the presence of persistent fever without bacteremia or a new murmur. *(Level of Evidence: C)***

**Class IIb**

**Transthoracic echocardiography may be considered for the re-evaluation of prosthetic valve endocarditis during antibiotic therapy in the absence of clinical deterioration. *(Level of Evidence: C)***

**Class III**

**Transthoracic echocardiography is not indicated to re-evaluate uncomplicated (including no regurgitation on baseline echocardiogram) native valve endo-carditis during antibiotic treatment in the absence of clinical deterioration, new physical findings, or persistent fever. *(Level of Evidence: C)***

### 2. Transesophageal Echocardiography in Endocarditis

**Class I**

1. **TEE is recommended to assess the severity of valvular lesions in symptomatic patients with infective endocarditis, if transthoracic echocardiography is nondiagnostic. *(Level of Evidence: C)***
2. **TEE is recommended to diagnose infective endocarditis in patients with valvular heart disease and positive blood cultures, if transthoracic echocardiography is nondiagnostic. *(Level of Evidence: C)***
3. **TEE is recommended to diagnose complications of infective endocarditis with potential impact on prognosis and management (e.g., abscesses, perforation, and shunts). *(Level of Evidence: C)***
4. **TEE is recommended as first-line diagnostic study to diagnose prosthetic valve endocarditis and assess for complications. *(Level of Evidence: C)***
5. **TEE is recommended for preoperative evaluation in patients with known infective endocarditis, unless the need for surgery is evident on transthoracic imaging and unless preoperative imaging will delay surgery in urgent cases. *(Level of Evidence: C)***
6. **Intraoperative TEE is recommended for patients undergoing valve surgery for infective endocarditis. *(Level of Evidence: C)***

**Class IIa**

**TEE is reasonable to diagnose possible infective endocarditis in patients with persistent staphylococcal bacteremia without a known source. *(Level of Evidence: C)***

**Class IIb**

**TEE might be considered to detect infective endocarditis in patients with nosocomial staphylococcal bacteremia. *(Level of Evidence: C)***

### C. Indications for Surgery in Patients With Acute 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 proven infective endocarditis if the patient has reasonable prospects of recovery with satisfactory quality of life after the operation (378,440,443–453). 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. Consulta-

tion with a cardiovascular surgeon is recommended in a patient with complicated endocarditis so that the surgical team is aware of the patient who may suddenly need surgery. Surgery is recommended in patients with annular or aortic abscesses, heart block, recurrent emboli on appropriate antibiotic therapy, infections resistant to antibiotic therapy, and fungal endocarditis. Prosthetic valve endocarditis and native valve endocarditis caused by *S. aureus* are almost always surgical diseases. Early surgery in MV endocarditis caused by virulent organisms (such as *S. aureus* or fungi) may make repair possible. Echocardiography, especially with transesophageal imaging, identifies vegetations and provides size estimation in many instances. Patients with a vegetation diameter greater than 10 mm have a significantly higher incidence of embolization than those with a vegetation diameter less than or equal to 10 mm (438), and this risk appears to be higher in patients with MV endocarditis than in those with aortic valve endocarditis. However, surgery on the basis of vegetation size alone is controversial.

Patients with prosthetic valves who receive warfarin anticoagulation and develop endocarditis should have their warfarin discontinued and replaced with heparin. This recommendation is less related to the possibility of hemorrhagic complications of endocarditis (454) than to the possibility of urgent surgery. 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 magnetic resonance imaging or computed tomographic scanning.

### 1. Surgery for Native Valve Endocarditis

#### Class I

1. **Surgery of the native valve is indicated in patients with acute infective endocarditis who present with valve stenosis or regurgitation resulting in heart failure. *(Level of Evidence: B)***
2. **Surgery of the native valve is indicated in patients with acute infective endocarditis who present with AR or MR with hemodynamic evidence of elevated LV end-diastolic or left atrial pressures (e.g., premature closure of MV with AR, rapid decelerating MR signal by continuous-wave Doppler [*v*-wave cutoff sign], or moderate or severe pulmonary hypertension). *(Level of Evidence: B)***
3. **Surgery of the native valve is indicated in patients with infective endocarditis caused by fungal or other highly resistant organisms. *(Level of Evidence: B)***
4. **Surgery of the native valve is indicated in patients with infective endocarditis complicated by heart block, annular or aortic abscess, or destructive penetrating lesions (e.g., sinus of Valsalva to right atrium, right ventricle, or left atrium fistula; mitral leaflet perforation with aortic valve endocarditis; or infection in annulus fibrosa). *(Level of Evidence: B)***

#### Class IIa

**Surgery of the native valve is reasonable in patients with infective endocarditis who present with recurrent emboli and persistent vegetations despite appropriate antibiotic therapy. *(Level of Evidence: C)***

#### Class IIb

**Surgery of the native valve may be considered in patients with infective endocarditis who present with mobile vegetations in excess of 10 mm with or without emboli. *(Level of Evidence: C)***

### 2. Surgery for Prosthetic Valve Endocarditis

#### Class I

1. **Consultation with a cardiac surgeon is indicated for patients with infective endocarditis of a prosthetic valve. *(Level of Evidence: C)***
2. **Surgery is indicated for patients with infective endocarditis of a prosthetic valve who present with heart failure. *(Level of Evidence: B)***
3. **Surgery is indicated for patients with infective endocarditis of a prosthetic valve who present with dehiscence evidenced by cine fluoroscopy or echocardiography. *(Level of Evidence: B)***
4. **Surgery is indicated for patients with infective endocarditis of a prosthetic valve who present with evidence of increasing obstruction or worsening regurgitation. *(Level of Evidence: C)***
5. **Surgery is indicated for patients with infective endocarditis of a prosthetic valve who present with complications (e.g., abscess formation). *(Level of Evidence: C)***

#### Class IIa

1. **Surgery is reasonable for patients with infective endocarditis of a prosthetic valve who present with evidence of persistent bacteremia or recurrent emboli despite appropriate antibiotic treatment. *(Level of Evidence: C)***
2. **Surgery is reasonable for patients with infective endocarditis of a prosthetic valve who present with relapsing infection. *(Level of Evidence: C)***

#### Class III

**Routine surgery is not indicated for patients with uncomplicated infective endocarditis of a prosthetic valve caused by first infection with a sensitive organism. *(Level of Evidence: C)***

## 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 that is accompanied by a commensurate increase in cardiac output that usually peaks between the midportion of the second and third trimesters. Because of the effects of uterine circulation and endogenous hormones, systemic vascular resistance falls with a disproportionately 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, which leads to hypotension.

There is an 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 (455).

Pregnancy is also associated with a hypercoagulable state due to relative decreases in protein S activity, stasis, and venous hypertension (456). Estrogens can interfere with collagen deposition within the media of the medium and large 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 (457). Relaxin, an insulin-like growth factor hormone, is detectable in serum during pregnancy and causes a decrease in collagen synthesis and may predispose to aortic dissection during pregnancy (458).

The increased blood volume and enhanced cardiac output associated with normal pregnancy can accentuate the murmurs associated with stenotic heart valve lesions (e.g., MS and AS). On the other hand, murmurs of AR, MR, and ventricular septal defect can actually attenuate or become inaudible as systemic vascular resistance is lowered (459).

### 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 (460). Most women will demonstrate Doppler evidence of "physiological" MR in the absence of structural valve disease. Atrioventricular valve regurgitation may result from the annular dilatation that accompanies ventricular enlargement. Appreciation of these echocardiographic and Doppler findings in normal individuals is an important foundation for the noninvasive evaluation of subjects with suspected valvular disease. The use of ultrasound during pregnancy poses no risk to the mother or fetus.

### C. Management Guidelines

Clinical experience has identified several cardiac conditions in which the physiological changes of pregnancy are poorly tolerated. For some conditions, such as cyanotic heart disease, Eisenmenger syndrome, or severe pulmonary hypertension, pregnancy should be discouraged. Valvular heart lesions associated with high maternal and fetal risk during pregnancy include severe AS with or without symptoms, MR or AR with NYHA functional class III or IV symptoms, MS with NYHA functional class II to IV symptoms, mechanical valves that require chronic anticoagulation, AR associated with Marfan syndrome, bicuspid aortic valves with aortic root dilatation, and any condition that results in LV systolic dysfunction or pulmonary hypertension (461–464). Outcomes data are limited for pregnant patients with valvular heart disease, except for those with MS.

Individual counseling usually requires a multidisciplinary approach and should include information regarding 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 rectified before conception and pregnancy. Contemporaneous management with a dedicated obstetric team accustomed to working with high-risk patients is encouraged.

#### 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. Diuretics are given to relieve pulmonary and excess systemic venous congestion, but care must be taken to avoid vigorous volume depletion to protect against uteroplacental hypoperfusion. Beta blockers are chiefly indicated to treat or prevent tachycardia to optimize diastolic filling. Although the nonselective beta blocker propranolol has been in use for decades, some authorities recommend a cardioselective beta blocker such as metoprolol or atenolol to prevent the potential deleterious effects of epinephrine blockade on myometrial activity.

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 (465). Percutaneous mitral balloon valvotomy should only be performed in experienced centers and only after aggressive medical measures have been exhausted.

### 2. Mitral Regurgitation

MVP is the most common cause of MR in pregnant women. MR can usually be managed medically, although on rare occasions, MV surgery is required because of ruptured chordae and acute, severe worsening of MR. Medical management includes diuretics for the rare patient with pulmonary congestion. Vasodilator therapy is indicated only in the presence of concomitant systemic hypertension. ACE inhibitors are considered unsafe and are contraindicated because of their multiple adverse effects on fetal development. When MV surgery is required, repair is always preferred.

### 3. Aortic Stenosis

Patients with mild AS and normal LV systolic function can be managed conservatively throughout the entire pregnancy. Patients with moderate to severe obstruction (Table 1) or symptoms should be advised to delay conception until relief of AS can be obtained. Women with severe AS who become pregnant but who remain asymptomatic or have mild symptoms may often be managed conservatively during pregnancy with bed rest, oxygen, and beta blockers. In women with severe AS who develop symptoms, consideration may have to be given to either percutaneous aortic balloon valvotomy (466,467) or surgery (depending on the anatomic findings) before labor and delivery. These procedures are fraught with danger to both the mother and fetus, although successful outcomes have been reported. Aortic root dilatation in patients with bicuspid aortic valves 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 (468). ACE inhibitors are considered unsafe and are contraindicated because of their multiple adverse effects on fetal development. Women with symptoms or signs of LV failure should be closely monitored throughout labor and delivery with strict attention to volume status and blood pressure. Surgery for AR during pregnancy should be contemplated only for control of refractory NYHA functional class III or IV symptoms. The recommendations for AVR based on LV size that apply to nonpregnant patients should not be used for pregnant patients.

### 5. Pulmonic 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. Tricuspid Valve Disease

Tricuspid valve disease may be congenital (Ebstein's anomaly, tricuspid atresia) or acquired (endocarditis, myxomatous replacement/proliferation, carcinoid). The approach to the patient with tricuspid valve involvement as part of a more complex congenital heart disease syndrome is predicated on the features of the associated lesions. Isolated TR should not pose a significant problem during pregnancy, although care should be taken to prevent diuretic-induced hypoperfusion.

### 7. Marfan Syndrome

Spontaneous aortic dissection or rupture is the most feared cardiovascular complication associated with pregnancy in the Marfan syndrome (457,469,470). Dissection can occur at any point along the aorta but most commonly originates in the ascending portion. Enlargement of the aortic root to greater than 4.0 cm identifies a particularly high-risk group, although a normal dimension is by no means a guarantee against this catastrophic complication. Aortic root enlargement may or may not be accompanied by AR. MVP with MR is also frequently detected.

Any woman with Marfan syndrome should be counseled against pregnancy, because aortic rupture or dissection can occur in any root size. All patients with Marfan syndrome should have a screening transthoracic echocardiogram with assessment of aortic root dimensions. Enlargement greater than 4.5 cm is generally considered an indication for elective repair before conception. If any degree of aortic root enlargement (greater than 4.0 cm) is first detected during pregnancy, some authorities recommend termination of the pregnancy with prompt aortic repair, although this is controversial. Less controversial is the recommendation for prompt repair if serial imaging studies demonstrate progressive dilatation over time. Dissection and rupture are most likely to occur during the third trimester or near the time of delivery. The use of prophylactic beta blockade throughout the pregnancy is strongly recommended. Successful surgical correction does not confer a normal risk during subsequent pregnancy. Special care must be taken during labor and delivery to provide adequate analgesia to prevent wide surges in blood pressure. Obstetric techniques to shorten the second stage of labor are appropriate. General anesthesia and caesarean section may allow more optimal hemodynamic control.

### D. Endocarditis Prophylaxis

The Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the AHA does not recommend routine antibiotic prophylaxis in patients with valvular heart disease undergoing uncomplicated vaginal delivery or caesarean section unless infection is suspected (8). 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.

### E. Cardiac Valve Surgery

Cardiac valve surgery is a difficult and complex undertaking in the pregnant patient. Even under ideal conditions, there is a high incidence of fetal distress, growth retardation, or wastage (471–475). If possible, it is always preferable to delay surgery until the time the fetus is viable and a caesarean section can be performed as part of a concomitant procedure (476,477). Surgery should be pursued only in the setting of medically refractory cardiac symptoms (pulmonary congestion), especially if a low-output syndrome intervenes.

For suitable valve lesions, repair is always preferred over replacement, and percutaneous mitral balloon valvotomy is preferred over MV replacement in patients with MS. If valve replacement is necessary, the choice of a heart valve substitute can be problematic.

### F. Anticoagulation During Pregnancy

#### 1. Warfarin

Warfarin crosses the placenta and has been associated with an increased incidence of spontaneous abortion, prematurity, stillbirth, and fetal bleeding. The true incidence of warfarin embryopathy has been difficult to ascertain. It has ranged from less than 5% to as high as 67% (478–481), and an estimate of 4% to 10% seems reasonable (482,483). However, the risk of clinically important embryopathy may be lower if the dose of warfarin is less than or equal to 5 mg per day.

Warfarin is probably safe during the first 6 weeks of gestation, but there is a risk of embryopathy if warfarin is taken between 6 and 12 weeks of gestation. For women requiring long-term warfarin therapy who are attempting pregnancy, it is wise to perform frequent pregnancy tests with the substitution of unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) for warfarin when pregnancy is achieved. Warfarin is also relatively safe during the second and third trimesters of pregnancy but must be discontinued and switched to a heparin compound several weeks before delivery.

#### 2. Unfractionated Heparin

Heparin does not cross the placenta and does not have the potential to cause fetal bleeding or teratogenicity. Thus, heparin is generally considered safer than warfarin during pregnancy in terms of the development of embryopathy (482,484). However, bleeding at the uteroplacental junction is possible, and numerous case series and patient registries attest to a high incidence of thromboembolic complications (12% to 24%), including fatal valve thrombosis, in high-risk pregnant women managed with subcutaneous UFH or LMWH (482,485–487). When heparin is used during the

first trimester, the risks of maternal thromboembolism and maternal death are more than doubled.

During pregnancy, the activated partial thromboplastin time (aPTT) response to heparin is often attenuated because of increased levels of factor VIII and fibrinogen. Adjusted-dose subcutaneous UFH can cause a persistent anticoagulant effect at the time of delivery, which can complicate its use before labor.

#### 3. Low-Molecular-Weight Heparins

LMWHs have potential advantages over UFH during pregnancy (488) because they 1) cause less heparin-induced thrombocytopenia; 2) have a longer plasma half-life and a more predictable dose response than UFH; 3) have greater ease of administration, with lack of need for laboratory monitoring and the potential for once-daily dosing administration; 4) are likely associated with a lower risk of heparin-induced osteoporosis; and 5) appear to have a low risk of bleeding complications. They do not cross the placenta and are likely safe for the fetus.

As the pregnancy progresses (and most women gain weight), the potential volume of distribution for LMWH changes. It is thus necessary to measure plasma anti-Xa levels 4 to 6 hours after the morning dose and adjust the dose of LMWH to achieve an anti-Xa level of approximately 0.7 to 1.2 units per ml.

The use of LMWH during pregnancy remains controversial because of an early warning by the manufacturer and the Food and Drug Administration in July 2001 regarding safety concerns in this situation. In 2004, labeling approved by the Food and Drug Administration indicated specifically that use of LMWH for thromboprophylaxis in pregnant women with mechanical prosthetic heart valves has not been studied adequately.

#### 4. Selection of Anticoagulation Regimen in Pregnant Patients With Mechanical Prosthetic Valves

#### Class I

1. **All pregnant patients with mechanical prosthetic valves must receive continuous therapeutic anticoagulation with frequent monitoring (see Section IX-A). *(Level of Evidence: B)***
2. **For women requiring long-term warfarin therapy who are attempting pregnancy, pregnancy tests should be monitored with discussions about subsequent anticoagulation therapy, so that anticoagulation can be continued uninterrupted when pregnancy is achieved. *(Level of Evidence: C)***
3. **Pregnant patients with mechanical prosthetic valves who elect to stop warfarin between weeks 6 and 12 of gestation should receive continuous intravenous UFH, dose-adjusted UFH, or dose-adjusted subcutaneous LMWH. *(Level of Evidence: C)***
4. **For pregnant patients with mechanical prosthetic valves, up to 36 weeks of gestation, the therapeutic**

choice of continuous intravenous or dose-adjusted sub-cutaneous UFH, dose-adjusted LMWH, or warfarin should be discussed fully. If continuous intravenous UFH is used, the fetal risk is lower, but the maternal risks of prosthetic valve thrombosis, systemic embolization, infection, osteoporosis, and heparin-induced thrombocytopenia are relatively higher. *(Level of Evidence: C)*

5. **In pregnant patients with mechanical prosthetic valves who receive dose-adjusted LMWH, the LMWH should be administered twice daily subcutaneously to maintain the anti-Xa level between 0.7 and 1.2 U per ml 4 h after administration.** *(Level of Evidence: C)*

6. **In pregnant patients with mechanical prosthetic valves who receive dose-adjusted UFH, the aPTT should be at least twice control.** *(Level of Evidence: C)*

7. **In pregnant patients with mechanical prosthetic valves who receive warfarin, the INR goal should be 3.0 (range 2.5 to 3.5).** *(Level of Evidence: C)*

8. **In pregnant patients with mechanical prosthetic valves, warfarin should be discontinued and continuous intravenous UFH given starting 2 to 3 weeks before planned delivery.** *(Level of Evidence: C)*

**Class IIa**

1. **In patients with mechanical prosthetic valves, it is reasonable to avoid warfarin between weeks 6 and 12 of gestation owing to the high risk of fetal defects.** *(Level of Evidence: C)*

2. **In patients with mechanical prosthetic valves, it is reasonable to resume UFH 4 to 6 h after delivery and begin oral warfarin in the absence of significant bleeding.** *(Level of Evidence: C)*

3. **In patients with mechanical prosthetic valves, it is reasonable to give low-dose aspirin (75 to 100 mg per day) in the second and third trimesters of pregnancy in addition to anticoagulation with warfarin or heparin.** *(Level of Evidence: C)*

**Class III**

1. **LMWH should not be administered to pregnant patients with mechanical prosthetic valves unless anti-Xa levels are monitored 4 to 6 h after administration.** *(Level of Evidence: C)*

2. **Dipyridamole should not be used instead of aspirin as an alternative antiplatelet agent in pregnant patients with mechanical prosthetic valves because of its harmful effects on the fetus.** *(Level of Evidence: B)*

In April 2004, labeling approved by the Food and Drug Administration stated that pregnancy alone conferred an increased risk for thromboembolism and an even higher risk with thrombotic disease and certain high-risk pregnancy conditions. Although not adequately studied, women with mechanical prosthetic heart valves may be at higher risk for thromboembolism during pregnancy regardless of the anticoagulant used, and when pregnant, they have a higher rate of fetal loss from stillbirth, spontaneous abortion, and premature delivery.

In patients receiving UFH, therapy requires aggressive monitoring and appropriate dose adjustment. A minimum target aPTT ratio of 1.5 times the control is likely to be inadequate. A target aPTT ratio of at least twice the control should be attained.

There are still insufficient grounds to make definitive recommendations about optimal antithrombotic therapy in pregnant patients with mechanical heart valves, because properly designed studies have not been performed. Substantial concern remains about the fetal safety of warfarin, the efficacy of subcutaneous UFH and of LMWH in preventing thromboembolic complications, and the risks of maternal bleeding with various regimens.

The American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy (489,490) concluded that it is reasonable to use one of the following 3 regimens: 1) either LMWH or UFH between 6 and 12 weeks and close to term only, with warfarin used at other times; 2) aggressive dose-adjusted UFH throughout pregnancy; or 3) aggressive adjusted-dose LMWH throughout pregnancy. Before any of these approaches is used, it is crucial to explain the risks in detail to the patient. If warfarin is used, the dose should be adjusted to attain a target INR of 3.0 (range 2.5 to 3.5). If subcutaneous UFH is used, it should be initiated in high doses (17 500 to 20 000 U every 12 h) and adjusted to prolong a 6-h postinjection aPTT of at least twice the control. Adjusted-dose LMWH appears to be a reasonable substitute for UFH, but further information is required about dosing during pregnancy; if LMWH is used during pregnancy, it has been recommended that LMWH be administered twice daily and dosed to achieve anti-Xa levels of 0.7 to 1.2 U per ml 4 to 6 h after injection (489,491).

The addition of aspirin 75 to 100 mg can be considered in an attempt to further reduce the risk of thrombosis, with the recognition that it can increase the risk of bleeding (485). Dipyridamole should not be considered as an alternative antiplatelet agent because of its harmful effects on the fetus. Neither warfarin nor heparin is contraindicated in postpartum mothers who breast-feed (484).

# VI. MANAGEMENT OF CONGENITAL VALVULAR HEART DISEASE IN ADOLESCENTS AND YOUNG ADULTS

The management of valvular abnormalities associated with complex congenital heart disease is beyond the scope of these guidelines. Rather, this section concerns isolated valve involvement when it is the primary anatomic abnormality.

In evaluating valvular stenosis in children, severity is usually reported as the peak ventricular-to-peak great artery systolic gradient at cardiac catheterization or maximum instantaneous or mean gradient by Doppler echocardiogra-

phy rather than valve area. With the development of Doppler echocardiographic assessment of valvular obstruction, many pediatric cardiologists have continued to rely on gradients calculated from peak velocity for the semilunar valves rather than on mean gradient or valve area. The peak gradient measured by Doppler velocity (based on maximum instantaneous velocity) is almost always higher than the peak ventricular–to–peak great vessel gradient measured at catheterization. The difference between Doppler peak instantaneous and catheterization peak-to-peak gradients is greater with AS than with pulmonic stenosis and has resulted in most cardiologists using mean gradients, especially in patients with AS. Significant valvular regurgitation may exacerbate the differences. In contrast to children and adolescents, valve area is used by many centers in evaluation of the young adult.

### A. Aortic Stenosis

Adolescents and young adults with isolated AS almost always have congenital fusion of 1 or more commissures that results in a bicuspid or unicuspid valve. Although the prevalence of bicuspid and unicuspid valves may be as high as 1% to 2%, only 1 of 50 children born with these abnormalities will actually have significant obstruction or regurgitation by adolescence. For purposes of these guidelines, adolescents and young adults are defined as patients with minimally calcified valves who are less than 30 years old. Some adults with minimally calcified valves who are more than 30 years old may also benefit under these guidelines.

As the aortic annulus and aortic valve must grow in parallel with somatic growth throughout childhood, the rate of progression of AS during childhood and adolescent growth can be different from that in the adult with acquired AS (see Section III-A).

### 1. Evaluation of Asymptomatic Adolescents or Young Adults With Aortic Stenosis

#### Class I

1. **An ECG is recommended yearly in the asymptomatic adolescent or young adult with AS who has a Doppler mean gradient greater than 30 mm Hg or a peak velocity greater than 3.5 m per second (peak gradient greater than 50 mm Hg) and every 2 years if the echocardiographic Doppler mean gradient is less than or equal to 30 mm Hg or the peak velocity is less than or equal to 3.5 m per second (peak gradient less than or equal to 50 mm Hg). *(Level of Evidence C)***
2. **Doppler echocardiography is recommended yearly in the asymptomatic adolescent or young adult with AS who has a Doppler mean gradient greater than 30 mm Hg or a peak velocity greater than 3.5 m per second (peak gradient greater than 50 mm Hg) and every 2 years if the Doppler gradient is less than or equal to 30 mm Hg or the peak jet velocity is less**

than or equal to 3.5 m per second (peak gradient less than or equal to 50 mm Hg). *(Level of Evidence C)*
3. **Cardiac catheterization for the evaluation of AS is an effective diagnostic tool in the asymptomatic adolescent or young adult when results of Doppler echocardiography are equivocal regarding severity of AS or when there is a discrepancy between clinical and noninvasive findings regarding severity of AS. *(Level of Evidence: C)***
4. **Cardiac catheterization is indicated in the adolescent or young adult with AS who has symptoms of angina, syncope, or dyspnea on exertion if the Doppler mean gradient is greater than 30 mm Hg or the peak velocity is greater than 3.5 m per second (peak gradient greater than 50 mm Hg). *(Level of Evidence C)***
5. **Cardiac catheterization is indicated in the asymptomatic adolescent or young adult with AS who develops T-wave inversion at rest over the left precordium if the Doppler mean gradient is greater than 30 mm Hg or the peak velocity is greater than 3.5 m per second (peak gradient greater than 50 mm Hg). *(Level of Evidence C)***

#### Class IIa

1. **Graded exercise testing is a reasonable diagnostic evaluation in the adolescent or young adult with AS who has a Doppler mean gradient greater than 30 mm Hg or a peak velocity greater than 3.5 m per second (peak gradient greater than 50 mm Hg) if the patient is interested in athletic participation, or if the clinical findings and Doppler findings are disparate. *(Level of Evidence: C)***
2. **Cardiac catheterization for the evaluation of AS is a reasonable diagnostic tool in the asymptomatic adolescent or young adult who has a Doppler mean gradient greater than 40 mm Hg or a peak velocity greater than 4 m per second (peak gradient greater than 64 mm Hg). *(Level of Evidence C)***
3. **Cardiac catheterization for the evaluation of AS is reasonable in the adolescent or young adult who has a Doppler mean gradient greater than 30 mm Hg or a peak velocity greater than 3.5 m per second (peak gradient greater than 50 mm Hg) if the patient is interested in athletic participation or becoming pregnant, or if the clinical findings and Doppler echocardiographic findings are disparate. *(Level of Evidence C)***

The diagnosis of AS can usually be made clinically, with severity estimated by ECG and Doppler echocardiographic studies. Diagnostic cardiac catheterization is occasionally required if there is a discrepancy among clinical evaluation, ECG, and/or Doppler echocardiographic findings. Exercise testing may be useful, especially in those interested in athletic participation. Diagnostic cardiac catheterization

may be helpful if the clinical findings and the Doppler echocardiographic assessment are disparate.

## 2. Indications for Aortic Balloon Valvotomy in Adolescents and Young Adults

### Class I

1. **Aortic balloon valvotomy is indicated in the adolescent or young adult patient with AS who has symptoms of angina, syncope, or dyspnea on exertion and a catheterization peak LV-to-peak aortic gradient greater than or equal to 50 mm Hg without a heavily calcified valve.** *(Level of Evidence: C)*\*
2. **Aortic balloon valvotomy is indicated for the asymptomatic adolescent or young adult patient with AS who has a catheterization peak LV-to-peak aortic gradient greater than 60 mm Hg.** *(Level of Evidence: C)*\*
3. **Aortic balloon valvotomy is indicated in the asymptomatic adolescent or young adult patient with AS who develops ST or T-wave changes over the left precordium on ECG at rest or with exercise and who has a catheterization peak LV-to-aortic gradient greater than 50 mm Hg.** *(Level of Evidence: C)*\*

### Class IIa

1. **Aortic balloon valvotomy is reasonable in the asymptomatic adolescent or young adult patient with AS when catheterization peak LV-to-peak aortic gradient is greater than 50 mm Hg and the patient wants to play competitive sports or desires to become pregnant.** *(Level of Evidence: C)*\*
2. **In the adolescent or young adult patient with AS, aortic balloon valvotomy is probably recommended over valve surgery when balloon valvotomy is possible. Patients should be referred to a center with expertise in balloon valvotomy.** *(Level of Evidence: C)*\*

### Class III

**Aortic balloon valvotomy should not be performed when the asymptomatic adolescent or young adult patient with AS has a catheterization peak LV-to-peak aortic gradient less than 40 mm Hg without symptoms or ECG changes.** *(Level of Evidence: C)*\*

*\*Gradients are usually obtained with patients sedated. If general anesthesia is used, the gradients may be somewhat lower.*

Balloon valvotomy is an efficacious treatment in children and adolescents with AS due to fusion of commissures, whereas it is rarely recommended in older adults with calcific valves, 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. Because balloon valvotomy has resulted in good midterm palliation with little morbidity and little or no short- or intermediate-term mortality in children, adolescents, and young adults, the indications for intervention are considerably more liberal than those in older adults, in whom intervention usually involves AVR. Surgical valvotomy is of historical interest and is now rarely used except in situations in which interventional cardiologists are not available.

Children and young adults with peak Doppler gradients of 64 mm Hg or more or mean gradients greater than 40 mm Hg and those with symptoms may be considered for cardiac catheterization and possible balloon dilation. Patients with lower gradients (50 mm Hg peak or 30 mm Hg mean) are sometimes referred for catheterization if they are interested in participating in athletics, are contemplating pregnancy, or have developed ST-T-wave changes over the left precordium at rest or with exercise. In those children who have had a balloon valvuloplasty when younger, a repeat attempt is usually tried before surgical valve replacement using the above criteria if significant AR is not present.

When balloon aortic valvotomy is ineffective or significant AR is present, surgical valve repair or replacement may be necessary. Because degeneration of homograft or bioprosthetic valves is usually accelerated in the young (see Sections VII-A and VII-B), AVR is usually performed with a mechanical valve. Recently, there has been a renewed interest in valve repair or the Ross operation (81,492–495). The most common complications of the Ross procedure are AR, usually secondary to neoaortic root dilation, and RV outflow tract obstruction, with intervention necessary in roughly 10% of patients within 7 to 10 years. The indications for surgery with the Ross operation or heterograft homograft do not differ from those for mechanical valve replacement.

## B. Aortic Regurgitation

### Class I

1. **An adolescent or young adult with chronic severe AR\* with onset of symptoms of angina, syncope, or dyspnea on exertion should receive aortic valve repair or replacement.** *(Level of Evidence: C)*
2. **Asymptomatic adolescent or young adult patients with chronic severe AR\* with LV systolic dysfunction (ejection fraction less than 0.50) on serial studies 1 to 3 months apart should receive aortic valve repair or replacement.** *(Level of Evidence: C)*
3. **Asymptomatic adolescent or young adult patients with chronic severe AR\* with progressive LV enlargement (end-diastolic dimension greater than 4 standard deviations above normal) should receive aortic valve repair or replacement.** *(Level of Evidence: C)*
4. **Coronary angiography is recommended before AVR in adolescent or young adult patients with AR in whom a pulmonary autograft (Ross operation) is contemplated when the origin of the coronary arter-**

ies has not been identified by noninvasive techniques. *(Level of Evidence: C)*

**Class IIb**

1. An asymptomatic adolescent with chronic severe AR* with moderate AS (peak LV–to–peak aortic gradient greater than 40 mm Hg at cardiac catheterization) may be considered for aortic valve repair or replacement. *(Level of Evidence: C)*
2. An asymptomatic adolescent with chronic severe AR* with onset of ST depression or T-wave inversion over the left precordium on ECG at rest may be considered for aortic valve repair or replacement. *(Level of Evidence: C)*

*See Table 1 (7).*

AR is an uncommon isolated congenital lesion, although it may occasionally develop in adolescents and young adults with a bicuspid aortic valve, discrete sub-aortic obstruction, or prolapse of 1 aortic cusp into a ventricular septal defect. It is commonly the consequence of attempts to relieve stenosis of the valve by either balloon dilation or surgical valvulotomy, or after the Ross procedure. The indications for surgery with severe isolated AR or mixed aortic valve disease are similar to those for adults, that is, symptoms, LV dysfunction (ejection fraction less than 0.50), or severely increased LV end-diastolic or end-systolic diameter, taking into account variations in body size. As noted above, surgery has usually involved mechanical or biological valve replacement (see SectionVII-A), but the Ross operation or aortic valve repair are viable alternatives in some centers. Indications for surgery in patients with AR and dilated aortic roots or ascending aortas are the same as those for older adult patients (see Sections III-B-3 and III-C).

### C. Mitral Regurgitation

**Class I**

1. MV surgery is indicated in the symptomatic adolescent or young adult with severe congenital MR* with NYHA functional class III or IV symptoms. *(Level of Evidence: C)*
2. MV surgery is indicated in the asymptomatic adolescent or young adult with severe congenital MR* and LV systolic dysfunction (ejection fraction less than or equal to 0.60). *(Level of Evidence: C)*

**Class IIa**

MV repair is reasonable in experienced surgical centers in the asymptomatic adolescent or young adult with severe congenital MR* with preserved LV systolic function if the likelihood of successful repair

without residual MR is greater than 90%. *(Level of Evidence: B)*

**Class IIb**

The effectiveness of MV surgery is not well established in asymptomatic adolescent or young adult patients with severe congenital MR* and preserved LV systolic function in whom valve replacement is highly likely. *(Level of Evidence: C)*

*See Table 1 (7).*

MR caused by myxomatous MV disease and MVP is a common congenital lesion. MR also develops commonly in children with primum atrioventricular septal defects, which may involve an isolated ostium primum atrial septal defect; ventricular septal defect in the inlet (posterior) septum; abnormalities of the mitral or tricuspid valve, including clefts; or a combination of these disorders. Repair of the defects in early childhood is now commonplace, with low mortality and morbidity. The most common long-term sequela of surgery is MR, which can be mild, moderate, or severe.

The pathophysiology, diagnosis, and therapy of residual MR in atrioventricular septal defects, rheumatic fever, or MVP are similar to those discussed for the adult with MR (Section III-F). When patients with MR develop symptoms or deteriorating LV systolic function, surgery should be performed. MV repair is usually possible in MR after atrioventricular septal defect repair or MR secondary to MVP. Rarely, MV replacement with a mechanical or biological valve is necessary.

### D. Mitral Stenosis

**Class I**

MV surgery is indicated in adolescent or young adult patients with congenital MS who have symptoms (NYHA functional class III or IV) and mean MV gradient greater than 10 mm Hg on Doppler echocardiography.* *(Level of Evidence: C)*

**Class IIa**

1. MV surgery is reasonable in adolescent or young adult patients with congenital MS who have mild symptoms (NYHA functional class II) and mean MV gradient greater than 10 mm Hg on Doppler echocardiography.* *(Level of Evidence: C)*
2. MV surgery is reasonable in the asymptomatic adolescent or young adult with congenital MS with pulmonary artery systolic pressure 50 mm Hg or greater and a mean MV gradient greater than or equal to 10 mm Hg.* *(Level of Evidence: C)*

**Class IIb**

The effectiveness of MV surgery is not well established in the asymptomatic adolescent or young adult with congenital MS and new-onset atrial fibrillation

**or multiple systemic emboli while receiving adequate anticoagulation.\* *(Level of Evidence: C)***

***\*See Table 1 (7).***

In developed countries, MS in adolescents and young adults is often congenital in origin. In 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 bicuspid aortic valve and AS, supravalvar mitral ring, and coarctation of the aorta.

The clinical, electrocardiographic, and radiologic features of congenital MS are similar to those of acquired MS in adults. The echocardiogram is essential in evaluating the MV 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 in adolescents and young adults, but TEE is sometimes necessary.

Medical management including beta blockers and diuretics may be of some utility with mild MS. It is important to prevent and treat common complications such as pulmonary infections, endocarditis, and atrial fibrillation. Surgical intervention may be necessary in severe cases. The surgical management of congenital MS has improved considerably with the improved appreciation of the mechanism of MV function and the improved ability to visualize the valve afforded by TEE. In those patients with a parachute MV, creation of fenestrations among the fused chordae may increase effective orifice area and improve symptoms dramatically. MV replacement may occasionally be necessary but is especially problematic in those with a hypoplastic mitral annulus, in whom an annulus-enlarging operation may be necessary. Recently, balloon dilation of congenital MS has been attempted (496), but its utility is limited in patients with significant stenosis of the subvalvular apparatus. 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 procedure. In adolescent and young adult patients with rheumatic MS, the results of balloon dilation are similar to those in older adults (see Section III-D-8).

### E. Tricuspid Valve Disease

Acquired disease of the tricuspid valve is very uncommon in adolescents and young adults and is usually related to 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 wide variation in the severity of valve leaflet abnormalities in Ebstein's anomaly. An interatrial communication, usually in the form of a patent foramen ovale, is present in most cases. 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 approximately 25%. Patients with Ebstein's anomaly may be asymptomatic with no cyanosis and no atrial arrhythmias, but they often are cyanotic owing to right-to-left shunting (497), which is associated with exercise intolerance. RV dysfunction may eventually lead to right-sided heart failure, frequently exacerbated by an atrial arrhythmia such as atrial tachycardia, atrial flutter, or atrial fibrillation. Exercise testing may be useful in determining symptom status and degree of exercise-induced arterial desaturation.

Predictors of poor outcome include NYHA functional class III or IV symptoms, cardiothoracic ratio greater than 65%, atrial fibrillation, severity of cyanosis, and magnitude of TR. However, patients with Ebstein's anomaly who reach late adolescence and adulthood often have an excellent outcome (498).

### 1. Evaluation of Tricuspid Valve Disease in Adolescents and Young Adults

**Class I**

1. **An ECG is indicated for the initial evaluation of adolescent and young adult patients with TR, and serially every 1 to 3 years, depending on severity. *(Level of Evidence: C)***
2. **Chest X-ray is indicated for the initial evaluation of adolescent and young adult patients with TR, and serially every 1 to 3 years, depending on severity. *(Level of Evidence: C)***
3. **Doppler echocardiography is indicated for the initial evaluation of adolescent and young adult patients with TR, and serially every 1 to 3 years, depending on severity. *(Level of Evidence: C)***
4. **Pulse oximetry at rest and/or during exercise is indicated for the initial evaluation of adolescent and young adult patients with TR if an atrial communication is present, and serially every 1 to 3 years, depending on severity. *(Level of Evidence: C)***

**Class IIa**

1. **If there is a symptomatic atrial arrhythmia, an electrophysiology study can be useful for the initial evaluation of adolescent and young adult patients with TR. *(Level of Evidence: C)***
2. **Exercise testing is reasonable for the initial evaluation of adolescent and young adult patients with TR, and serially every 1 to 3 years. *(Level of Evidence: C)***

**Class IIb**

**Holter monitoring may be considered for the initial evaluation of asymptomatic adolescent and young adult patients with TR, and serially every 1 to 3 years. *(Level of Evidence: C)***

## 2. Indications for Intervention in Tricuspid Regurgitation

### Class I

1. **Surgery for severe TR is recommended for adolescent and young adult patients with deteriorating exercise capacity (NYHA functional class III or IV). *(Level of Evidence: C)***
2. **Surgery for severe TR is recommended for adolescent and young adult patients with progressive cyanosis and arterial saturation less than 80% at rest or with exercise. *(Level of Evidence: C)***
3. **Interventional catheterization closure of the atrial communication is recommended for the adolescent or young adult with TR who is hypoxemic at rest and with exercise intolerance due to increasing hypoxemia with exercise, when the tricuspid valve appears difficult to repair surgically. *(Level of Evidence: C)***

### Class IIa

1. **Surgery for severe TR is reasonable in adolescent and young adult patients with NYHA functional class II symptoms if the valve appears to be repairable. *(Level of Evidence: C)***
2. **Surgery for severe TR is reasonable in adolescent and young adult patients with atrial fibrillation. *(Level of Evidence: C)***

### Class IIb

1. **Surgery for severe TR may be considered in asymptomatic adolescent and young adult patients with increasing heart size and a cardiothoracic ratio of more than 65%. *(Level of Evidence: C)***
2. **Surgery for severe TR may be considered in asymptomatic adolescent and young adult patients with stable heart size and an arterial saturation of less than 85% when the tricuspid valve appears repairable. *(Level of Evidence: C)***
3. **In adolescent and young adult patients with TR who are mildly cyanotic at rest but who become very hypoxemic with exercise, closure of the atrial communication by interventional catheterization may be considered when the valve does not appear amenable to repair. *(Level of Evidence: C)***
4. **If surgery for Ebstein's anomaly is planned in adolescent and young adult patients (tricuspid valve repair or replacement), a preoperative electrophysiological study may be considered to identify accessory pathways. If present, these may be considered for mapping and ablation either preoperatively or at the time of surgery. *(Level of Evidence: C)***

Surgical management of Ebstein's anomaly remains challenging (499). For adolescents and young adults, tricuspid valve repair may be performed, especially when there is a mobile anterior leaflet free of tethering to the ventricular septum. If TR is mild and hypoxemia at rest or exercise is problematic, closure of the atrial septal defect in the catheterization laboratory has been successful in eliminating the hypoxemia. Occasionally, the tricuspid valve is not reparable, and valve replacement with a bioprosthesis or a mechanical valve may be necessary (500).

### 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 are congenital in origin. Most patients with stenosis have a conical or dome-shaped pulmonary valve formed by fusion of the valve leaflets. Occasionally, the valve may be thickened and dysplastic, with the stenosis caused by inability of the valve leaflets to separate 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 in severe pulmonic stenosis with systemic or suprasystemic RV pressures, with decreased preload or dehydration, or with a low systemic vascular resistance state (such as pregnancy). Eventually, with long-standing untreated severe obstruction, TR and RV failure may occur. At any age, if the foramen ovale is patent, RV compliance may be reduced sufficiently to elevate right atrial pressure, which allows right-to-left shunting and cyanosis.

### 1. Evaluation of Pulmonic Stenosis in Adolescents and Young Adults

#### Class I

1. **An ECG is recommended for the initial evaluation of pulmonic stenosis in adolescent and young adult patients, and serially every 5 to 10 years for follow-up examinations. *(Level of Evidence: C)***
2. **Transthoracic Doppler echocardiography is recommended for the initial evaluation of pulmonic stenosis in adolescent and young adult patients, and serially every 5 to 10 years for follow-up examinations. *(Level of Evidence: C)***
3. **Cardiac catheterization is recommended in the adolescent or young adult with pulmonic stenosis for evaluation of the valvular gradient if the Doppler peak jet velocity is greater than 3 m per second (estimated peak gradient greater than 36 mm Hg) and balloon dilation can be performed if indicated. *(Level of Evidence: C)***

#### Class III

> **Diagnostic cardiac catheterization is not recommended for the initial diagnostic evaluation of pulmonic stenosis in adolescent and young adult patients. *(Level of Evidence: C)***

### 2. Indications for Balloon Valvotomy in Pulmonic Stenosis

**Class I**

1. **Balloon valvotomy is recommended in adolescent and young adult patients with pulmonic stenosis who have exertional dyspnea, angina, syncope, or presyncope and an RV-to-pulmonary artery peak-to-peak gradient greater than 30 mm Hg at catheterization.** *(Level of Evidence: C)*
2. **Balloon valvotomy is recommended in asymptomatic adolescent and young adult patients with pulmonic stenosis and an RV-to-pulmonary artery peak-to-peak gradient greater than 40 mm Hg at catheterization.** *(Level of Evidence: C)*

**Class IIb**

**Balloon valvotomy may be reasonable in asymptomatic adolescent and young adult patients with pulmonic stenosis and an RV-to-pulmonary artery peak-to-peak gradient 30 to 39 mm Hg at catheterization.** *(Level of Evidence: C)*

**Class III**

**Balloon valvotomy is not recommended in asymptomatic adolescent and young adult patients with pulmonic stenosis and an RV–to–pulmonary artery peak-to-peak gradient less than 30 mm Hg at catheterization.** *(Level of Evidence: C)*

The clinical course of children and young adults with pulmonary valve stenosis has been well described. The second Natural History of Congenital Heart Defects study (501) reported that the probability of 25-year survival was 96%. Fewer than 20% of patients managed medically required a valvotomy, and only 4% of the patients who had undergone surgery required a second operation. For patients who had an initial transpulmonary gradient less than 25 mm Hg, 96% were free of cardiac operation over a 25-year period.

Infective endocarditis was uncommon. Only 1 case developed in the 592 patients followed up for a median of 18 years, 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 in the United States for the typically domed, thickened valve (502–504). Although long-term follow-up of pulmonary balloon valvotomy is not yet available, the early and midterm results (up to 10 years) (505) suggest that the long-term results will be similar to surgical valvotomy, with little or no recurrence over a 22- to 30-year period.

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.

### G. Pulmonary Regurgitation

Pulmonic valve regurgitation is unusual as an isolated congenital defect, but it is an almost unavoidable result of either surgical or balloon valvuloplasty of valvular pulmonic stenosis or surgical repair of tetralogy of Fallot. Among patients with pulmonic stenosis who undergo surgical valvotomy, 87% have pulmonary regurgitation by Doppler echocardiography (501), although it was audible in only 58%.

Most physicians would perform pulmonary valve replacement in patients with NYHA class II or III symptoms and severe pulmonary regurgitation, but the indications in asymptomatic patients on the basis of regurgitant fraction, RV end-diastolic or end-systolic volume, or RV ejection fraction remain unclear.

## VII. SURGICAL CONSIDERATIONS

### A. Aortic Valve Surgery

The types of operations available to treat aortic valve dysfunction include AVR with a mechanical or bioprosthetic valve, AVR with an allograft (homograft) valve, pulmonic valve autotransplantation (Ross operation) (81,492,493,495,506), aortic valve repair, and left ventricle to–descending aorta shunt. Each has specific advantages and disadvantages. Cardiopulmonary bypass is used in aortic valve operations, and these procedures are usually performed through a median sternotomy incision, although partial sternotomy (minimally invasive incisions) is gaining acceptance. See Sections III-A-6 and III-B-2-g for indications for AVR or repair in patients with AS and AR.

### 1. Antithrombotic Therapy for Patients With Aortic Mechanical Heart Valves

After mechanical AVR, the goal of antithrombotic therapy is usually to achieve an INR of 2.5 to 3.5 for the first 3 months after surgery and 2.0 to 3.0 beyond that time (see Section IX-A). Low-dose aspirin (75 to 100 mg per day) is also indicated in addition to warfarin (485), as discussed in Section IX-A-1. At that level of anticoagulation, the risk of significant hemorrhage appears to be 1% to 2% per year.

### 2. Stented and Nonstented Heterografts

#### a. Aortic Valve Replacement With Stented Heterografts

The first-generation stented heterografts (porcine heterografts) exhibited a freedom from structural valve deterioration of approximately 40% by 18 postoperative years. However, the rate of structural valve deterioration is age-related (96,507–519), being increased for younger patients, and in patients less than 40 years of age, approximately half of all porcine valves fail by 10 years. Bovine pericardial valves appear to have a lower rate of structural valve deterioration,

with 15-year data indicating that 77% of valves in surviving patients of all ages are functioning without explantation, and among patients undergoing primary AVR at an age greater than 65 years, fewer than 10% underwent valve explantation by 15 postoperative years (96,515). The reported rate of structural valve deterioration for second-generation porcine valves appears so far to be equivalent to that of stented bovine valves.

### b. Aortic Valve Replacement With Stentless Heterografts

The major goal of stentless heterografts is to achieve enhanced hemodynamic efficiency relative to stented valves (520–525). The long-term importance of hemodynamic efficiency of prosthetic heart valves is currently a subject of investigation and disagreement. The argument favoring the use of stentless valves is that stented valves of any kind are at least partially stenotic (particularly in small sizes) and that even small postoperative gradients may lead to incomplete LV mass regression postoperatively (522,524–526), which will, in turn, lead to impaired long-term survival and symptom status.

Stentless heterografts have the disadvantages that their implantation is more complex than that for stented valves and their long-term outcomes are unknown. There is a low incidence (7% to 10%) of early mild AR in some series (522,523,525), which may progress with time. Observational studies with 8- to 10-year follow-up (527) appear to show a low risk of structural valve deterioration with stentless heterografts.

### 3. Aortic Valve Homografts

It had been hoped that aortic valve homografts would outlast heterografts, particularly in young patients, but to date, long-term data do not support this view. One possible advantage of homografts is in the avoidance of early endocarditis and in the treatment of aortic valve endocarditis (528–531), particularly complex aortic root endocarditis. The risk of thromboembolism is very low after homograft implantation, and hemodynamic efficiency is excellent even in small sizes. The biggest disadvantage of homografts is that reoperation after homograft AVR is more difficult than reoperation after placement of standard prostheses, because the entire homograft may become severely calcified.

### 4. Pulmonic Valve Autotransplantation

Pulmonic valve autotransplantation (Ross operation) has been performed in small numbers, and long-term follow-up studies have been inconsistent, which makes analysis of long-term advantages and disadvantages difficult. The known advantages of the procedure are that the autograft may grow in children, warfarin is not required, there is a low incidence of thromboembolism, the autograft is a hemodynamically efficient valve, and the incidence of endocarditis is low (81,492,493,495,506,532). The disadvantage of pulmonic autotransplantation is that the operation is much more complex than standard AVR and in most series has

been associated with at least some increase in in-hospital mortality. There is also an incidence of early aortic valve failure based on technical considerations or dilatation of the aortic root, and the homograft used to replace the pulmonic valve is also subject to failure, sometimes early, within a few years of operation (506). Deterioration of the pulmonary homograft often offsets potential advantages of the autograft.

### 5. Aortic Valve Repair

Multiple strategies for aortic valve repair have been explored, some successfully. In particular, repair of insufficient bicuspid aortic valves in the adult has been increasingly successful at limited numbers of centers (533–535). Among the advantages of this strategy are the lack of need for anticoagulation, a low thromboembolic risk, a low endocarditis risk, a hemodynamically efficient valve, and a straightforward reoperation, if needed. The disadvantages are lack of uniform applicability, lack of widespread experience with surgical techniques, and the need for reoperation. Long-term data are limited, but the risk of reoperation appears to be about 15% by 10 postoperative years.

Much progress has been made in the repair of aortic valves rendered insufficient by aortic root pathology (228,536–541). When an aortic root aneurysm exists, the operation to restore competence to the aortic valve involves resecting the aorta and resuspending the valve in association with a Dacron graft that is used to replace the aorta. Advantages of this strategy include avoidance of warfarin, a low thromboembolic risk, a very efficient valve, and what appears to be a low risk of prosthetic valve endocarditis. The disadvantages are, again, limited applicability in the setting of intrinsic leaflet pathology and the high level of surgical expertise and experience required.

### 6. Major Criteria for Aortic Valve Selection

#### Class I

1. **A mechanical prosthesis is recommended for AVR in patients with a mechanical valve in the mitral or tricuspid position.** *(Level of Evidence: C)*
2. **A bioprosthesis is recommended for AVR in patients of any age who will not take warfarin or who have major medical contraindications to warfarin therapy.** *(Level of Evidence: C)*

#### Class IIa

1. **Patient preference is a reasonable consideration in the selection of aortic valve operation and valve prosthesis. A mechanical prosthesis is reasonable for AVR in patients under 65 years of age who do not have a contraindication to anticoagulation. A bioprosthesis is reasonable for AVR in patients under 65 years of age who elect to receive this valve for lifestyle considerations after detailed discussions of the risks of anticoagulation versus the likelihood that a second**

AVR may be necessary in the future. *(Level of Evidence: C)*

2. **A bioprosthesis is reasonable for AVR in patients aged 65 years or older without risk factors for thromboembolism. *(Level of Evidence: C)***

3. **Aortic valve re-replacement with a homograft is reasonable for patients with active prosthetic valve endocarditis. *(Level of Evidence: C)***

**Class IIb**

A bioprosthesis might be considered for AVR in a woman of childbearing age *(see Sections V–E and V–F)*. *(Level of Evidence: C)*

*B. Mitral Valve Surgery*

**1. Mitral Valve Repair**

*a. Myxomatous Mitral Valve*

**Class I**

1. **MV repair is recommended when anatomically possible for patients with severe degenerative MR who fulfill clinical indications, and patients should be referred to surgeons who are expert in repair. *(Level of Evidence: B)***

2. **Patients who have undergone successful MV repair should continue to receive antibiotics as indicated for endocarditis prophylaxis. *(Level of Evidence: C)***

3. **Patients who have undergone successful MV repair and have chronic or paroxysmal atrial fibrillation should continue to receive long-term anticoagulation with warfarin. *(Level of Evidence: B)***

4. **Patients who have undergone successful MV repair should undergo 2D and Doppler echocardiography before discharge or at the first postoperative outpatient visit. *(Level of Evidence: C)***

5. **Tricuspid valve repair is beneficial for severe TR in patients with MV disease that requires MV surgery. *(Level of Evidence: B)***

**Class IIa**

1. **Oral anticoagulation is reasonable for the first 3 months after MV repair. *(Level of Evidence: C)***

2. **Long-term treatment with low-dose aspirin (75 to 100 mg per day) is reasonable in patients who have undergone successful MV repair and remain in sinus rhythm. *(Level of Evidence: C)***

3. **Tricuspid annuloplasty is reasonable for mild TR in patients undergoing MV repair when there is pulmonary hypertension or tricuspid annular dilatation. *(Level of Evidence: C)***

**Class IIb**

In patients with MR and a history of atrial fibrillation, a Maze procedure may be considered at the time of MV repair. *(Level of Evidence: B)*

Myxomatous MV disease produces MR based on rupture or elongation of chordae tendineae, valve leaflet instability, annulus dilatation, or multiple causes that result in excessive MV leaflet motion. In the majority of these conditions, experienced surgeons can repair the MV using strategies that involve removal of unsupported leaflet structures, transfer of chordae (357,358), or the use of artificial chordae to support unstable areas of the leaflet, the sliding of supported areas of the leaflet to cover the MV orifice, and stabilization of the size and shape of the MV annulus with an artificial ring (318,319, 27,343–348). MV repair is the treatment of choice for degenerative valve disease, because patients in sinus rhythm do not need warfarin, the thromboembolism rate is low, valve efficiency and hemodynamics are good, there is little adverse effect on LV function, the risk of endocarditis is low, and the long-term survival rate is favorable compared with MV replacement (see Section III-F-3). Concomitant tricuspid valve repair should be performed when there is severe TR or mild-to-moderate TR and tricuspid annular dilatation (see Section III-H-2). In patients presenting for MV repair with chronic atrial fibrillation, a concomitant surgical procedure to eliminate atrial fibrillation may prevent future embolic events by restoring normal sinus rhythm (370–376). The decision to proceed with a surgical procedure to eliminate atrial fibrillation should be made based on the age and health of the patient, as well as the surgical expertise, because this procedure may add to the morbidity of the operation (see Section III-F-3-b).

The likelihood of a successful MV repair is related to the extent of the MV dysfunction (with isolated posterior leaflet dysfunction being the most favorable condition); the presence and extent of calcification; the amount of pliable, noncalcified valve tissue; and surgeon experience. Recurrent MR after repair may occur with time, but in favorable situations, more than 90% of valves are still functioning well after 10 years (318,319).

*b. Rheumatic Heart Disease*

**Class I**

Percutaneous or surgical MV commissurotomy is indicated when anatomically possible for treatment of severe MS, when clinically indicated. *(Level of Evidence: C)*

Rheumatic MR is inconsistently reparable, and the long-term outcomes after repair are not as good as for valve repair for degenerative MV disease. Rheumatic pathology often leads to leaflet and chordal scarring, which restricts the leaflet motion, and leaflet scarring may be progressive after repair. Rheumatic MS that is not associated with severe chordal fusion or shortening or with calcification may be treated with either percutaneous or open mitral commissurotomy with a high degree of long-term success. Clinical indications for these procedures are discussed in Sections III-D-8 and III-D-9.

### c. Ischemic Mitral Valve Disease

By definition, all patients with ischemic MR have significant CAD that usually has a significant effect on long-term survival. The pathology of ischemic MR has multiple subgroups, with the most common situation being functional MR, in which the valve leaflets are structurally normal, but LV chamber enlargement and papillary muscle displacement tether the MV via the chordal attachments and prevent leaflet coaptation (379–386). When functional MR is severe, it may be corrected by placement of an annuloplasty ring that decreases the annular circumference, shortens the intertrigonal distance, reduces the septal-lateral (anterior-posterior) annular diameter, and restores the geometry of the annulus, thereby allowing the MV leaflets to coapt (387–390,396–405). This strategy acutely decreases or eliminates MR, but because the fundamental abnormality is related to LV function, the late survival rate of these patients is relatively low compared with patients with other MV pathologies, and the recurrence rate of MR is higher. For patients with moderate functional MR, it is not yet clear whether MV repair improves outcomes.

Patients with ischemic MV disease who have anatomic MR based on infarction or rupture of the papillary muscles benefit from either mitral repair or MV replacement. Papillary muscle rupture often produces severe MR and hemodynamic decompensation, which is an indication for emergency surgery.

### d. Mitral Valve Endocarditis

With increased surgical experience in mitral reparative techniques, MV endocarditis has become more consistently treatable with repair (542–544). There appears to be a low risk of recurrent infection, and in experienced hands, it is often possible to avoid the need for an MV prosthesis (see Section IV-C-1). Surgery, however, must not be delayed until extensive valve disruption has occurred.

### 2. Selection of Mitral Valve Prostheses (Mechanical or Bioprostheses)

#### Class I

**A bioprosthesis is indicated for MV replacement in a patient who will not take warfarin, is incapable of taking warfarin, or has a clear contraindication to warfarin therapy. *(Level of Evidence: C)***

#### Class IIa

1. **A mechanical prosthesis is reasonable for MV replacement in patients under 65 years of age with long-standing atrial fibrillation. *(Level of Evidence: C)***
2. **A bioprosthesis is reasonable for MV replacement in patients 65 years of age or older. *(Level of Evidence: C)***
3. **A bioprosthesis is reasonable for MV replacement in patients under 65 years of age in sinus rhythm who elect to receive this valve for lifestyle considerations after detailed discussions of the risks of anticoagula-**

**tion versus the likelihood that a second MV replacement may be necessary in the future. *(Level of Evidence: C)***

The selection of a valve is a multifactorial decision. The STS National Cardiac Surgery Database (93) indicates that the numbers of MV reparative procedures are increasing relative to MV replacement. Among patients receiving an MV replacement, more patients received mechanical valves than bioprostheses. Medicare data indicate that the mortality for isolated MV replacement in patients older than 65 years is 14.1%, which increases to 20.5% in low-volume centers (95).When MV pathology is combined with CAD, the risks of surgery increase.

### 3. Choice of Mitral Valve Operation

MV repair should be able to be achieved by experienced surgeons for the majority of patients with degenerative MV disease and ischemic valve disease, and patients should be referred to surgeons expert in repair. For patients with rheumatic MV disease and endocarditis, repair may be more difficult.

For patients undergoing MV replacement, preservation of the chordal apparatus preserves LV function and enhances postoperative survival compared with MV replacement, in which the apparatus is disrupted (345,353–356), as discussed in Section III-F-3. In the randomized trials, there was no difference in survival rate based on valve type. However, the failure rate of bioprostheses has been higher in the mitral than in the aortic position (96,507–509,512–516,518,545), which adds impetus to the use of mechanical prostheses in younger patients.

The availability of surgical ablation procedures for atrial fibrillation offers the possibility of converting the patient to sinus rhythm and avoiding anticoagulation after MV repair or replacement with a bioprosthesis (370–376). If patients can be maintained in sinus rhythm, the advantage of a bioprosthesis is enhanced. For patients with a history of atrial fibrillation who are undergoing MV repair, a Maze-type procedure results in sinus rhythm in 75% to 90% of cases by 6 postoperative months, with long-term data indicating sustained results up to 8 years and reduced risk of stroke (373,376).

### C. Tricuspid Valve Surgery

#### Class I

**Severe TR in the setting of surgery for multivalvular disease should be corrected. *(Level of Evidence: C)***

#### Class IIa

**Tricuspid annuloplasty is reasonable for mild TR in patients undergoing MV surgery when there is pulmonary hypertension or tricuspid annular dilatation. *(Level of Evidence: C)***

The most common cause of TR is dilatation of the tricuspid valve annulus caused by pulmonary hypertension. The

tricuspid leaflets are usually normal, and tricuspid valve annuloplasty usually corrects or improves the situation. Severe TR should be treated with annuloplasty during operations for multivalvular disease (see Section III-H-2). When leaflet anatomy is severely abnormal, tricuspid valve replacement may be needed, but this situation is not common. There are no data clearly showing the advantage of one type of tricuspid prosthesis over another.

### D. Valve Selection for Women of Child-Bearing Age

There is no ideal valve prosthesis for women of childbearing age who might wish to become pregnant. Bioprostheses may be subject to premature heterograft or homograft failure. Because mechanical valves require anticoagulation, there is an increased risk of fetal abnormalities and mortality, and there may be an increased risk of maternal complications, including thromboembolism. Discussion with the patient concerning the risk of the prosthesis is important.

## VIII. INTRAOPERATIVE ASSESSMENT

### Class I

1. **Intraoperative TEE is recommended for valve repair surgery.** *(Level of Evidence: B)*
2. **Intraoperative TEE is recommended for valve replacement surgery with a stentless xenograft, homograft, or autograft valve.** *(Level of Evidence: B)*
3. **Intraoperative TEE is recommended for valve surgery for infective endocarditis.** *(Level of Evidence: B)*

### Class IIa

**Intraoperative TEE is reasonable for all patients undergoing cardiac valve surgery.** *(Level of Evidence: C)*

Detailed and comprehensive evaluation of valve lesions during cardiac surgery has become possible and common since the development of TEE. This includes confirmation of the preoperative diagnosis and associated pathology, provision of additional detail and depth about the severity and mechanism of valve dysfunction, detection of previously undiagnosed conditions, and evaluation of the surgical result in the operating room, which makes possible the immediate correction of detected problems. Studies have documented the impact of intraoperative TEE on valve surgery, with changes in the operative plan based on TEE findings reported in 11% to 14% of cases and detection of problems with surgical procedure and subsequent need to return to cardiopulmonary bypass reported in 2% to 6% (546–549). Other important aspects of TEE during valve surgery include assessment of ventricular function and detection of intracardiac air and aortic dissection.

Intraoperative TEE is especially important during valve repair surgery. Examination before cardiopulmonary bypass provides insight into the mechanism of valve dysfunction and therefore facilitates surgical planning. More importantly, intraoperative TEE allows immediate assessment of the repair after cardiopulmonary bypass. Intraoperative TEE during valve replacement surgery with a stented prosthetic valve is also useful, although there will be a lower rate of problems detected after cardiopulmonary bypass. Valve replacement with a stentless xenograft, homograft, or autograft valve will have a higher likelihood of technical problems during surgery, and therefore, TEE is virtually essential in this setting because it is currently the best way to assess valve function intraoperatively.

The committee recommends that institutions performing valve surgery establish consistent and credible intraoperative echocardiography programs with knowledgeable echocardiographers committed to and capable of providing accurate anatomic and functional information relevant to valve operations.

## IX. MANAGEMENT OF PATIENTS WITH PROSTHETIC HEART VALVES

The results of valve surgery with regard to survival, functional class, valve function, and complications are dependent on patient-related factors, cardiac function, type of surgery, type of prosthesis, and medical comorbidities (550).

### A. Antithrombotic Therapy

### Class I

1. **After AVR with bileaflet mechanical or Medtronic Hall prostheses, in patients with no risk factors,\* warfarin is indicated to achieve an INR of 2.0 to 3.0. If the patient has risk factors, warfarin is indicated to achieve an INR of 2.5 to 3.5.** *(Level of Evidence: B)*
2. **After AVR with Starr-Edwards valves or mechanical disc valves (other than Medtronic Hall prostheses), in patients with no risk factors,\* warfarin is indicated to achieve an INR of 2.5 to 3.5.** *(Level of Evidence: B)*
3. **After MV replacement with any mechanical valve, warfarin is indicated to achieve an INR of 2.5 to 3.5.** *(Level of Evidence: C)*
4. **After AVR or MV replacement with a bioprosthesis and no risk factors,\* aspirin is indicated at 75 to 100 mg per day.** *(Level of Evidence: C)*
5. **After AVR with a bioprosthesis and risk factors,\* warfarin is indicated to achieve an INR of 2.0 to 3.0.** *(Level of Evidence: C)*
6. **After MV replacement with a bioprosthesis and risk factors,\* warfarin is indicated to achieve an INR of 2.5 to 3.5.** *(Level of Evidence: C)*
7. **For those patients who are unable to take warfarin after MV replacement or AVR, aspirin is indicated in a dose of 75 to 325 mg per day.** *(Level of Evidence: B)*
8. **The addition of aspirin 75 to 100 mg once daily to therapeutic warfarin is recommended for all patients with mechanical heart valves and those patients with**

**biological valves who have risk factors.\*** *(Level of Evidence: B)*

**Class IIa**

1. **During the first 3 months after AVR with a mechanical prosthesis, it is reasonable to give warfarin to achieve an INR of 2.5 to 3.5.** *(Level of Evidence: C)*
2. **During the first 3 months after AVR or MV replacement with a bioprosthesis, in patients with no risk factors,\* it is reasonable to give warfarin to achieve an INR of 2.0 to 3.0.** *(Level of Evidence: C)*

**Class IIb**

**In high-risk patients with prosthetic heart valves in whom aspirin cannot be used, it may be reasonable to give clopidogrel (75 mg per day) or warfarin to achieve an INR of 3.5 to 4.5.** *(Level of Evidence: C)*

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

All patients with mechanical valves require warfarin therapy, as indicated in Table 2 (568). Aspirin is recommended for all patients with prosthetic heart valves: aspirin alone in patients with bioprostheses and no risk factors, and aspirin combined with warfarin in patients with mechanical heart valves and high-risk patients with bioprostheses. In high-risk patients who cannot take aspirin, the addition of clopidogrel to warfarin therapy should be considered. Even with the use of warfarin, risk of thromboembolism is 1% to 2% per year (99,100,102,551–553), but the risk is considerably higher without treatment with warfarin (554).

Almost all studies have shown that the risk of embolism is greater with a valve in the mitral position (mechanical or biological) than with one in the aortic position (100,106,553–555). 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 (556), before the valve is fully endothelialized (480).

### 1. Mechanical Valves

All patients with mechanical valves require anticoagulation. For mechanical prostheses in the aortic position, the INR with warfarin therapy 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 disc valves and Starr-Edwards valves. For prostheses in the mitral position, the INR should be maintained between 2.5 and 3.5 for all mechanical valves. There is a difference of opinion regarding the Starr-Edwards valve in the aortic position, with the minority opinion recommending that INR be maintained between 2.0 and 3.0. In patients with aortic mechanical prostheses who are at higher risk of thromboembolic complications, INR should be maintained at 2.5 to 3.5, and the addition of aspirin should be considered (see below). These include patients with atrial fibrillation, previous thromboembolism, and a hypercoagulable state. Many would also include patients with severe LV dysfunction in this higher-risk group (557).

The addition of low-dose aspirin (75 to 100 mg per day) to warfarin therapy (INR 2.0 to 3.5) not only further decreases the risk of thromboembolism (485,558–562) but also decreases mortality due to other cardiovascular diseases. A slight increase in the risk of bleeding with this combination should be kept in mind (558,563). The addition of aspirin (75 to 100 mg per day) to warfarin should be strongly considered unless there is a contraindication to the use of aspirin. This combination is particularly appropriate

**Table 2.** Recommendations for Antithrombotic Therapy in Patients With Prosthetic Heart Valves

| Valve Type | Aspirin (75–100 mg) | Warfarin (INR 2.0–3.0) | Warfarin (INR 2.5–3.5) | No Warfarin |
|---|---|---|---|---|
| Mechanical prosthetic | | | | |
|   AVR—low risk | | | | |
|     Less than 3 months | Class I | Class I | Class IIa | |
|     Greater than 3 months | Class I | Class I | | |
|   AVR—high risk | Class I | | Class I | |
|   MVR | Class I | | Class I | |
| Biological prosthetic | | | | |
|   AVR—low risk | | | | |
|     Less than 3 months | Class I | Class IIa | | Class IIb |
|     Greater than 3 months | Class I | | | Class IIa |
|   AVR—high risk | Class I | Class I | | |
|   MVR—low risk | | | | |
|     Less than 3 months | Class I | Class IIa | | |
|     Greater than 3 months | Class I | | | Class IIa |
|   MVR—high risk | Class I | Class I | | |

Depending on patients' clinical status, antithrombotic therapy must be individualized (see special situations in text). In patients receiving warfarin, aspirin is recommended in virtually all situations. Risk factors: atrial fibrillation, left ventricular dysfunction, previous thromboembolism, and hypercoagulable condition. International normalized ratio (INR) should be maintained between 2.5 and 3.5 for aortic disc valves and Starr-Edwards valves. Modified from McAnulty JH, Rahimtoola SH. Antithrombotic therapy in valvular heart disease. In: Schlant R, Alexander RW, editors. Hurst's The Heart. New York, NY: McGraw-Hill, 1998:1867–74. Reprinted with permission from the McGraw-Hill Companies (568).
    AVR indicates aortic valve replacement; and MVR, mitral valve replacement.

in patients who have had an embolus while undergoing warfarin therapy, those with known vascular disease, and those who are known to be particularly hypercoagulable. As an example, such combination therapy is recommended by a committee concerning the use of antithrombotic therapy in women during pregnancy (484). The method of anticoagulation in pregnant patients is controversial and is discussed in Section V-F.

It is important to note that thromboembolic risk is increased early after insertion of the prosthetic heart valve. The use of UFH early after prosthetic valve replacement, before warfarin achieves therapeutic levels, is controversial. Many centers start UFH as soon as the risk of increased surgical bleeding is reduced (usually within 24 to 48 h), with maintenance of aPTT between 55 and 70 s. After an overlap of UFH and warfarin for 3 to 5 days, UFH is discontinued when an INR of 2.0 to 3.0 is achieved. In some patients, achievement of therapeutic INR must be delayed several days after surgery because of mitigating complications.

## 2. Biological Valves

Because of an increased risk of thromboembolism during the first 3 months after implantation of a biological prosthetic valve, anticoagulation with warfarin is often used, especially when the valve is in the mitral position (556), although most centers use only aspirin for biological valves in the aortic position. The risk is particularly high in the first few days after surgery, and many centers start UFH as soon as the risk of increased surgical bleeding is reduced (usually within 24 to 48 h), with maintenance of aPTT between 55 and 70 s. After an overlap of UFH and warfarin for 3 to 5 days, UFH may be discontinued when an INR of 2.0 to 3.0 is achieved. After 3 months, the tissue valve can be treated like native valve disease, and warfarin can be discontinued in more than two thirds of patients with biological valves (102,556,564). In the remaining patients with associated risk factors for thromboembolism, such as atrial fibrillation, previous thromboembolism, or 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 less than 0.30) (557).

## 3. Embolic Events During Adequate Antithrombotic Therapy

In the patient who has a definite embolic episode(s) while undergoing adequate antithrombotic therapy, the dosage of antithrombotic therapy should be increased, when clinically safe, as follows:

- **Warfarin, INR 2.0 to 3.0: 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 taking aspirin: aspirin 75 to 100 mg per day should be initiated;**

- **Warfarin plus aspirin 75 to 100 mg per day: aspirin dose may also need to be increased to 325 mg per day 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 per day, clopidogrel 75 mg per day added, and/or warfarin added.**

## 4. Excessive Anticoagulation

In most patients with INR above the therapeutic range, excessive anticoagulation can be managed by withholding warfarin and monitoring the level of anticoagulation with serial INR determinations (480). Excessive anticoagulation (INR greater than 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 an INR of 5 to 10 who are not bleeding can be treated by withholding warfarin and administering 1 to 2.5 mg of oral vitamin K1 (phytonadione) (480,565). The INR should be determined after 24 h and subsequently as needed. Warfarin therapy is restarted and adjusted dose appropriately to ensure that the INR is in the therapeutic range. In emergency situations, the use of fresh frozen plasma is preferable to high-dose vitamin K1 (566), especially parenteral vitamin K1, because use of the latter increases the risk of overcorrection to a hypercoagulable state. Low-dose intravenous vitamin K (less than 1 mg) appears safe in this situation (567).

## 5. Bridging Therapy in Patients With Mechanical Valves Who Require Interruption of Warfarin Therapy for Noncardiac Surgery, Invasive Procedures, or Dental Care

### Class I

1. **In patients at low risk of thrombosis, defined as those with a bileaflet mechanical AVR with no risk factors,\* it is recommended that warfarin be stopped 48 to 72 h before the procedure (so the INR falls to less than 1.5) and restarted within 24 h after the procedure. Heparin is usually unnecessary.** *(Level of Evidence: B)*
2. **In patients at high risk of thrombosis, defined as those with any mechanical MV replacement or a mechanical AVR with any risk factor, therapeutic doses of IV UFH should be started when the INR falls below 2.0 (typically 48 h before surgery), stopped 4 to 6 h before the procedure, restarted as early after surgery as bleeding stability allows, and continued until the INR is again therapeutic with warfarin therapy.** *(Level of Evidence: B)*

### Class IIa

**It is reasonable to give fresh frozen plasma to patients with mechanical valves who require interruption of warfarin therapy for emergency noncardiac surgery, invasive procedures, or dental care. Fresh frozen**

plasma is preferable to high-dose vitamin K1. *(Level of Evidence: B)*

**Class IIb**

In patients at high risk of thrombosis (see above), therapeutic doses of subcutaneous UFH (15 000 U every 12 h) or LMWH (100 U per kg every 12 h) may be considered during the period of a subtherapeutic INR. *(Level of Evidence: B)*

**Class III**

In patients with mechanical valves who require interruption of warfarin therapy for noncardiac surgery, invasive procedures, or dental care, high-dose vitamin K1 should not be given routinely, because this may create a hypercoagulable condition. *(Level of Evidence: B)*

*\*Risk factors: atrial fibrillation, previous thromboembolism, LV dysfunction, hypercoagulable conditions, older generation thrombogenic valves, mechanical tricuspid valves, or more than 1 mechanical valve.*

The risk of increased bleeding during a procedure performed with a patient receiving antithrombotic therapy has to be weighed against the increased risk of a 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.

Management of antithrombotic therapy must be individualized, but some generalizations apply (568). Antithrombotic therapy should not be stopped for procedures in which bleeding is unlikely or would be inconsequential if it occurred, for example, surgery on the skin, dental cleaning, or simple treatment for dental caries. Eye surgery, particularly for cataracts or glaucoma, is usually associated with very little bleeding and thus is frequently performed without alterations to antithrombotic treatment. When bleeding is likely or its potential consequences are severe, antithrombotic treatment should be altered.

For patients with a bileaflet mechanical aortic valve and no risk factors, warfarin should be stopped before the procedure so that the INR is less than 1.5 (which is often 48 to 72 h after warfarin is discontinued) (568,569) and restarted within 24 h after a procedure. Admission to the hospital or a delay in discharge to give heparin is usually unnecessary.

Patients at high risk of thrombosis include all patients with mechanical mitral or tricuspid valve replacements and patients with an AVR and any risk factors. Such risk factors include atrial fibrillation, previous thromboembolism, hypercoagulable condition, older-generation mechanical valves, LV dysfunction (ejection fraction less than 0.30), or more than 1 mechanical valve (570–572). When UFH is used, it should be started when INR falls below 2.0 (i.e., 48 h before surgery) and stopped 4 to 6 h before the procedure. UFH should be restarted as early after surgery as bleeding stability allows, and the aPTT should be maintained at 55 to 70 s until warfarin is therapeutic. LMWH is attractive because it is more easily used outside the hospital; however, concerns about the use of LMWH for mechanical valves persists, and package inserts continue to list a warning for this use of these medications (490).

High-dose vitamin K1 should not be given routinely, because this may create a hypercoagulable condition. For emergency situations, fresh frozen plasma is preferable to high-dose vitamin K1 (see Section IX-A-4).

**6. Antithrombotic Therapy in Patients Who Need Cardiac Catheterization/Angiography**

In an emergency or semiurgent situation, cardiac catheterization can be performed in a patient taking warfarin, but preferably, the drug should be stopped so that INR is less than 1.5. The drug should be restarted as soon as the procedure is completed. If a patient has more than 1 risk factor that predisposes to thromboembolism, heparin should be started when INR falls below 2.0 and should be continued when warfarin is restarted. After an overlap of 3 to 5 days, heparin may be discontinued when the desired INR is achieved. If the catheterization procedure is to include a transseptal puncture (especially in a patient who has not had previous opening of the pericardium), patients should be removed from all antithrombotic therapy, and INR should be less than 1.2.

**7. Thrombosis of Prosthetic Heart Valves**

**Class I**

1. Transthoracic and Doppler echocardiography is indicated in patients with suspected prosthetic valve thrombosis to assess hemodynamic severity. *(Level of Evidence: B)*
2. TEE and/or fluoroscopy is indicated in patients with suspected valve thrombosis to assess valve motion and clot burden. *(Level of Evidence: B)*

**Class IIa**

1. Emergency operation is reasonable for patients with a thrombosed left-sided prosthetic valve and NYHA functional class III–IV symptoms. *(Level of Evidence: C)*
2. Emergency operation is reasonable for patients with a thrombosed left-sided prosthetic valve and a large clot burden. *(Level of Evidence: C)*
3. Fibrinolytic therapy is reasonable for thrombosed right-sided prosthetic heart valves with NYHA class III–IV symptoms or a large clot burden. *(Level of Evidence C)*

**Class IIb**

1. Fibrinolytic therapy may be considered as a first-line therapy for patients with a thrombosed left-sided

prosthetic valve, NYHA functional class I–II symptoms, and a small clot burden. *(Level of Evidence: B)*

2. **Fibrinolytic therapy may be considered as a first-line therapy for patients with a thrombosed left-sided prosthetic valve, NYHA functional class III–IV symptoms, and a small clot burden if surgery is high risk or not available. *(Level of Evidence: B)***

3. **Fibrinolytic therapy may be considered for patients with an obstructed, thrombosed left-sided prosthetic valve who have NYHA functional class II–IV symptoms and a large clot burden if emergency surgery is high risk or not available. *(Level of Evidence: C)***

4. **Intravenous UFH as an alternative to fibrinolytic therapy may be considered for patients with a thrombosed valve who are in NYHA functional class I–II and have a small clot burden. *(Level of Evidence: C)***

Fibrinolytic therapy for a left-sided prosthetic valve obstructed by thrombus is associated with significant risks (cerebral emboli in 12% to 15% of cases) and is often ineffective. Fibrinolytic therapy in such patients is reserved for those in whom surgical intervention carries a high risk and those with contraindications to surgery (573–580).

In patients with a "small clot" who are in NYHA functional class I or II, treatment with short-term intravenous UFH therapy or continuous infusion of fibrinolytic therapy may be considered (576–580). The size threshold for this recommendation is difficult to define because of the lack of large cohort studies and differing thresholds from small studies (ranging from 5 to 10 mm, as determined by TEE) below which intravenous UFH or fibrinolytic therapy is safe and effective (575,578–580). Factors that identify patients at risk for adverse outcomes of fibrinolytic therapy include active internal bleeding, history of hemorrhagic stroke, recent cranial trauma of neoplasm, diabetic hemorrhagic retinopathy, large thrombi, mobile thrombi, hypertension (greater than 200 over 120 mm Hg), hypotension or shock, and NYHA functional class III–IV symptoms. If fibrinolytic therapy is successful, it should be followed by intravenous UFH until warfarin achieves an INR of 3.0 to 4.0 for aortic prosthetic valves and 3.5 to 4.5 for mitral prosthetic valves. If partially successful, fibrinolytic therapy may be followed by a combination of subcutaneous UFH twice daily (to achieve an aPTT of 55 to 80 s) plus warfarin (INR 2.5 to 3.5) for a 3-month period (576).

Patients with small thrombi who receive intravenous UFH as first-line therapy and who do not respond successfully may receive a trial of continuous-infusion fibrinolytic therapy. If fibrinolytic therapy is unsuccessful or there is an increased risk associated with fibrinolytic therapy, reoperation should be considered. An alternative in patients who remain hemodynamically stable is to convert intravenous UFH to combined therapy with subcutaneous UFH (twice daily to an aPTT of 55 to 80 s) and warfarin (INR 2.5 to 3.5) for 1 to 3 months on an outpatient basis to allow for endogenous fibrinolysis (576). If intravenous UFH, fibrino-

lytic therapy, combined UFH/fibrinolytic therapy, or combined UFH/warfarin is successful, warfarin doses should be increased so that INR is between 3.0 and 4.0 (approximately 3.5) for prosthetic aortic valves and between 3.5 and 4.5 (approximately 4.0) for prosthetic MVs. These patients should also receive low-dose aspirin.

Thrombosis of mechanical tricuspid valve prostheses may be treated with fibrinolytic therapy, although experience with this is limited (581,582).

### B. Follow-Up Visits

**Class I**

1. **For patients with prosthetic heart valves, a history, physical examination, and appropriate tests should be performed at the first postoperative outpatient evaluation, 2 to 4 weeks after hospital discharge. This should include a transthoracic Doppler echocardiogram if a baseline echocardiogram was not obtained before hospital discharge. *(Level of Evidence: C)***

2. **For patients with prosthetic heart valves, routine follow-up visits should be conducted annually, with earlier re-evaluations (with echocardiography) if there is a change in clinical status. *(Level of Evidence: C)***

**Class IIb**

**Patients with bioprosthetic valves may be considered for annual echocardiograms after the first 5 years in the absence of a change in clinical status. *(Level of Evidence: C)***

**Class III**

**Routine annual echocardiograms are not indicated in the absence of a change in clinical status in patients with mechanical heart valves or during the first 5 years after valve replacement with a bioprosthetic valve. *(Level of Evidence: C)***

### 1. First Outpatient Postoperative Visit

The first outpatient evaluation after valve surgery usually occurs 3 to 4 weeks after hospital discharge. By this time, the patient's physical capabilities and expected improvement in functional capacity can be assessed. The workup on this visit should include an interval or complete history and physical examination, ECG, chest X-ray, 2D and Doppler echocardiography, complete blood count, blood urea nitrogen/creatinine, electrolytes, lactate dehydrogenase, 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, LV and RV hypertrophy, LV and RV size and function, and pericardial effusion/thickening. It is an essential component of the first postoperative visit because it allows an assessment of the effects and results of surgery, as well as serving as a baseline

for comparison should complications 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. The clinical course of patients with prosthetic heart valves is influenced by several factors (550), including LV dysfunction, progression of other valve disease, pulmonary hypertension, other cardiac diseases, complications of prosthetic heart valves, and clinical heart failure. The interval between routine follow-up visits depends on the patient's needs.

The asymptomatic uncomplicated patient needs to be seen only at 1-year intervals, at which time a complete history and thorough physical examination should be performed. No further echocardiographic testing is required after the initial postoperative evaluation in patients with mechanical valves who are stable and who have no symptoms or clinical evidence of LV dysfunction, prosthetic valve dysfunction, or dysfunction of other heart valves (1). Once regurgitation is detected, close follow-up with 2D and Doppler echocardiography every 3 to 6 months is indicated. Echocardiography is indicated in any patient with a prosthetic heart valve whenever there is evidence of a new murmur or change in clinical status, when there are questions about prosthetic valve integrity and function, and when there are concerns about ventricular function.

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

### Class I

**Patients with LV systolic dysfunction after valve surgery should receive standard medical therapy for systolic heart failure. This therapy should be continued even if there is improvement of LV dysfunction.** *(Level of Evidence: B)*

LV dysfunction and clinical heart failure after valve replacement may be the result of preoperative LV dysfunction that persists or improves only partially, perioperative myocardial damage, other valve disease that has progressed, complications of prosthetic heart valves, and 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 2D and Doppler echocardiography and, if necessary, TEE and cardiac catheterization with angiography to determine the cause. Patients with postoperative LV systolic dysfunction, even if asymptomatic, should receive standard medical therapy for systolic heart failure, and this therapy should be continued indefinitely even if there is improvement in systolic function and/or symptoms. All patients should also receive primary and secondary prevention measures to reduce the risk of future cardiovascular events.

## X. EVALUATION AND TREATMENT OF CORONARY ARTERY DISEASE IN PATIENTS WITH VALVULAR HEART DISEASE

Many patients with valvular heart disease have concomitant CAD, but there are only limited data regarding the 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 the smaller published series of patients undergoing surgical treatment of valvular heart disease.

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

The prevalence of CAD in patients with valvular heart disease is determined by the same variables as in the general population (583), and risk factors should be approached with the prevention and risk reduction strategies that have been recommended for the general population (584).

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 (585), and RV hypertrophy (586). Angina is thus a less specific indicator of CAD in patients with valvular heart disease than in the general population.

Among patients with severe AS, angina is a common symptom in young patients with normal coronary arteries and congenital or rheumatic AS. On the other hand, CAD is a common finding in older symptomatic men with AS. In elderly patients (greater than 70 years old), angina is a strong determinant of CAD (sensitivity 78%, specificity 82%) (587). Calcification of the aortic valve is also associated with a high presence of CAD (90%) (588). In general, because angina is a poor marker of CAD in patients with AS, coronary angiography is recommended in symptomatic patients before AVR in men older than 35 years; premenopausal women older than 35 years with coronary risk factors, as well as asymptomatic men older than 45 years; women older than 55 years; or those with 2 or more coronary risk factors.

CAD is less prevalent in patients with AR than in those with AS, and the prevalence of CAD in patients with MS is lower than in patients with aortic valve disease, an observation explained principally on the basis of differences in age and gender. Nonetheless, because of the impact of untreated CAD on perioperative and long-term postoperative survival, preoperative identification of CAD is of great importance in patients with AR or MS and those with AS. Thus, in symptomatic patients and/or those with LV dysfunction, preoperative coronary angiography is recommended in men aged greater than 35 years, premenopausal women aged greater than 35 years 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 Sections III-F-4 and VII-B-1-c. Neither angina nor heart failure symptoms are reliable markers

of CAD in these patients. In patients undergoing catheterization to evaluate the cause and severity of MR, CAD is present in an average of 33% (589,590). In patients undergoing catheterization for acute ischemic syndromes, an average of 20% have associated MR (591). Those with chronic CAD and MR usually have lower LV ejection fractions and more extensive CAD than those without MR.

### B. Diagnosis of Coronary Artery Disease

#### Class I

1. **Coronary angiography is indicated before valve surgery (including infective endocarditis) or mitral balloon commissurotomy in patients with chest pain, other objective evidence of ischemia, decreased LV systolic function, history of CAD, or coronary risk factors (including age). Patients undergoing mitral balloon valvotomy need not undergo coronary angiography solely on the basis of coronary risk factors.** *(Level of Evidence: C)*
2. **Coronary angiography is indicated in patients with apparently mild to moderate valvular heart disease but with progressive angina (Canadian Heart Association functional class II or greater), objective evidence of ischemia, decreased LV systolic function, or overt congestive heart failure.** *(Level of Evidence: C)*
3. **Coronary angiography should be performed before valve surgery in men aged 35 years or older, premenopausal women aged 35 years or older who have coronary risk factors, and postmenopausal women.** *(Level of Evidence: C)*

#### Class IIa

**Surgery without coronary angiography is reasonable for patients having emergency valve surgery for acute valve regurgitation, aortic root disease, or infective endocarditis.** *(Level of Evidence: C)*

#### Class IIb

**Coronary angiography may be considered for patients undergoing catheterization to confirm the severity of valve lesions before valve surgery without pre-existing evidence of CAD, multiple coronary risk factors, or advanced age.** *(Level of Evidence: C)*

#### Class III

1. **Coronary angiography is not indicated in young patients undergoing nonemergency valve surgery when no further hemodynamic assessment by catheterization is deemed necessary and there are no coronary risk factors, no history of CAD, and no evidence of ischemia.** *(Level of Evidence: C)*
2. **Patients should not undergo coronary angiography before valve surgery if they are severely hemodynamically unstable.** *(Level of Evidence: C)*

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 reduces the accuracy of the ECG at rest and during exercise for the diagnosis of concomitant CAD.

Given the importance of determining the presence of CAD, coronary angiography remains the most appropriate method for the 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, but it has a limited role in patients with severe valvular heart disease.

In patients undergoing emergency valve surgery for acute AR, aortic dissection, or endocarditis with hemodynamic instability, cardiac catheterization, aortography, and coronary angiography are rarely required, are associated with increased risk, and might delay urgent surgery unnecessarily (136,139–142). Angiography should be considered only when the valve diagnosis cannot be determined by noninvasive imaging and when patients have known CAD, especially those with previous CABG (see Section III-B-1-b).

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

#### Class I

**Patients undergoing AVR with significant stenoses (greater than or equal to 70% reduction in luminal diameter) in major coronary arteries should be treated with bypass grafting.** *(Level of Evidence: C)*

#### Class IIa

1. **In patients undergoing AVR and coronary bypass grafting, use of the left internal thoracic artery is reasonable for bypass of stenoses of the left anterior descending coronary artery greater than or equal to 50% to 70%.** *(Level of Evidence: C)*
2. **For patients undergoing AVR with moderate stenosis (50% to 70% reduction in luminal diameter), it is reasonable to perform coronary bypass grafting in major coronary arteries.** *(Level of Evidence: C)*

As noted previously, more than 33% of patients with AS undergoing AVR have concomitant CAD, and more than 50% of patients older than 70 years have CAD. The addition of CABG to AVR has had little or no adverse effect on operative mortality. Moreover, combined CABG 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. 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

**Class I**

**AVR is indicated in patients undergoing CABG who have severe AS who meet the criteria for valve replacement (see Section III-A-6). *(Level of Evidence: C)***

**Class IIa**

**AVR is reasonable in patients undergoing CABG who have moderate AS (mean gradient 30 to 50 mm Hg or Doppler velocity 3 to 4 m per second). *(Level of Evidence: B)***

**Class IIb**

**AVR may be considered in patients undergoing CABG who have mild AS (mean gradient less than 30 mm Hg or Doppler velocity less than 3 m per second) when there is evidence, such as moderate-severe valve calcification, that progression may be rapid. *(Level of Evidence: C)***

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

Confirmation by cardiac catheterization is especially important in patients with reduced stroke volumes, mixed valve lesions, or intermediate mean aortic valve gradients (between 30 and 50 mm Hg) by Doppler echocardiography, because many such patients may actually have severe AS (as discussed in Section III-A-5). The more complex and controversial issue is the decision to replace the aortic valve for only mild AS at the time of CABG, because the degree of AS may become more severe within a few years, necessitating a second, more difficult AVR operation in a patient with patent bypass grafts.

It is difficult to predict whether a given patient with CAD and mild AS is likely to develop significant AS in the years after CABG. As noted previously (see Section III-A-2), 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$^2$ per year and an increase in pressure gradient of up to 15 to 19 mm Hg per year; however, the majority may show little or no change (20,22–26,37,592–597). The average rate of reduction in valve area is on average 0.12 cm$^2$ per year (20), but the rate of change in an individual patient is difficult to predict.

Retrospective studies of patients who have come to AVR after previous CABG have been reported in which the mean time to reoperation was 5 to 8 years (598–603). The aortic valve gradient at the primary operation was small, less than 20 mm Hg, but the mean gradient increased significantly to greater than 50 mm Hg at the time of the second operation. It is important to note that these reports represent selected patients in whom AS progressed to the point that AVR was warranted. The number of patients in these surgical series who had similar gradients at the time of the primary operation but who did not have significant progression of AS is unknown.

Although definitive data are not yet available, patients with intermediate aortic valve gradients (30 to 50 mm Hg mean gradient at catheterization or transvalvular velocity of 3 to 4 m per second by Doppler echocardiography) who are undergoing CABG may warrant AVR at the time of revascularization (108–112), whereas patients with gradients below 10 mm Hg do not need valve replacement. The degree of mobility and calcification are also important factors predicting more rapid progression of aortic disease and should be taken into consideration, particularly in those with gradients between 10 and 25 mm Hg (29,108,112–114,604–607).

### E. Management of Concomitant Mitral Valve Disease and Coronary Artery Disease

Most patients with both MV disease and CAD have ischemic MR, as discussed in Sections III-F-4 and VII-B-1-c. In patients with 1 to 2+ MR, ischemic symptoms usually dictate the need for revascularization. Patients with more severe ischemic MR usually have significant LV dysfunction, and the decision to perform revascularization and MV repair is based on symptoms, severity of CAD, LV dysfunction, and inducible myocardial ischemia.

In patients with MV disease due to diseases other than ischemia, significantly obstructed coronary arteries identified at preoperative cardiac catheterization are generally revascularized at the time of MV surgery. There are no data to indicate the wisdom of this general policy, but because revascularization usually adds little morbidity or mortality to the operation, the additional revascularization surgery is usually recommended.

### APPENDIX 1. Abbreviation List

ACC = American College of Cardiology
ACE = angiotensin-converting enzyme
AHA = American Heart Association
aPTT = activated partial thromboplastin time
AR = aortic regurgitation
AS = aortic stenosis
AVR = aortic valve replacement
CABG = coronary artery bypass graft surgery
CAD = coronary artery disease
ECG = electrocardiogram
INR = international normalized ratio
LMWH = low-molecular-weight heparin
LV = left ventricular

## APPENDIX 1. Continued

MR = mitral regurgitation
MS = mitral stenosis
MV = mitral valve
MVP = mitral valve prolapse
NYHA = New York Heart Association
RV = right ventricular
TEE = transesophageal echocardiography
TR = tricuspid regurgitation
UFH = unfractionated heparin
2D = 2-dimensional

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