Valvular Heart Disease: Diagnosis and Management

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On completion of this article, you should be able to (1) summarize important basic and clinical concepts of valvular heart disease, (2) recognize the full array of valvular disorders so as to provide enhanced care for patients with valvular heart disease, and (3) treat patients in accordance with new recommendations from recent clinical trials and clinical practice guidelines.

Valvular heart disease (VHD) encompasses a number of common cardiovascular conditions that account for 10% to 20% of all cardiac surgical procedures in the United States. A better understanding of the natural history coupled with the major advances in diagnostic imaging, interventional cardiology, and surgical approaches have resulted in accurate diagnosis and appropriate selection of patients for therapeutic interventions. A thorough understanding of the various valvular disorders is important to aid in the management of patients with VHD. Appropriate work-up for patients with VHD includes a thorough history for evaluation of causes and symptoms, accurate assessment of the severity of the valvular abnormality by examination, appropriate diagnostic testing, and accurate quantification of the severity of valve dysfunction and therapeutic interventions, if necessary. It is also important to understand the role of the therapeutic interventions vs the natural history of the disease in the assessment of outcomes. Prophylaxis for infective endocarditis is no longer recommended unless the patient has a history of endocarditis or a prosthetic valve.

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AR = aortic regurgitation; AS = aortic stenosis; AVR = aortic valve replacement; CAD = coronary artery disease; CMR = cardiac magnetic resonance imaging; CT = computed tomography; ECG = electrocardiography; LV = left ventricular; MR = mitral regurgitation; MS = mitral stenosis; MV = mitral valve; RV = right ventricular

Degenerative valve disease is the most common form of valvular heart disease in the United States, whereas rheumatic heart disease accounts for most valve pathology in developing nations. As the US population ages, physicians are likely to see more patients with degenerative valve disorders. Because people continue to immigrate to the United States from developing nations, rheumatic valve disease may be seen more frequently. Thus, an understanding of the full array of valvular disorders is imperative to the provision of quality patient care.

AORTIC STENOSIS

ETIOLOGY AND PATHOPHYSIOLOGY

Aortic stenosis (AS) is the most prevalent form of cardiovascular disease in the Western world after hypertension and coronary artery disease. It is usually caused by either degenerative calcification of a trileaflet valve or progressive stenosis of a congenital bicuspid valve. Rheumatic

heart disease, the most common etiology worldwide, is less common in the United States. Aortic stenosis develops from progressive calcification of leaflets with restriction of leaflet opening over time. The risk factors for the development of degenerative calcific AS, which are similar to those for the development of vascular atherosclerosis, include diabetes, hypertension, smoking, and elevated levels of low-density lipoprotein cholesterol and lipoprotein(a).¹ Obstruction of left ventricular (LV) outflow can also occur at the subvalvular level (discrete subvalvular obstruction, hypertrophic cardiomyopathy) or above the valve (supra-valvular stenosis).

In patients with valvular AS, the severity of stenosis increases gradually over many years. The left ventricle adapts to the obstruction by increasing wall thickness while maintaining normal LV chamber size (concentric hypertrophy). The development of hypertrophy is a compensatory mechanism to normalize the LV wall stress and appears to be a critical determinant of ventricular performance in patients with AS. Left ventricular systolic function is usually preserved, and cardiac output is maintained for many years despite the pressure gradient across the aortic valve. In many patients, this compensatory mechanism cannot be maintained indefinitely, and systolic function begins to decline as a result of the pressure overload. If LV systolic dysfunction is present, it often improves after aortic valve replacement (AVR). However, LV function will not improve if myocardial contractile dysfunction is irreversible.² Differentiation between reversible and irreversible LV dysfunction is not possible on the basis of a preoperative resting imaging study alone.

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Concentric hypertrophy as an adaptive response to obstruction can also be maladaptive. As stenosis severity progresses, the left ventricle becomes less compliant and the LV diastolic pressure increases even though the ventricular size is normal. Thus, dyspnea on exertion may result from LV systolic dysfunction or elevated diastolic filling pressures with preserved systolic function. The increased wall thickness can also lead to reduced coronary artery blood flow per gram of muscle and reduced coronary flow reserve, resulting in angina pectoris even if the epicardial coronary arteries are normal.

Eventually, with progression of stenosis severity, symptoms of angina (35% of patients), syncope (15% of patients), or dyspnea and/or heart failure (50% of patients) develop.³ The symptoms are typically noted with exertion. Once symptoms develop, prompt surgical intervention is needed because the average survival is only 2 to 3 years with an increased risk of sudden death.^{4,5} Therefore, careful history regarding the onset of symptoms is essential. Prognosis of patients with asymptomatic severe AS is more difficult to determine; however, AS is a progressive disease, and so patients with severe AS have a high likelihood of developing symptoms in the course of 3 to 5 years.⁶ Atrial fibrillation in particular is tolerated poorly in patients with severe AS because the loss of atrial contraction as well as the rapid ventricular response limits diastolic filling of the left ventricle.

PHYSICAL EXAMINATION

The spectrum of findings on physical examination varies with the severity of valve calcification, the severity of stenosis, and LV function. In general, in patients with severe AS the arterial pulse is slow to increase and has a reduced peak (*pulsus parvus et tardus*), which is best appreciated by palpating the carotid pulse. This may not be present in elderly patients because of the rigidity of the vasculature. The carotid pulse may also demonstrate a systolic thrill. The jugular venous pulse is usually normal, but prominent *a* waves may be present, reflecting reduced right ventricular (RV) compliance due to hypertrophy of the interventricular septum. The *v* wave may be prominent if there is RV failure. The apical cardiac impulse is usually normal in location unless LV dysfunction has developed but is often sustained in nature because of LV hypertrophy. The S_1 is usually normal or soft. The S_2 may be single because the aortic and pulmonic valve components are superimposed, or the aortic valve component is absent or soft because the aortic valve is calcified and immobile. An S_4 may be palpable and audible because of a vigorous atrial contraction. Presence of an S_4 in a young patient with AS is a marker of LV hypertrophy and typically indicates that the AS is severe in the absence of other disorders that could lead to LV hypertrophy.

The characteristic murmur of AS is a crescendo-decrescendo systolic murmur along the left sternal border that radiates to the upper right sternal border and into the carotid arteries. However, it may also radiate to the LV apex (the Gallavardin phenomenon) and may be mistaken for a murmur of mitral regurgitation (MR). The intensity of the murmur does not correspond to the severity of AS. As the severity of the AS increases, the duration of the murmur increases, and it is more likely to peak at mid to late systole. A diastolic murmur may be heard if aortic regurgitation (AR) is also present, a characteristic finding in patients with rheumatic AS. In young patients with bicuspid AS, the systolic murmur may be preceded by a systolic ejection click. This sound tends to disappear with aging as the valve calcifies and the severity of AS increases. In the presence of severe heart failure, the apical impulse may be diffuse and laterally displaced, a third heart sound may be present, the jugular venous pulse may be elevated, and the systolic murmur may be soft or absent.^{1,7}

DIAGNOSTIC TESTING

Chest Radiography. Cardiac size is often normal in patients with AS, with rounding of the LV border and apex due to the LV hypertrophy. Aortic valve and aortic root calcification are best appreciated in the lateral projections on fluoroscopy. They are rarely detected on anteroposterior or posteroanterior projections. The proximal ascending aorta may be dilated, particularly in patients with bicuspid valves. Cardiomegaly is a late feature in patients with AS. In patients with heart failure, the heart is enlarged, with congestion of pulmonary vasculature. In cases of advanced heart failure, the right atrium and right ventricle may also be enlarged.

Electrocardiography. The typical finding on electrocardiography (ECG) in patients with AS is LV hypertrophy, often with secondary repolarization abnormalities. This is found in 85% of patients with severe AS. However, its absence does not preclude AS. Left atrial enlargement and conduction abnormalities are also common, including left and right bundle branch block. This may be due to extension of the calcification into the surrounding conduction system. The axis may be shifted leftward or rightward. Atrial fibrillation can also develop, particularly in older patients and those with hypertension. A sample ECG from a patient with AS is shown in Figure 1.

Echocardiography. Echocardiography is the imaging modality of choice to help diagnose and estimate the severity of AS. Two-dimensional echocardiography demonstrates the morphology of the aortic valve and can often delineate if it is trileaflet or bicuspid. The spectrum of calcific aortic valve disease ranges from aortic sclerosis without obstruction to ventricular outflow to severe AS. Aortic

FIGURE 1. Electrocardiogram of a patient with severe aortic stenosis showing marked left ventricular hypertrophy with repolarization abnormalities.

sclerosis is common and is often seen in people older than 65 years. On echocardiography, it is characterized by focal areas of valve thickening, typically located in the leaflet center with commissural sparing and normal leaflet mobility. Diffuse leaflet thickening is not characteristic of aortic sclerosis; instead, it suggests normal aging changes, a different valvular pathology, or an imaging artifact. With aortic sclerosis, valvular hemodynamics are within normal limits, with an aortic valve velocity of less than 2.5 m/s.^{8,9} Several studies have documented clinical factors associated with calcific aortic valve disease that are similar to atherosclerotic heart disease, with an increase in cardiovascular morbidity and mortality.¹⁰⁻¹⁴

In patients with AS, the aortic valve is usually thickened and calcified, with limited excursion and a reduced aortic valve area (Figure 2). Doming of the aortic leaflets due to asymmetry and restriction is often seen in young patients with bicuspid aortic valves. The ascending aorta should also be evaluated and measured to detect associated aortic aneurysms, which are particularly common in patients with bicuspid valves. In the absence of heart failure, the LV cavity is usually of normal size or small. Left ventricular hypertrophy is often present, as is left atrial enlargement. Left ventricular systolic function is usually normal. If heart failure has developed, the left ventricle may be enlarged and systolic function depressed.

Doppler echocardiography is an excellent tool for both evaluating the severity of AS by measuring jet velocity and gradients and calculating the aortic valve area. It also aids in detecting other associated valve lesions and in estimating pulmonary artery systolic pressure. The classification

of the severity of AS on the basis of findings on Doppler echocardiography is shown in Table 1.⁸

As the aortic valve area decreases with time, the velocity of forward flow across the valve increases. This hallmark of AS is one of the principal means of assessing the severity of AS with echocardiography, which has largely obviated the need for cardiac catheterization for hemodynamic assessment. Assessing the severity of AS using Doppler criteria is dependent not only on the severity of AS but also on the aortic flow. In patients with low cardiac output, such as patients with LV dysfunction, the calculated gradients and aortic valve area may not be representative of the

FIGURE 2. Parasternal short-axis echocardiographic view of a patient with severe aortic stenosis due to a congenital bicuspid aortic valve. The leaflets are heavily calcified (arrow).

TABLE 1. Classification of Aortic Stenosis Severity Using Doppler Examination

	Aortic sclerosis	Mild	Moderate	Severe
Aortic jet velocity (m/s)	≤2.5	2.6-2.9	3.0-4.0	>4.0
Mean gradient (mm Hg)	...	<20 (30 ^a)	20-40 ^b (30-50 ^a)	>40 ^b (>50 ^a)
Aortic valve area (cm ²)	...	>1.5	1.0-1.5	<1.0
Indexed aortic valve area (cm ² /m ²)	...	>0.85	0.60-0.85	<0.6
Velocity ratio	...	>0.50	0.25-0.50	<0.25

^a European Society of Cardiology guidelines.^b American Heart Association/American College of Cardiology guidelines.Adapted from *J Am Soc Echocardiogr*,⁸ with permission.

true severity of stenosis. In such cases of “low-output, low-gradient” AS, the administration of low-dose dobutamine may be needed to truly assess the severity of AS and to differentiate patients with anatomically severe AS from those with “pseudo” AS.^{15,16} An algorithm for managing patients with low-output, low-gradient AS is provided in Figure 3.

Computed Tomography. Both electron beam and multislice cardiac computed tomography (CT) can provide quantitative assessment of valve calcification and have been shown to correlate with echocardiographic assessment and clinical outcome.¹⁷ The role of CT in clinical management is not yet well defined, but CT has an established role in

evaluating the presence and severity of aortic root and ascending aortic dilatation in patients with associated aortic aneurysms.

Cardiac Magnetic Resonance Imaging. Cardiac magnetic resonance imaging (CMR) is useful for detecting and reliably measuring the anatomic valve area. Velocity-encoded CMR is currently being investigated for assessment of velocity across the stenotic aortic valves. As with cardiac CT, the role of this modality in the management of AS is currently not well defined,¹⁸ but it has an established role in evaluating aortic root and ascending aortic anatomy.

FIGURE 3. Algorithm for management of low-output, low-gradient aortic stenosis. AS = aortic stenosis; AVA = aortic valve area; DSE = dobutamine stress echocardiography; LV = left ventricular; LVOT = LV outflow tract.

Cardiac Catheterization. Because of the accuracy of echocardiographic assessment of the severity of AS, cardiac catheterization is currently used most often to identify the presence of associated coronary artery disease (CAD) rather than to define hemodynamic abnormalities. However, invasive hemodynamic measurements are helpful in patients in whom the noninvasive tests are inconclusive or provide discrepant results regarding the severity of AS. Coronary arteriography is recommended before surgical AVR in all patients at risk of CAD. Coronary angiography is indicated in patients with chest pain, objective evidence of ischemia, LV systolic dysfunction, and a history of CAD or coronary risk factors, including older age. This procedure should also be performed preoperatively in younger patients who will be undergoing the Ross procedure if the origin of the coronary arteries cannot be identified by noninvasive imaging.

Exercise Testing. Many patients with AS do not recognize symptoms that may develop gradually and cannot differentiate fatigue and dyspnea from aging and physical deconditioning. Other patients modify their lifestyle to prevent symptoms from occurring. In apparently asymptomatic patients with severe AS, exercise testing may have a role in eliciting symptoms or an abnormal blood pressure response to exercise. Such testing should be performed with close physician supervision and should not be performed on patients with symptoms.^{2,15}

TREATMENT

Patients with AS who are asymptomatic should be followed up with serial clinical examinations, and careful attention should be paid to any change in symptoms. Because the rate of progression of AS varies considerably, closer follow-up of patients with severe AS may be appropriate. As noted previously, a peak jet velocity of 4 m/s or greater represents severe AS.² Although the rate of progression can vary greatly among patients, peak jet velocity increases annually by an average of 0.3 m/s and the aortic valve area decreases by an average of 0.1 cm² in patients with moderate AS.²

Currently, no medical treatments are recommended to delay the progression of AS. Because of the association between AS and other risk factors for CAD, statin therapy has been proposed as a possible therapeutic intervention to delay the progression of AS. However, the results of small randomized trials using statin therapy have been negative to date.¹⁹

In patients who develop symptoms, AVR is the treatment of choice. It is also recommended in asymptomatic patients with LV dysfunction. Even in the setting of LV dysfunction, surgical treatment offers a better survival benefit. Successful AVR results in substantial clinical and he-

modynamic improvement. The management of severe AS is delineated in Figure 4.²

Percutaneous balloon valvotomy of the aortic valve may be a reasonable option for the treatment of adolescents and young adults with noncalcified aortic valves. However, if older individuals are optimal surgical candidates, percutaneous balloon valvotomy is not the procedure of choice because of the high rate of restenosis of calcific AS and failure to improve long-term survival.²⁰ Nevertheless, this procedure may be a reasonable option for highly symptomatic patients who are not surgical candidates or in those who need this procedure as a bridge to surgery in the near future. Implantation of bioprosthetic valves using percutaneous catheter-based interventions is currently under study and offers an exciting new era of treatment for patients with severe AS who are not ideal candidates for surgical AVR.²¹ These devices are already approved in Europe for use in high-risk surgical candidates, with over 10,000 implantations.

AORTIC REGURGITATION

ETIOLOGY

Aortic regurgitation results from abnormalities of the aortic leaflets, their supporting structures in the aortic root and annulus, or both. Rheumatic heart disease remains the most common cause of severe AR worldwide. However, diseases involving the aortic root and ascending aorta have become more frequent causes of AR in the western hemisphere.

Abnormalities of the aortic cusps that may result in AR include congenital leaflet abnormalities, such as bicuspid, unicuspid, or quadricuspid valves or rupture of a congenitally fenestrated valve; other congenital defects such as subaortic membranes; rheumatic heart disease with fusion of the commissures and retraction of the aortic valve leaflets due to scarring and fibrosis; myxomatous infiltration of the aortic valve; tumors; infective endocarditis; atherosclerotic degeneration; connective tissue disorders such as Marfan syndrome; ingestion of ergot-derived compounds; inflammatory diseases such as aortitis; antiphospholipid syndrome; and the use of anorectic drugs. Other systemic disorders that may affect the aortic valve include lupus erythematosus, giant cell arteritis, Takayasu arteritis, ankylosing spondylitis, Jaccoud arthropathy, Whipple disease, and Crohn disease.¹

Diseases that primarily affect the annulus or aortic root include idiopathic aortic root dilatation, degeneration of the extracellular matrix as an isolated condition or associated with Marfan syndrome or congenitally bicuspid aortic valves, Ehlers-Danlos syndrome, osteogenesis imperfecta, syphilitic aortitis, aortitis noted with other connective tissue diseases such as ankylosing spondylitis, giant cell

FIGURE 4. Management strategy in patients with severe aortic stenosis. Preoperative coronary angiography should be performed routinely as determined by age, symptoms, and coronary risk factors. AVA = aortic valve area; CABG = coronary artery bypass graft; LV = left ventricular; $V_{\max}$ = maximum velocity. Adapted from *Circulation*.²

arteritis, the Behçet syndrome, psoriatic arthritis, other forms of arthritis associated with ulcerative colitis, relapsing polychondritis, and the Reiter syndrome. Aortic root enlargement causes AR by annular dilatation, resulting in leaflet separation and loss of coaptation. Bicuspid aortic valves are commonly associated with dilatation of the aortic root as well as congenital leaflet abnormality because of abnormalities in the aortic matrix.²² Similarly, ankylosing spondylitis can result in abnormalities of both the leaflets and the aortic root. It is important to note that chronic AR by itself may lead to progressive aortic root dilatation over time.

PATHOPHYSIOLOGY

In chronic AR, a combined preload and afterload excess is imposed on the left ventricle. The excess preload reflects the volume overload that is directly related to the severity of AR. Left ventricular afterload is also increased because

the elevated end-diastolic volume increases LV wall stress. In addition, the increased stroke volume that is ejected into the high-impedance aorta often creates systolic hypertension, which in turn further increases LV afterload. The combination of preload and afterload excess with severe AR ultimately leads to progressive LV dilatation with resultant systolic dysfunction. Left ventricular dysfunction may be associated with symptoms of heart failure, such as dyspnea on exertion, orthopnea, and paroxysmal nocturnal dyspnea.

In early, compensated severe AR, the left ventricle adapts to the volume overload by development of eccentric hypertrophy, with replication of sarcomeres in series and elongation of myocytes and myofibers. This eccentric hypertrophy helps to maintain the ratio of the LV cavity radius to wall thickness, thereby regulating the LV wall stress to normal levels (*Laplace's law*: $[\text{Ventricular Pressure} \times \text{Radius}] / [\text{Wall Thickness} \times 2]$). Increased systolic wall stress

and afterload lead to further concentric hypertrophy. The systolic function is thus preserved as a result of the combination of chamber dilatation and hypertrophy. Despite the large regurgitant volume with increases in preload and afterload, these compensatory changes seek to maintain normal LV systolic function and allow patients to remain asymptomatic for many years. However, with progressive LV dilatation, preload reserve may be exhausted, leading to an afterload mismatch and deterioration of systolic function.²³⁻²⁵ This process is initially reversible, and LV systolic function can improve after restoration of normal loading conditions by AVR. With time, however, myocardial contractile dysfunction may develop, at which point there is the risk of irreversible LV dysfunction.

With progression of LV dysfunction, LV end-diastolic pressure increases, resulting in elevated left atrial and pulmonary artery capillary wedge pressures. Patients experience dyspnea, initially with exercise and then ultimately at rest as heart failure ensues. Angina can also occur because of a reduction in coronary flow reserve.

PHYSICAL EXAMINATION

The findings on physical examination in patients with chronic AR are primarily related to the increased stroke volume and widened pulse pressure. The peripheral pulses demonstrate an abrupt rise of the upstroke and a quick collapse (water-hammer or Corrigan pulse). A bisferiens pulse may be palpable. "Pistol shot" sounds may be heard over the femoral arteries. Capillary pulsations can be appreciated at the fingertips, lips, and tongue. Systolic blood pressure is generally elevated and diastolic pressure is low with a widened pulse pressure. The apical impulse is diffuse, hyperdynamic, and displaced laterally and inferiorly. A rapid filling wave can often be palpated at the apex. A systolic thrill may be heard at the base of the heart, the suprasternal notch, and the carotid arteries as a result of the increased stroke volume. At times, a carotid shudder is palpable.

The intensity of the S_2 may be increased or decreased depending on the etiology of the AR. A loud closure sound is associated with a dilated aortic root and a soft S_2 with abnormally thickened and retracted leaflets. Aortic ejection sounds can be heard in young patients with bicuspid valves.²⁴ An S_3 may be present as a manifestation of LV dilatation and does not necessarily indicate a failing left ventricle.²⁵

The classic murmur of AR is a high-frequency, blowing, and decrescendo diastolic murmur, usually heard in the aortic area but also audible in the left third and fourth intercostal spaces along the sternal border. The murmur is best heard with the diaphragm of the stethoscope while the patient is sitting up and leaning forward after deep expira-

tion. The murmur is increased by maneuvers that increase peripheral vascular resistance, such as squatting or isometric exercise. The murmur decreases with maneuvers that decrease blood pressure, such as standing, amyl nitrate inhalation, or the strain phase of the Valsalva maneuver. Mild degrees of AR result in a murmur only in early diastole. As the severity of AR increases, the murmur becomes more holodiastolic. However, when the left ventricle decompensates, the gradient between the left ventricle and the aorta at end diastole is diminished, shortening the murmur.^{25,26}

The Austin-Flint murmur, a mid to late diastolic rumble heard best at the apex, is similar to the murmur heard in mitral stenosis (MS) but occurs in patients with no mitral valve (MV) abnormalities. This murmur is low-pitched and has been postulated to represent physiologic MS caused by the rapid increase in LV diastolic pressure and by the high-pressure jet of AR impeding the opening of the MV.²⁶ Others have surmised that the vibrations caused by the AR jet being directed at the anterior mitral leaflet and the LV free wall could be mistakenly appreciated on auscultation as a diastolic rumble.²⁴

DIAGNOSTIC TESTING FOR ACUTE AR

Acute AR is often a catastrophic illness. Because the ventricle has not had time to compensate, diagnosis is often difficult. In these patients, tachypnea and tachycardia are common and pulmonary edema is possible. With acute reduction in forward stroke volume, cardiac output is maintained by compensatory tachycardia. The patient may present in cardiogenic shock. The precordium is usually quiet. The S_1 is soft because of the early closure of the MV and a short diastolic murmur. Early closure of the MV noted on echocardiography is a poor prognostic sign and should prompt rapid surgical correction. Rapid diagnosis and prompt surgical correction for acute severe AR are imperative because medical therapy (eg, therapies that reduce heart rate) can often worsen hemodynamics. Aortic balloon counterpulsation is absolutely contraindicated.²⁷

Chest Radiography. In patients with acute AR, chest radiography reveals minimal cardiac enlargement. The aortic root and arch are normal. Pulmonary vascular congestion is noted. In patients with chronic AR, chest radiography demonstrates an enlarged cardiac silhouette with LV dilatation. The ascending aorta may also be enlarged when an aortic aneurysm or aortic dissection is present. Pulmonary congestion is noted when heart failure has developed. A chest radiograph from a patient with severe AR is shown in Figure 5.

Electrocardiography. Findings on ECG may be normal early in the disease or show LV hypertrophy with or without associated repolarization abnormalities. Left axis deviation may also be present. With early LV volume over-

FIGURE 5. Chest radiograph of a patient with severe aortic regurgitation showing cardiomegaly and bilateral pleural effusions.

load, there are prominent Q waves in leads I, aVL, and V3 through V6. As the disease progresses, the prominent initial forces decrease, but the total QRS amplitude increases.¹

Echocardiography. Echocardiography is the most widely used diagnostic tool to assess LV dimensions, volumes, and ejection fraction. It also allows the morphological assessment of the aortic valve, annulus, and root, thereby helping determine the etiology of AR (Figure 6). Color-flow and spectral Doppler echocardiography are then used to further quantify the severity of AR (Figure 7) and to identify lesions in the other valves.²⁴ No single method provides an entirely accurate quantitative assessment of the severity of valve regurgitation, and the complex interaction of anatomic and hemodynamic variables can add to these potential difficulties.

Although cardiac ultrasonographic techniques provide important clinical information in patients with AR, physicians interpreting the results of such testing should be mindful not only of the clinical findings but also of the advantages and limitations of cardiac ultrasonography. A combination of different parameters is used in quantifying the severity of AR because no single method provides the necessary quantitative information.

If a patient has poor acoustic windows, obtaining quantitative information from the study is unlikely. In such patients, alternative imaging modalities such as transesophageal echocardiography may be considered.

The recent development of real-time 3-dimensional echocardiography shows promise for accurate calculation

FIGURE 6. Transesophageal echocardiographic short-axis view of a patient with a bicuspid aortic valve. Note that there are 2 leaflets instead of 3 (arrows).

of LV volumes and ejection fraction. Although not specifically studied in patients with AR, LV-volume assessment using real-time 3-dimensional echocardiography has been shown to be accurate, rapid, and superior to standard 2-dimensional echocardiographic techniques, particularly in abnormally shaped hearts. The major limitation of this technique is the reduced accuracy in patients with poor acoustic windows.

Cardiac Catheterization. Cardiac catheterization is primarily used to assess coronary anatomy before surgery in patients with the appropriate age and risk factor profile. Invasive assessment of LV function and AR severity is reserved for selected patients in whom noninvasive imaging is inconclusive.

FIGURE 7. Transesophageal echocardiographic long-axis view with color-flow Doppler imaging in a patient with a bicuspid aortic valve with severe aortic regurgitation (arrow). Ao = aorta; LV = left ventricle.

Cardiac Magnetic Resonance Imaging. Cardiac magnetic resonance imaging provides highly accurate assessment of LV volumes, mass, and ejection fraction; it can also provide excellent visualization of the aortic root and ascending aorta. In addition to providing superb anatomic information, CMR can be used to obtain accurate information regarding regurgitant volumes and flow. Although cine CMR is not as well validated as echocardiography, it can be useful for detecting progressive LV dilatation and for planning the timing of surgery for asymptomatic patients with severe AR. Velocity-encoded imaging is another useful technique that allows quantification of both forward and regurgitant flow.²⁸

Exercise Testing. Exercise testing is useful as a measure of functional capacity when it is unclear whether symptoms are present. However, exercise LV ejection fraction is often abnormal in asymptomatic patients with severe AR and has not been shown to provide additional prognostic information when resting LV size and function are already known.²

TREATMENT

Patients with chronic AR may remain asymptomatic for many years. In patients with normal LV systolic function, published data indicate that the rate of progression to asymptomatic LV systolic dysfunction is less than 3.5% per year; the development of symptoms or LV dysfunction, less than 6% per year; and the risk of sudden death, less than 0.2% per year.^{2,29} However, the mortality rate is much greater among patients older than 50 years with severe AR, and the higher mortality rate in this age group is an important consideration in the timing of AVR.³⁰ When patients develop LV systolic dysfunction while asymptomatic, most will become symptomatic and require AVR within 2 to 3 years. In asymptomatic patients with LV systolic dysfunction, progression to symptoms is greater than 25% per year.² Asymptomatic patients with normal LV function generally have a favorable prognosis.³⁰ A progressive increase in LV dimensions or a decline in resting ejection fraction during serial follow-up may identify high-risk patients who require careful monitoring. Patients with even moderate symptoms or evidence of severe LV dilatation are at higher risk and should be considered for early intervention. These findings emphasize the importance of close follow-up of patients with chronic AR, including those who are asymptomatic.²

Asymptomatic patients with severe AR and normal LV size and function should undergo clinical examination and echocardiography yearly unless symptoms arise beforehand. Patients with substantial LV dilatation (end-diastolic dimension >60 mm) require clinical evaluations every 6 months and echocardiographic imaging every 6 to 12 months. Patients with very severe LV dilatation (end-diastolic dimension >70

mm or end-systolic dimension >50 mm) may be considered for AVR (New York Heart Association class II indication for AVR).² However, body surface area should be considered when assessing the LV dimensions because the very large LV dimensions may never be reached in women or small men.

The benefits of long-term vasodilator therapy in asymptomatic patients with severe AR and normal ejection fraction remain controversial, with no definitive trial proving or disproving its benefit. Vasodilators may be helpful in patients who have symptoms and/or LV dysfunction but are poor surgical candidates because of additional cardiac or noncardiac comorbid conditions. They may also be helpful for improving the hemodynamic profile of patients with severe heart failure before they undergo AVR. Lastly, they have been considered as long-term therapy to prolong the compensated phase of asymptomatic patients with preserved ejection fraction but with substantial LV dilatation²; definitive data regarding the benefit of long-term vasodilator therapy are lacking. The goal of vasodilator therapy is the reduction of systolic blood pressure. Vasodilators such as hydralazine, nifedipine, or angiotensin-converting enzyme inhibitors are preferred.³¹⁻³³ β -Blocking agents have no proven benefit and, in theory, could increase the aortic regurgitant volume because the resultant bradycardia would prolong the diastolic-filling interval. Vasodilator therapy is not recommended in patients with mild or moderate AR and normal LV function in the absence of systemic hypertension because the prognosis of these patients is excellent without treatment. Patients should be referred for AVR when symptoms develop, LV dilatation is severe, or the ejection fraction decreases.^{2,29,30} The management of patients with chronic severe AR is outlined in Figure 8.²

MITRAL REGURGITATION

ETIOLOGY AND PATHOPHYSIOLOGY

Mitral regurgitation may result from disorders of the valve leaflets themselves or from any of the surrounding structures that comprise the mitral apparatus. The leading cause of MR is rheumatic heart disease in developing areas of the world and degenerative forms of MV disease (myxomatous disease and fibroelastic deficiency) in the United States and other developed countries. Less common conditions include mitral annular calcification and congenital anomalies such as cleft MVs; other rare causes of MR are endomyocardial fibrosis, carcinoid disease with right-to-left shunting, ergotamine toxicity, radiation therapy, systemic lupus erythematosus, and diet-drug toxicity. The second leading cause of MR in developed countries is “functional” MR, which results from dilatation of the MV annulus or from myocardial infarction. In particular, infarctions involving the inferolateral and the posteromedial papillary muscle

FIGURE 8. Management strategy for patients with chronic severe aortic regurgitation. AVR = aortic valve replacement; DD = diastolic diameter; echo = echocardiography; EF = ejection fraction; LV = left ventricular; MRI = magnetic resonance imaging; RVG = radionuclide ventriculography; SD = systolic diameter. Adapted from *Circulation*.²

produce tethering of the mitral leaflets that prohibits normal coaptation, leading to “functional” MR even though the valve leaflets themselves are normal.³⁴

Patients who develop acute severe MR usually present with symptomatic heart failure because their ventricles are ill prepared to accept the sudden increase in volume load.

However, if the patient survives the acute episode or has slowly progressive worsening of MR, the left ventricle is able to develop compensatory changes. Symptoms are therefore either absent or slowly progressive over many years. The adaptive changes of the ventricle to the volume overload include LV dilatation and eccentric hypertrophy.

FIGURE 9. Electrocardiogram from a patient with severe mitral regurgitation showing both left ventricular hypertrophy and left atrial enlargement.

The left atrium also enlarges, thus allowing accommodation of the regurgitant volume at a lower pressure.²⁹

Although patients with compensated chronic MR may remain asymptomatic for many years, decompensation may eventually develop if the regurgitation is sufficiently severe. The LV ejection fraction in chronic MR may be greater than normal because of the increase in preload and the afterload-reducing effect of ejection into the low-impedance left atrium. Therefore, LV ejection fraction can be misleading as a measure of contractile function in this disorder. Advanced myocardial dysfunction may occur while LV ejection fraction is still well within the normal range.³⁵ Thus, outcome after MV surgery is poorer in patients with a preoperative ejection fraction of less than 60% than in those with higher ejection fractions.^{35,36}

PHYSICAL EXAMINATION

The examination of the patient with chronic severe MR varies according to the degree of decompensation. The carotid upstroke is sharp in patients with compensated MR, but the volume of the carotid pulse is reduced in the presence of advanced heart failure.¹ The apical impulse is usually brisk and hyperdynamic; in those with severe MR it may be enlarged and displaced laterally. The S_1 is usually soft, and a widely split S_2 is common. A diastolic rumble and S_3 may be present and do not necessarily indicate LV dysfunction.² The systolic murmur of MR varies according to the etiology of the regurgitation. The murmur is usually heard best at the apex in the left lateral decubitus position. With severe degenerative MR, the murmur is holosystolic,

radiating into the axilla. Early systolic murmurs are typical of acute MR. Late systolic murmurs are typical of MV prolapse or papillary muscle dysfunction. Signs of pulmonary hypertension, such as a loud P_2 , are usually ominous and represent advanced disease.

DIAGNOSTIC TESTING

Chest Radiography. Cardiomegaly due to LV and left atrial enlargement is common in patients with chronic MR. In patients with pulmonary hypertension, right-sided chamber enlargement is also a common finding. Kerley B lines and interstitial edema can be seen in patients with acute MR or progressive LV failure.¹

Electrocardiography. Left atrial enlargement and atrial fibrillation are the most common ECG findings in patients with MR. Left ventricular enlargement is noted in approximately one-third of patients, and RV hypertrophy is observed in 15%.¹ A sample ECG of a patient with severe MR is depicted in Figure 9.

Echocardiography. Echocardiography is the most commonly used tool to evaluate the patient with suspected MR. It provides information about the mechanism and severity of MR, the size and function of the left and right ventricle, the size of the left atrium, the degree of pulmonary hypertension, and the presence of other associated valve lesions.³⁶ Doppler evaluation provides quantitative measures of the severity of MR that have been shown to be important predictors of outcome.^{35,36} Echocardiographic examples of a patient with MV prolapse and a patient with severe MR are depicted in Figures 10 and 11, respectively.

FIGURE 10. Parasternal long-axis echocardiographic view of a patient with bileaflet mitral valve prolapse (arrows). LA = left atrium; LV = left ventricle.

Exercise Testing. Exercise testing is useful in determining functional capacity, particularly when symptoms are unclear. Measurement of MR severity and pulmonary artery systolic pressure before and after exercise using Doppler echocardiography can provide additional useful information, especially if surgical intervention is being contemplated.² This technique is especially useful in symptomatic patients in whom there is a discrepancy between symptoms and resting measures of LV function and pulmonary artery pressure.

Cardiac Catheterization. Cardiac catheterization is generally performed to assess the hemodynamic severity

FIGURE 11. Apical 4-chamber echocardiographic view with color-flow Doppler imaging in a patient with mitral valve prolapse and severe mitral regurgitation (arrow). LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

of MR when noninvasive testing is inconclusive or a discrepancy exists between clinical and noninvasive findings. Coronary angiography is indicated for patients who are planning to undergo surgery and are at risk of CAD.¹

TREATMENT

Patients with chronic MR can remain asymptomatic for years. However, serial clinical evaluations and noninvasive tests are necessary because LV dysfunction can develop in the absence of symptoms. Patients with mild MR and an otherwise normal heart may be followed up with annual clinical examinations, undergoing echocardiography only if their clinical status changes (eg, the intensity of the murmur changes). In patients with moderate to severe MR, clinical examination and echocardiography should be performed yearly or sooner if symptoms develop. In view of the loading conditions that enhance LV shortening in severe MR, LV systolic dysfunction in severe MR is defined as an ejection fraction of 60% or less or an end-systolic dimension of 40 mm or greater.² Such conditions should prompt surgical referral.

Similarly, asymptomatic patients with severe MR should be considered for surgical correction, especially if the valve can be repaired, after discussions regarding the benefit of early referral for surgery. If such patients decline surgery, they should be followed up with clinical examinations and echocardiography every 6 to 12 months and should be referred for surgery promptly if they develop symptoms, atrial fibrillation, pulmonary hypertension, or LV systolic dysfunction.² Recent data have shown that this “watchful waiting” approach does not adversely affect survival as long as patients are carefully monitored.³⁷

The timing of surgical correction is in part related to whether the patient is a candidate for MV repair or will require MV replacement. It is therefore critical that patients with severe MR who may require surgery are referred to experienced, high-volume surgical centers, where the chances of a successful repair are high.^{2,38} Nonrheumatic posterior MV prolapse due to degenerative MV disease or ruptured chordae tendineae can usually be repaired. Involvement of the anterior mitral leaflet or both the leaflets decreases the likelihood of repair because it requires accompanying interventions, such as chordal shortening or chordal transfers. Thus, surgical skill and experience are the primary predictors of an acceptable outcome. In contrast, calcified mitral annulus or rheumatic involvement of the MV diminishes the likelihood of repair, even in experienced hands.² The management of patients with severe MR is outlined in Figure 12.²

For patients with asymptomatic degenerative MR, no accepted medical therapy has been shown to delay the need for surgical intervention. In asymptomatic patients with severe

FIGURE 12. Management strategy for patients with chronic severe mitral regurgitation. AF = atrial fibrillation; EF = ejection fraction; ESD = end-systolic dimension; HT = hypertension; LV = left ventricular; MV = mitral valve; MVR = MV replacement.

* Mitral valve repair may be performed in asymptomatic patients with normal LV function if performed by an experienced surgical team and if the likelihood of successful MV repair is >90%.

Adapted from *Circulation*.²

MR and normal LV function, repair of a severely regurgitant valve may be contemplated to prevent sequelae of chronic severe MR. This should be considered only when the likelihood of successful valve repair is greater than 90% in an experienced center.² In patients with functional MR associated

with LV dysfunction, angiotensin-converting enzyme inhibitors, β -blockers, and biventricular pacing have been shown to produce beneficial reverse remodeling, and the reduction in LV end-diastolic and end-systolic volumes with these therapies is associated with decreased severity of MR.³⁹⁻⁴¹

TABLE 2. Classification of Mitral Stenosis Severity

	Mild	Moderate	Severe
Specific findings			
Valve area (cm ²)	>1.5	1.0-1.5	<1.0
Supportive findings			
Mean gradient (mm Hg) ^a	<5	5-10	>10
Pulmonary artery pressure (mm Hg)	<30	30-50	>50

^a At heart rates of 60-80 beats/min and in sinus rhythm.
Adapted from *J Am Soc Echocardiogr*,⁸ with permission.

Percutaneous techniques for MV repair are under development, and several are currently undergoing clinical trials.⁴² These approaches are unlikely to be as effective as surgical MV repair performed at experienced centers. However, because percutaneous approaches to MV repair likely pose less risk to patients than open heart surgery, they may be effective enough to be used in selected higher-risk populations, such as elderly patients with multiple comorbid conditions or patients with severe LV dysfunction.

MITRAL STENOSIS

ETIOLOGY AND PATHOPHYSIOLOGY

The most common cause of MS worldwide is rheumatic fever. Isolated MS is twice as common in women as in men.² Other causes of MS are very rare and include congenital anomalies, prior exposure to chest radiation, mucopolysaccharidosis, severe mitral annular calcification, and left atrial myxoma.

FIGURE 13. Chest radiograph of a patient with severe mitral stenosis showing left atrial enlargement and pulmonary congestion.

Rheumatic disease is associated with fibrosis, calcification and fusion of commissures, leaflet thickening, and chordal fusion resulting in MS. A normal MV area is 4.0 to 5.0 cm². Symptoms usually develop when the valve area decreases below 1.5 cm² and also below 2.5 cm², particularly when the heart rate is elevated, as during exercise.² In some patients with chronic severe MS, pulmonary edema may not occur because of increased alveolar basement membrane thickening and decreased pulmonary microvascular permeability. The pulmonary arterioles may react with vasoconstriction, intimal hyperplasia, and medial hypertrophy, often resulting in pulmonary arterial hypertension. In some patients, a secondary obstruction may also develop at the level of the pulmonary veins.

Resting symptoms usually develop when the valve area is less than 1.0 cm². However, symptoms often occur in patients with larger valve areas if the time of diastolic filling decreases and/or transmitral flow increases, as is the case with exercise, atrial fibrillation, pregnancy, infection, or emotional stress.

The first symptoms of MS are usually exertional dyspnea and fatigue. However, patients may also present with pulmonary edema, atrial fibrillation, or an embolic event. Rarely, patients may present with hoarseness, hemoptysis, or dysphagia. Survival is good (80% in 10 years) in patients who are asymptomatic or minimally symptomatic. Once severe symptoms develop, however, survival decreases to 0% to 15% at 10 years. If severe pulmonary hypertension develops, average survival is less than 3 years.² Table 2 outlines the classification of the severity of MS.⁸

PHYSICAL EXAMINATION

Classic physical examination findings in patients with MS include a normal apical LV impulse, an accentuated S₁, and an opening snap followed by a diastolic rumble with presystolic accentuation heard best at the apex in the left lateral decubitus position. These findings, however, may not be present in patients with severe pulmonary hypertension, low cardiac output, or a heavily calcified and immobile valve. The diastolic rumble of MS can be heard best using the bell of the stethoscope with the patient in the left lateral decubitus position. A prominent right ventricular impulse is often present.

DIAGNOSTIC TESTING

Chest Radiography. The most common chest radiographic finding in patients with severe MS is left atrial enlargement (Figure 13). Enlargement of the right atrium, right ventricle, and pulmonary artery also occurs in patients with advanced MS with pulmonary hypertension.

Electrocardiography. The most common ECG finding in patients with MS is left atrial enlargement (P-wave duration in lead II ≥0.12 s and/or a P-wave axis between +45°

and -30°).¹ Atrial fibrillation is also a common finding. Electrocardiographic evidence of RV hypertrophy occurs in individuals with pulmonary hypertension.

Echocardiography. Echocardiography is the primary imaging tool used to assess patients with MS. The anterior leaflet generally shows a “hockey stick” deformity because the restricted motion of the valve most commonly involves the leaflet tips. The posterior leaflet is often restricted in both systole and diastole. Echocardiography also provides information regarding the size of the left atrium and the size and function of the left ventricle and the right-sided chambers (Figure 14). Doppler examination provides information about the severity of MS, the presence of other associated valve lesions, and the degree of pulmonary hypertension.²³ The MV area can be determined from the diastolic jet velocity across the MV.

Cardiac Catheterization. Routine diagnostic cardiac catheterization is no longer performed in patients with MS because accurate hemodynamic information can usually be obtained from echocardiography. Diagnostic cardiac catheterization is necessary only when echocardiography is nondiagnostic or results are discordant with clinical findings. Catheterization-based hemodynamic assessment is also performed before, during, and after percutaneous balloon valvotomy.⁴³ Coronary angiography is performed in patients scheduled to undergo valve replacement surgery if there is a risk of CAD.

Exercise Testing. Exercise testing using either a treadmill or supine bicycle is useful to determine functional capacity, particularly if it is difficult to establish the presence of symptoms by history. Doppler echocardiography combined with exercise provides additional important hemodynamic data regarding the severity of the MV gradient and pulmonary artery pressure during exercise because symptoms are often most pronounced at higher heart rates.²

TREATMENT

Patients with MS caused by rheumatic heart disease should receive penicillin prophylaxis for β -hemolytic streptococcal infections to prevent recurrent rheumatic fever.² Anticoagulant therapy is indicated for prevention of systemic embolism in patients with atrial fibrillation (persistent or paroxysmal), any prior embolic events (even if in sinus rhythm), or documented left atrial thrombus.²

In asymptomatic patients with mild to moderate rheumatic MV disease, physical examination, chest radiography, and ECG should be performed yearly. No specific medical therapy is indicated. Echocardiography should be performed if clinical status changes or if severe MS is suspected. All patients with severe MS should be advised to avoid occupations requiring strenuous exertion.²

FIGURE 14. Apical 4-chamber echocardiographic view of a patient with severe mitral stenosis showing severe left atrial (LA) enlargement and a calcified mitral valve with reduced excursion (arrow). LV = left ventricle; RA = right atrium; RV = right ventricle.

Symptomatic patients with severe MS or those with pulmonary hypertension (>50 mm Hg at rest) should be considered for percutaneous balloon valvotomy. Patients with severe MR, severely thickened or highly calcified MV leaflets, and/or subvalvular apparatus are not optimal candidates for this procedure. Symptoms may be difficult to ascertain in patients who are sedentary. In such patients, exercise testing with the assessment of the MV gradient and pulmonary artery pressures before and after exercise may be useful in determining the possible cardiac etiology of symptoms.² Surgical valve replacement should be considered for patients who are not candidates for percutaneous intervention. The management strategy for MS is outlined in Figure 15.²

SPECIAL POPULATIONS

PREGNANCY

Important hemodynamic changes occur during pregnancy. Plasma volume increases during the first trimester and can reach as high as 50% above baseline by the second trimester. Plasma volume then plateaus for the rest of the pregnancy. The heart rate increases 10 to 20 beats/min above baseline. Uterine contraction and endogenous hormones result in a decline in peripheral vascular resistance and a widening of the pulse pressure. The gravid uterus can obstruct the inferior vena cava, potentially resulting in peripheral edema, weakness, and hypotension.

The added volume load may result in symptoms of dyspnea and heart failure in women with impaired LV function and those with limited cardiac reserve. Stenotic valvular lesions are less well tolerated than regurgitant ones. The increased heart rate associated with pregnancy reduces the

FIGURE 15. Management strategy for patients with severe mitral stenosis. AF = atrial fibrillation; LA = left atrial; MR = mitral regurgitation; MV = mitral valve; MVA = MV area; PAP = pulmonary artery pressure; PMBV = percutaneous mitral balloon valvotomy. Adapted from *Circulation*.²

time for diastolic filling, which can be extremely troublesome for many patients, especially those with MS.³⁰ It is not uncommon for women with MS to first come to clinical attention during pregnancy.

During delivery, uterine contraction results in up to 500 mL of blood being released into the circulation. During a normal vaginal delivery, the woman loses approximately 400 mL of blood. The risk of blood loss during a cesarean section is often greater, averaging about 800 mL. There is an abrupt increase in venous return after delivery, due to autotransfusion from the uterus and because the baby no longer compresses the inferior vena cava. In addition, there continues to be autotransfusion of blood for 24 to 72 hours after delivery. Thus, the risk of pulmonary edema extends for several days after delivery.⁴⁴

High-risk valvular lesions associated with pregnancy are listed in Table 3. Patients with moderate to severe valve lesions should be referred to a cardiovascular specialist for assistance in the care of the patient during the pregnancy and delivery. Ideally, the risks of surgery should be discussed with the patient before conception.

Women with mechanical prosthetic valves pose unique challenges during pregnancy. The anticoagulation management of a pregnant woman with a mechanical prosthetic valve is controversial²; the patient should discuss it in detail with a cardiovascular specialist, preferably before conception.

PROSTHETIC VALVES

In patients who require valve replacement surgery, the selection of a mechanical prosthesis vs a bioprosthesis must be individualized and requires a detailed discussion with the patient. Age, lifestyle, and medical comorbid conditions are the most important considerations in making this selection. Although the durability of mechanical valves is greater than that of tissue valves, patients with mechanical valves must be treated with life-long warfarin, with the addition of aspirin unless contraindicated. Mechanical mitral prostheses are more thrombogenic than those in the aortic position. The durability of a bioprosthesis increases as a function of age,⁴⁵ and thus a bioprosthesis is a reasonable choice in patients older than 65 years.² Many patients younger than 65 years will select a bioprosthesis for lifestyle considerations, with

TABLE 3. **Valvular Heart Lesions Associated With High Maternal and/or Fetal Risk During Pregnancy**

Severe aortic stenosis with or without symptoms
Aortic regurgitation with NYHA functional class III-IV symptoms
Mitral stenosis with NYHA functional class II-IV symptoms
Mitral regurgitation with NYHA functional class III-IV symptoms
Aortic and/or mitral valve disease resulting in severe pulmonary hypertension (pulmonary pressure >75% of systemic pressures)
Aortic and/or mitral valve disease with severe LV dysfunction (LVEF <40%)
Mechanical prosthetic valve requiring anticoagulation
Marfan syndrome with or without aortic regurgitation

LV = left ventricular; LVEF = LV ejection fraction; NYHA = New York Heart Association.

Adapted from *Circulation*.²

the understanding that a second valve replacement may be required in the future because of structural deterioration of the prosthesis. Whether percutaneous catheter-based valve replacement will be a viable option for patients with failing bioprostheses in the future remains to be determined, but this transcatheter “valve-in-valve” technique has already been performed in selected patients.²¹

It should be emphasized that most patients with MR in developed countries of the world have valves that can be

TABLE 4. **Indications for Anticoagulation Therapy in Patients With Mechanical Prosthetic Valves^a**

Class I

- Warfarin to achieve an INR goal of 2.0-3.0 after the following:
 - AVR with bileaflet mechanical or Medtronic Hall valves if no risk factors^b are present
 - After AVR with a bioprosthesis and risk factors^b
- Warfarin to achieve an INR goal of 2.5-3.5 after the following:
 - AVR with bileaflet mechanical or Medtronic Hall valves if risk factors^b are present
 - AVR Starr-Edwards valves or mechanical disc valves (other than Medtronic Hall prostheses) in patients with no risk factors
 - MVR with any mechanical valve
- Role of aspirin:
 - After AVR or MVR with a bioprosthesis and no risk factors,^b at a dose of 75-100 mg/d
 - In all patients with mechanical heart valves and in those patients with biological valves who have risk factors,^b at a dose of 75-100 mg/d
 - After AVR or MVR in patients who cannot take warfarin, at a dose of 75-325 mg/d

Class IIa

- During the first 3 mo after AVR with a mechanical prosthesis, administration of warfarin to achieve a goal of 2.5-3.5
- During the first 3 mo after AVR or MVR with a bioprosthesis, administration of warfarin to achieve a goal of 2.0-3.0

Class IIb

- In high-risk patients in whom aspirin cannot be used, clopidogrel (75 mg/d) or warfarin to achieve an INR goal of 3.5-4.5

^a AVR = aortic valve replacement; INR = international normalized ratio; MVR = mitral valve replacement.

^b Risk factors: atrial fibrillation, left ventricular dysfunction, previous thromboembolism, and hypercoagulable condition.

Adapted from *Circulation*.²

repaired successfully by a skilled surgical team, thereby eliminating the long-term risks of prosthetic heart valves. Thus, patients with MR requiring surgery should be referred to centers in which cardiologists and cardiac surgeons are skilled in the evaluation and repair of MR.²

Once patients undergo valve surgery, appropriate life-long follow-up is needed. All patients with prosthetic valves should receive appropriate prophylactic dental care and should comply with prophylactic antibiotics for prevention of infective endocarditis.⁴⁶ All patients with mechanical valves should receive appropriate anticoagulation and monitoring. Warfarin and aspirin are indicated in all patients with mechanical prostheses and in high-risk patients with bioprosthetic valves. Aspirin alone is indicated for low-risk patients with bioprosthetic valves.² The established anticoagulation regimens for prosthetic valves are listed in Table 4.

The asymptomatic, uncomplicated patient should be followed up yearly. Echocardiography is indicated in the initial outpatient visits after surgery, but serial echocardiography is needed only if clinical status has changed or if prosthetic valve malfunction is suspected.² Patients with symptoms or complicated prosthetic valve disorders should be followed up more closely. The frequency of clinical examinations, noninvasive imaging, and specific medical and/or surgical therapy should be individualized according to the patient and the specific underlying pathology.

CONCLUSION

Degenerative valve disorders will likely increase in frequency as the population ages. Rheumatic heart disease is common worldwide and is seen with increasing frequency in the United States as a result of the globalization of our society. Appropriate diagnosis, management, and follow-up of these patients are imperative to reduce long-term morbidity and mortality. A fundamental knowledge of valve disease is important for the primary care physician because the initial presentation of such patients often occurs in the primary care setting.

REFERENCES

1. Otto CM, Bonow RO. Valvular heart disease. In: Libby P, Bonow RO, Mann DL, Zipes DP, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia, PA: WB Saunders; 2007:1625-1712.
2. Bonow RO, Carabello BA, Chatterjee K, et al. 2008 Focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Valvular Heart Disease). *Circulation*. 2008;118:e523-e661.
3. Ross J Jr, Braunwald E. Aortic stenosis. *Circulation*. 1968;38(1)(suppl): 61-67.
4. Bouma BJ, van den Brink RBA, van der Meulen JH, et al. To operate or not in elderly patients with aortic stenosis: the decision and its consequences. *Heart*. 1999;82:143-148.

5. Bach DS, Siao D, Girard SE, Duvernoy C, McCallister BD Jr, Gualano SK. Evaluation of patients with severe symptomatic aortic stenosis who do not undergo aortic valve replacement: the potential role of subjectively overestimated operative risk. *Circ Cardiovasc Qual Outcomes*. 2009;2:533-539.
6. Pellikka PA, Sarano ME, Nishimura RA, et al. Outcome of 622 adults with asymptomatic, hemodynamically significant aortic stenosis during prolonged follow-up. *Circulation*. 2005;111(24):3290-3295.
7. Rahimtoola SH. Aortic valve disease. In: Fuster V, O'Rourke RA, Walsh RA, Poole-Wilson P, eds. *Hurst's The Heart*. 12th ed. New York, NY: McGraw-Hill; 2008:1697-1730.
8. Baumgartner H, Hung J, Bernejo J, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. *J Am Soc Echocardiogr*. 2009;22:1-23.
9. Lindroos M, Kupari M, Heikkilä J, Tilvis R. Prevalence of aortic valve abnormalities in the elderly: an echocardiographic study of a random population sample. *J Am Coll Cardiol*. 1993;21:1220-1225.
10. Stewart BF, Siscovick D, Lind BK, et al; Cardiovascular Health Study. Clinical factors associated with calcific aortic valve disease. *J Am Coll Cardiol*. 1997;29(3):630-634.
11. Otto CM, Lind BK, Kitzman DW, Gersh BJ, Siscovick DS. Association of aortic-valve sclerosis with cardiovascular mortality and morbidity in the elderly. *N Engl J Med*. 1999;341:142-147.
12. Aronow WS, Schwartz KS, Koenigsberg M. Correlation of serum lipids, calcium, and phosphorus, diabetes mellitus and history of systemic hypertension with presence or absence of calcified or thickened aortic cusps or root in elderly patients. *Am J Cardiol*. 1987;59:998-999.
13. Boon A, Cheriex E, Lodder J, Kessels F. Cardiac valve calcification: characteristics of patients with calcification of the mitral annulus or aortic valve. *Heart*. 1997;78:472-474.
14. Wilson PWF, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation*. 1998;97:1837-1847.
15. Picano E, Pibarot P, Lancellotti P, Monin JL, Bonow RO. The emerging role of exercise testing and stress echocardiography in valvular heart disease. *J Am Coll Cardiol*. 2009;54:2251-2260.
16. Connolly HM, Oh JK, Schaff HV, et al. Severe aortic stenosis with low transvalvular gradient and severe left ventricular dysfunction: result of aortic valve replacement in 52 patients. *Circulation*. 2000;101:1940-1946.
17. Messika-Zeitoun D, Aubry MC, Detaint D, et al. Evaluation and clinical implications of aortic valve calcification measured by electron-beam computed tomography. *Circulation*. 2004;110:356-362.
18. Kilner PJ, Manzara CC, Mohiaddin RH, et al. Magnetic resonance jet velocity mapping in mitral and aortic valve stenosis. *Circulation*. 1993;87:1239-1248.
19. Chan KL, Teo K, Dumesnil JG, et al. Effect of lipid lowering with rosuvastatin on progression of aortic stenosis: results of the Aortic Stenosis Progression Observation: Measuring Effects of Rosuvastatin (ASTRONOMER) trial. *Circulation*. 2010;121(2):306-314.
20. Lieberman EB, Bashore TM, Hermiller JB, et al. Balloon aortic valvuloplasty in adults: failure of procedure to improve long term survival. *J Am Coll Cardiol*. 1995;26:1522-1528.
21. Zajarias A, Cribier AG. Outcomes and safety of percutaneous aortic valve replacement. *J Am Coll Cardiol*. 2009;53(20):1829-1836.
22. Tadros TM, Klein MD, Shapira OM. Ascending aortic dilatation associated with bicuspid aortic valve: pathophysiology, molecular biology, and clinical implications. *Circulation*. 2009;119(6):880-890.
23. Otto CM. The left ventricular response to chronic pressure and/or volume overload and aortic regurgitation. In: Otto CM, ed. *Valvular Heart Disease*. 2nd ed. Philadelphia, PA: WB Saunders; 2003:302-335.
24. Rigolin VH, Bonow RO. Hemodynamic characteristics and progression to heart failure in regurgitant lesions. *Heart Fail Clin*. 2006;2:453-460.
25. Carabello BA. Progress in mitral and aortic regurgitation. *Prog Cardiovasc Dis*. 2001;43:457-475.
26. Enriquez-Sarano M, Tajik AJ. Clinical practice: aortic regurgitation. *N Engl J Med*. 2004;351:1539-1546.
27. Bekerredjian R, Grayburn PA. Valvular heart disease: aortic regurgitation. *Circulation*. 2005;112(1):125-134.
28. Roes SD, Hammer S, van der Geest RJ, et al. Flow assessment through four heart valves simultaneously using 3-dimensional 3-directional velocity-encoded magnetic resonance imaging with retrospective valve tracking in healthy volunteers and patients with valvular regurgitation [published online ahead of print August 29, 2009]. *Invest Radiol*. doi:10.1097/RLI.0b013e3181ae99b5.
29. Borer JS, Bonow RO. Contemporary approach to aortic and mitral regurgitation. *Circulation*. 2003;108:2432-2438.
30. Dujardin KS, Enriquez-Sarano M, Schaff HV, et al. Mortality and morbidity of aortic regurgitation in clinical practice: a long-term follow-up study. *Circulation*. 1999;99:1851-1857.
31. Greenberg BH, DeMots H, Murphy E, et al. Beneficial effects of hydralazine on rest and exercise hemodynamics in patients with chronic severe aortic insufficiency. *Circulation*. 1980;62:49-55.
32. Shen WF, Roubin GS, Hirasawa K, et al. Noninvasive assessment of acute effects of nifedipine on rest and exercise hemodynamics and cardiac function in patients with aortic regurgitation. *J Am Coll Cardiol*. 1984;4:902-907.
33. Lin M, Chiang HT, Lin SL, et al. Vasodilator therapy in chronic asymptomatic aortic regurgitation: enalapril versus hydralazine therapy. *J Am Coll Cardiol*. 1994;24:1046-1053.
34. Levine RA, Schwammenthal E. Ischemic mitral regurgitation on the threshold of a solution: from paradoxes to unifying concepts. *Circulation*. 2005;112:745-758.
35. Enriquez-Sarano M, Avierinos JF, Messika-Zeitoun D, et al. Quantitative determinants of the outcome of asymptomatic mitral regurgitation. *N Engl J Med*. 2005;352(9):875-883.
36. Zoghbi WA, Enriquez-Sarano M, Foster E, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr*. 2003;16:777.
37. Rosenhek R, Rader F, Klar U, et al. Outcome of watchful waiting in asymptomatic severe mitral regurgitation. *Circulation*. 2006;113(18):2238-2244.
38. Enriquez-Sarano M, Schaff HV, Orszulak TA, Tajik AJ, Bailey KR, Frye RL. Valve repair improves the outcome of surgery for mitral regurgitation: a multivariate analysis. *Circulation*. 1995;91:1022-1028.
39. Capomolla S, Febo O, Gnemmi M, et al. Beta blockade in chronic heart failure: diastolic function and mitral regurgitation improvement by carvedilol. *Am Heart J*. 2000;139:596-608.
40. Linde C, Leclercq C, Rex S, et al. Long term benefits of biventricular pacing in congestive heart failure: results from the Multisite STimulation In Cardiomyopathy (MUSTIC) study. *J Am Coll Cardiol*. 2002;40:111-118.
41. Breithardt OA, Sinha AM, Schramm E, et al. Acute effects of cardiac resynchronization therapy on functional mitral regurgitation in advanced systolic heart failure. *J Am Coll Cardiol*. 2003;41:765-770.
42. Alqoofi F, Feldman T. Percutaneous approaches to mitral regurgitation. *Curr Treat Options Cardiovasc Med*. 2009;11(6):476-482.
43. Wilkins GT, Weyman AE, Abascal VM, Block PC, Palacios IF. Percutaneous balloon dilation of the mitral valve: an analysis of echocardiographic variables related to outcome and the mechanism of dilatation. *Br Heart J*. 1988;60:299-308.
44. Warnes CA. Pregnancy and heart disease. In: Libby P, Bonow RO, Mann DL, Zipes DP, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia, PA: WB Saunders; 2007:1967-1982.
45. Banbury MK, Cosgrove DM III, White JA, Blackstone EH, Frater RW, Okies JE. Age and valve size effect on the long-term durability of the Carpentier-Edwards aortic pericardial bioprosthesis. *Ann Thorac Surg*. 2001;72:753-757.
46. Wilson W, Taubert KA, Gewitz M, et al. Prevention of endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation*. 2007;116:1736-1754.

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