

## Review Article

*Medical Progress*

## VALVULAR HEART DISEASE

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THE past 15 years have brought a remarkable improvement in the clinical outcome of patients with valvular heart disease. It is impossible to attribute the change to any single advance in the field. However, it is likely that more effective noninvasive monitoring of ventricular function, improvement in prosthetic valves, advances in valve-reconstruction techniques, and the development of useful guidelines for choosing the proper timing of surgical intervention have all worked in concert to improve prognosis. Moreover, advances in minimally invasive surgical techniques may make valve procedures more easily tolerated by the patient.<sup>1</sup>

All valvular heart diseases place a hemodynamic burden on the left or right ventricle, or on both ventricles, which is initially tolerated as the cardiovascular system compensates for the overload. However, hemodynamic overload eventually leads to muscle dysfunction and congestive heart failure, and sometimes sudden death. Two major questions must be answered in the management of every case of valvular heart disease: Is the valvular disease severe enough to cause morbidity or mortality for which mechanical intervention would be beneficial? And if the answer to this question is yes, what are the best medical therapy and the best time for surgical intervention to minimize or eliminate morbidity and mortality? We will discuss these questions for the four major acquired left-sided valvular lesions: aortic stenosis, mitral stenosis, nonischemic mitral regurgitation, and aortic regurgitation.

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## AORTIC STENOSIS

## Recognition

Acquired aortic stenosis is usually an idiopathic disease resulting from degeneration and calcification of the aortic leaflets.<sup>2,3</sup> Stenosis is more likely to occur in persons born with bicuspid aortic valves than in those with normal tricuspid valves, and it develops earlier, in the fourth and fifth decades of life, in such persons. When the disease is acquired in previously normal tricuspid aortic valves, stenosis develops in the sixth, seventh, and eighth decades. Why some persons are afflicted by this disease whereas others are spared is unknown, but it shares some of the pathologic features of coronary atherosclerosis and is associated with some of the same risk factors, such as hypertension and hypercholesterolemia.<sup>4</sup>

The classic symptoms of aortic stenosis are angina, syncope, and the symptoms of congestive heart failure. Angina develops in aortic stenosis in part because of reduced coronary flow reserve and in part because of increased myocardial oxygen demand caused by high afterload.<sup>5-7</sup>

The origin of exertional syncope in aortic stenosis remains controversial. According to one theory, an exercise-induced decrease in total peripheral resistance is uncompensated because cardiac output is restricted by the stenotic valve.<sup>8</sup> Another possible mechanism is the precipitation of a vasodepressor response.<sup>9</sup>

Heart failure in aortic stenosis can be caused by diastolic dysfunction, systolic dysfunction, or both. Diastolic dysfunction results from increased left-ventricular-wall thickness and increased collagen content.<sup>10</sup> Systolic dysfunction results from excess afterload, decreased contractility, or a combination of these factors.<sup>7</sup>

The most common sign of aortic stenosis is a systolic ejection murmur radiating to the neck. The murmur is usually heard best in the aortic area. It often disappears over the sternum and then reappears in the apical area, mimicking mitral regurgitation (Gallivardin's phenomenon). In mild aortic stenosis, the murmur usually peaks early in systole, it is often associated with a thrill, and the carotid upstrokes are well preserved. As the severity of stenosis increases, the murmur peaks progressively later in systole and may become softer as cardiac output diminishes. The carotid upstrokes classically become diminished in amplitude and delayed in time (*parvus et tardus*). The second heart sound may become single as the aortic closing component is lost, or S<sub>2</sub> may become paradoxically split because of delay in left ventricular emptying.

**Assessment of Severity**

**Echocardiography**

Although a reasonable estimate of the severity of aortic stenosis can be made during physical examination, echocardiography with Doppler examination of the aortic valve now provides a more accurate assessment of the transvalvular gradient and the area of the aortic valve. Since flow is the product of cross-sectional area and bloodstream velocity, as the bloodstream reaches a narrowing (Fig. 1), velocity must increase for flow to remain constant.<sup>11</sup> This increase in velocity, detected by the Doppler technique, can be translated into a gradient (four times the velocity squared) that accurately mirrors the gradient assessed by direct pressure measurement,<sup>12</sup> or the velocity can be used in the continuity equation to estimate aortic-valve area (Fig. 1). Echocardiography is also useful in assessing the extent of left ventricular hypertrophy and in estimating left ventricular ejection performance.

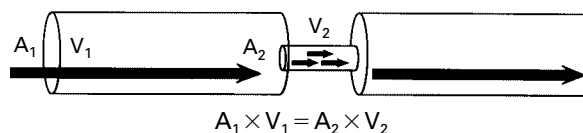
**Cardiac Catheterization and Coronary Angiography**

The severity of aortic stenosis can usually be gauged accurately by noninvasive techniques. However, because patients with aortic stenosis are often elderly and therefore at risk for coronary disease, coronary angiography is usually performed before valve replacement, especially in patients with angina.<sup>13,14</sup> Although initial attempts to detect coronary artery disease in patients with aortic stenosis by noninvasive techniques appear fruitful, further study will be required before this practice is adopted as routine.<sup>15,16</sup> In cases where the severity of aortic stenosis cannot be determined by noninvasive testing, invasive measurement of the pressure gradient and determination of cardiac output are performed to derive data from which to calculate the area of the aortic-valve orifice.<sup>17</sup>

**Timing of Surgery**

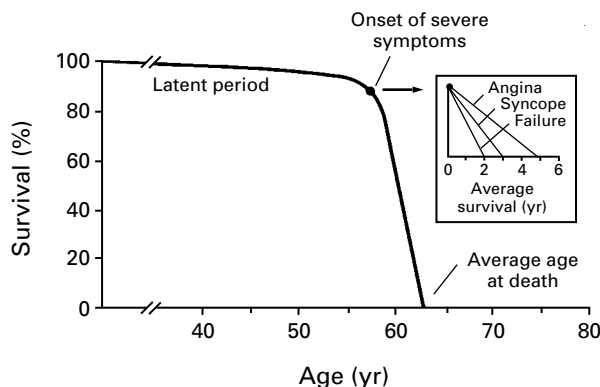
Except for prophylaxis against endocarditis, there is no proved medical therapy for aortic stenosis. The only effective relief of this mechanical obstruction to blood flow is aortic-valve replacement.<sup>18</sup> Although the noninvasive assessment of the severity of aortic stenosis is quite accurate and thus useful in determining the timing of surgery, it is not severity alone that determines the timing of aortic-valve replacement. Rather, the decision to replace the aortic valve is based on the presence of the classic symptoms of aortic stenosis (noted above) along with a severely stenotic valve.

As shown in Figure 2, the survival of patients with aortic stenosis is nearly normal until the onset of symptoms, when a precipitous decrease in survival occurs.<sup>19</sup> The prognostic importance of symptoms in an early study has been corroborated by more recent



**Figure 1.** Principles of the Use of Doppler Ultrasonography and the Continuity Equation in Estimating Aortic-Valve Area.

For blood flow ( $A_1 \times V_1$ ) to remain constant when it reaches a stenosis ( $A_2$ ), velocity must increase to  $V_2$ . Doppler examination of the stenosis detects the increase in velocity, which can be used to calculate the aortic-valve gradient or to solve the continuity equation for  $A_2$ . A denotes area, and V velocity.



**Figure 2.** Natural History of Aortic Stenosis.

There is a long latent period of increasing obstruction and myocardial overload, during which the asymptomatic patient has a normal life span. However, once angina, syncope, or heart failure develops, survival is greatly reduced. If the aortic valve is not replaced, approximately 50 percent of patients will be dead within five years after angina develops, 50 percent will be dead within three years after syncope develops, and 50 percent will be dead within only two years after heart failure develops. Adapted from Ross and Braunwald,<sup>19</sup> with the permission of the publisher.

studies in which Doppler echocardiography established the severity of stenosis in initially asymptomatic patients.<sup>20,21</sup> About 75 percent of patients with symptomatic aortic stenosis will be dead three years after the onset of symptoms unless the aortic valve is replaced.<sup>22</sup> Typically, a gradient of more than 50 mm Hg or a valve area of less than 0.8 cm<sup>2</sup> indicates critical stenosis that is capable of causing symptoms and death. However, there are exceptions to these rules. Some patients with larger valve areas or smaller gradients have symptoms that are clearly due to aortic stenosis. Such patients will benefit from aortic-valve replacement.

**Age**

It should be emphasized that even though most patients with aortic stenosis are elderly, the prognosis with surgery, even in an octogenarian, is excellent

in the absence of coexisting illnesses.<sup>23-25</sup> Thus, age is not a contraindication to surgery in such patients. Furthermore, the age-corrected survival after aortic-valve replacement in patients older than 65 is not different from that in the general population.<sup>26</sup>

#### **Balloon Aortic Valvotomy**

Balloon aortic valvotomy for adult acquired aortic stenosis is useful only for palliation of the disease. Although the procedure was initially greeted with enthusiasm, interest in balloon aortic valvotomy has waned in recent years. The rate of serious complications, including death, stroke, aortic rupture, aortic regurgitation, and vascular injury, exceeds 10 percent.<sup>27</sup> Furthermore, the mortality after this procedure is 60 percent at 18 months, a rate similar to that in an untreated population.<sup>28</sup> The event-free survival at two years is only 20 percent, and many patients thought to be candidates only for balloon valvotomy eventually have a good outcome with aortic-valve replacement.<sup>28,29</sup>

Although the procedure is not lifesaving, it may be useful in alleviating symptoms in patients who are clearly not candidates for aortic-valve replacement because of other medical problems. Some practitioners have successfully used balloon valvotomy as a bridge to aortic-valve replacement in very sick patients. However, no controlled data are available to prove this approach superior to direct aortic-valve replacement.

#### **Stress Testing**

Although the presence or absence of symptoms is the key factor in the management of aortic stenosis, in some patients who have vague symptoms or for whom a reliable history is difficult to obtain, exercise testing may be useful to establish the symptomatic state more objectively. However, this procedure is attended by increased risk in patients with aortic stenosis, and it is ill-advised to perform exercise testing in patients who are symptomatic.<sup>30</sup> The test can be performed safely in asymptomatic patients or those with vague symptoms if great caution is used and a physician is present.<sup>31-33</sup> In such patients, exercise testing may provide additional information on which to base clinical decision making.

#### **Patients with Congestive Heart Failure and Reduced Systolic Performance**

For most patients with advanced congestive heart failure, even those with a marked reduction in the ejection fraction, aortic-valve replacement provides remarkable relief of symptoms and improved ejection performance, because relieving the obstruction to outflow reduces left ventricular afterload and might also eventually lead to the restoration of contractile function.<sup>34-36</sup> However, a persistently problematic group of patients with aortic stenosis is the group

with a low ejection fraction and a low transvalvular gradient. Studies of this subgroup of patients have found high operative mortality and persistence of symptoms after surgery in many cases.<sup>34,37,38</sup> However, it is clear that other patients in this group improve after surgery.<sup>38</sup>

The criteria for deciding which patients in this group should have aortic-valve replacement continue to evolve. Initial studies indicate that patients in this group may have a favorable surgical outcome if both the cardiac output and the transvalvular gradient are increased by either inotropic stimulation or the administration of nitroprusside.<sup>39,40</sup> Patients in whom inotropic stimulation augments cardiac output but not the transvalvular gradient form a group with milder stenosis that was not the primary cause of left ventricular dysfunction. Such patients are unlikely to benefit from valve replacement.

#### **Women with Aortic Stenosis**

Recently, differences in left ventricular geometry between men and women with aortic stenosis have been recognized.<sup>41-43</sup> Women with aortic stenosis are likely to have thicker ventricular walls, which reduces wall stress (which, according to the Laplace equation, is calculated as the product of the left ventricular pressure and the radius, divided by two times the wall thickness), and higher ejection fractions. Preoperative recognition of these differences is important, because postoperative management of low cardiac output requires volume expansion rather than the use of pressor agents.<sup>44</sup>

In summary, aortic stenosis is a disease of aging that is likely to become more prevalent as the proportion of older people in our population increases. Once stenosis has been identified during physical examination, its severity can be accurately quantified by Doppler echocardiography. Asymptomatic patients with aortic stenosis are followed medically until the onset of one of the classic symptoms of aortic stenosis, at which time the aortic valve is replaced. Aortic-valve replacement is successful in most elderly patients and even in many patients with advanced heart failure.

### **MITRAL STENOSIS**

#### **Recognition and Assessment of Severity**

Mitral stenosis is a sequela of rheumatic heart disease that primarily affects women. Unfortunately, a reliable history of rheumatic fever is often difficult to obtain and thus cannot usually be used as a guide to the likely presence or absence of this disease. In developed countries, the steady decline in the incidence of rheumatic fever has reduced the incidence of mitral stenosis. Both rheumatic fever and mitral stenosis remain common in developing nations.

Patients with mitral stenosis usually have symptoms typical of left-sided heart failure: dyspnea on exertion, orthopnea, and paroxysmal nocturnal dyspnea. Less frequently, they have hemoptysis, hoarseness, and symptoms of right-sided heart failure; these symptoms are somewhat more specific for mitral stenosis. Often the patient remains asymptomatic until she becomes pregnant or has atrial fibrillation, when dyspnea and orthopnea are noted.

The symptoms of mitral stenosis stem from increased left atrial pressure and reduced cardiac output, primarily caused by mechanical obstruction of filling of the left ventricle. Although the symptoms are those of left ventricular failure, contractility of the left ventricle is usually normal in mitral stenosis.<sup>45</sup> However, in some cases, the left ventricular ejection fraction is reduced because of excessive afterload secondary to a reflexive increase in systemic vascular resistance. Since it is the right ventricle that ultimately bears the burden of propelling blood through the mitral valve, right ventricular function is compromised first by the afterload imposed on it by high left atrial pressure and then by the development of secondary pulmonary vasoconstriction.

During physical examination, mitral stenosis is suspected because of the presence of the classic diastolic rumble that follows an opening snap.  $S_1$  is characteristically loud, because the mitral valve is held open by the transmitral gradient until the force of ventricular systole closes the valve. The presence of a loud  $P_2$ , right ventricular lift, elevated neck veins, ascites, and edema indicates that pulmonary hypertension producing right ventricular overload has developed. This is an ominous sign in the progression of the disease, because pulmonary hypertension increases the risk associated with surgery.<sup>46</sup>

Echocardiography is the premier noninvasive diagnostic tool for assessing the severity of mitral stenosis and for judging the applicability of balloon mitral valvotomy. Echocardiography can usually permit an accurate planimetric calculation of valve area<sup>47</sup> and can also be used to assess the severity of stenosis by measuring the decay of the transvalvular gradient or the "pressure half-time," an empirical measurement.<sup>48,49</sup> The latter determination is based on the principle that as the severity of stenosis worsens, it takes progressively longer for the transmitral flow velocity to decay. By empirically dividing the constant of 220 by the pressure half-time, one can make an approximation of valve area.<sup>48</sup>

#### Therapy and Timing of Intervention

For the asymptomatic patient in sinus rhythm, prophylaxis against endocarditis is the only medical therapy indicated. When mild symptoms develop, diuretics are usually effective in lowering left atrial pressure and reducing symptoms. If atrial fibrillation develops, rate control with digoxin, a beta-blocker,

or a calcium-channel blocker is crucial, since a rapid heart rate further impairs left ventricular filling, simultaneously reducing cardiac output and increasing left atrial pressure. Anticoagulant therapy is required, since there is a high risk of embolism in patients with chronic atrial fibrillation and mitral stenosis.

If the symptoms are more than mild, or if there is evidence that pulmonary hypertension is beginning to develop, mechanical relief of the mitral stenosis is indicated, since further delay worsens the prognosis.<sup>50</sup> In many cases, balloon valvotomy provides excellent mechanical relief that usually results in prolonged benefit, unlike valvotomy in aortic stenosis.<sup>51</sup> The presence of heavy valvular calcification, severe subvalvular distortion, or more than mild mitral regurgitation militates against the use of balloon valvotomy.<sup>52</sup> In such cases, open commissurotomy, valve reconstruction, or mitral-valve replacement improves survival and reduces symptoms.

Still unresolved is the proper treatment of patients with mitral stenosis who are asymptomatic except for the presence of atrial fibrillation. This unwanted arrhythmia is associated with extensive morbidity and mortality.<sup>53</sup> It is often hoped that correction of mitral stenosis before the atrial fibrillation has become prolonged (and thus more likely to be permanent) will allow the reestablishment of sinus rhythm after valvotomy or surgery. However, there is currently no conclusive evidence that this management strategy is successful. Indeed, some now advocate a combination of the appropriate mitral-valve procedure and the Cox maze procedure in appropriate patients to ensure the maintenance of sinus rhythm postoperatively.<sup>54-56</sup>

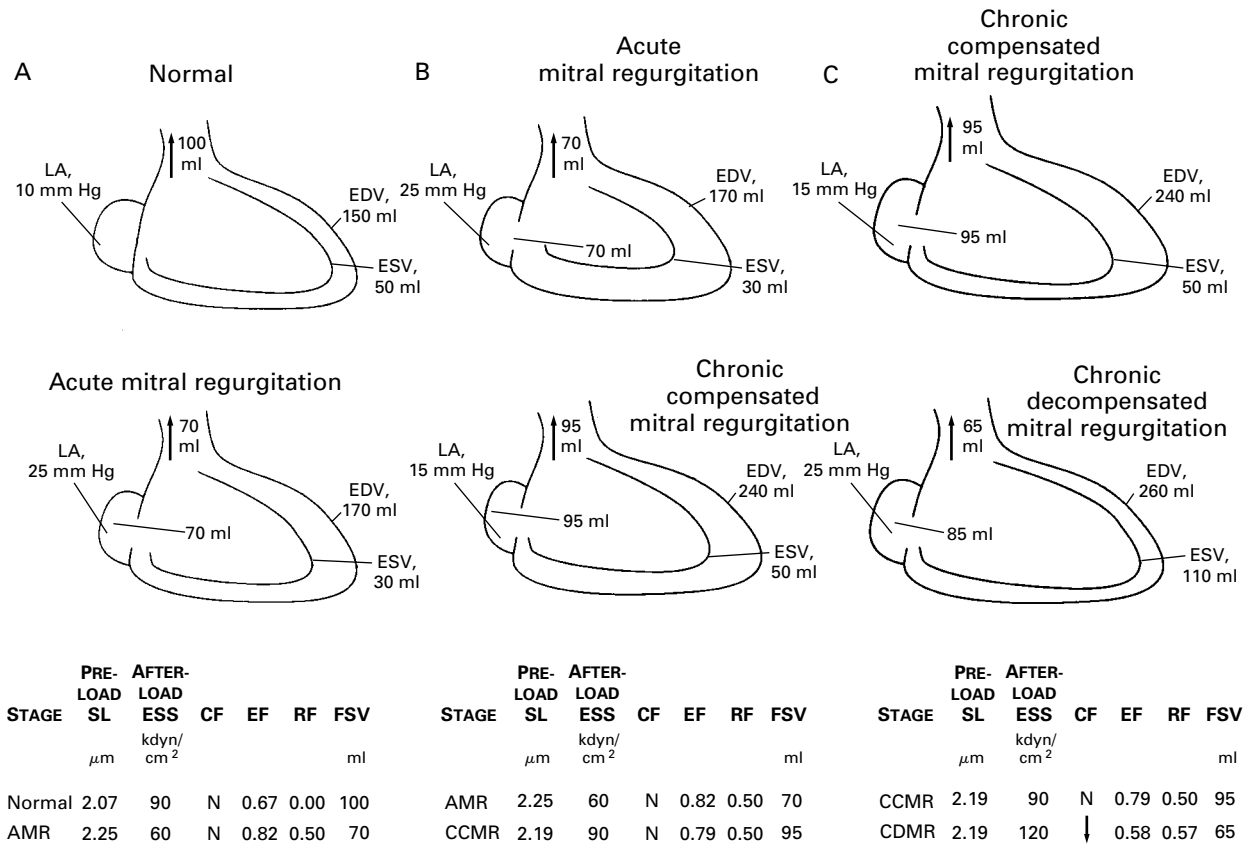
## NONISCHEMIC MITRAL REGURGITATION

### Recognition and Assessment of Severity

The usual causes of mitral regurgitation are infective endocarditis, myxomatous degeneration of the mitral valve (including the mitral valve prolapse syndrome), collagen vascular disease, spontaneous rupture of the chordae tendineae, and rheumatic fever.

Figure 3 depicts the pathophysiologic stages of mitral regurgitation, progressing from acute mitral regurgitation to chronic compensated mitral regurgitation and to chronic decompensated mitral regurgitation.<sup>57</sup>

Chronic mitral regurgitation is compensated by the development of eccentric cardiac hypertrophy, and cardiac enlargement should therefore be manifest on physical examination. A holosystolic apical murmur heard on physical examination alerts the examiner that mitral regurgitation is present. An  $S_3$  suggests that the disease is severe. However, an  $S_3$  heard in mitral regurgitation does not necessarily indicate the presence of congestive heart failure, since in this situation the sound is caused by rapid filling



**Figure 3.** Pathophysiologic Stages of Mitral Regurgitation.

Panel A shows the transition from normal physiology to acute mitral regurgitation (AMR). The volume overload of acute mitral regurgitation increases preload sarcomere length (SL) so that end-diastolic volume (EDV) increases from 150 to 170 ml. The presence of a new pathway for the ejection of blood into the left atrium (LA) reduces afterload, described as end-systolic stress (ESS), and therefore end-systolic volume (ESV) is reduced from 50 to 30 ml. The ejection fraction (EF) increases acutely, but because 50 percent of the total stroke volume is regurgitated into the left atrium, resulting in a regurgitant fraction (RF) of 0.50, forward stroke volume (FSV) is reduced from 100 to 70 ml. The increased volume in the left atrium raises pressure there from normal to 25 mm Hg. Panel B shows the transition from acute mitral regurgitation to chronic compensated mitral regurgitation (CCMR). The development of eccentric hypertrophy has increased end-diastolic volume from 170 to 240 ml. The now larger ventricle has an increase in afterload because the radius applied in the Laplace equation for stress has increased. This in turn increases end-systolic volume to normal. The presence of eccentric hypertrophy, however, allows for an increase in total stroke volume as well as forward stroke volume. Enlargement of the left atrium allows the volume overload there to be accommodated at a lower filling pressure (15 mm Hg). The ejection fraction is supernormal. Panel C shows the transition to chronic decompensated mitral regurgitation (CDMR). The now weakened ventricle can no longer contract well, and end-systolic volume therefore increases from 50 to 110 ml. Forward stroke volume is reduced, and cardiac dilatation leads to an increased regurgitant fraction. However, the still favorable loading conditions permit the ejection fraction to remain normal (0.58). CF denotes contractile function; N, normal; and the downward arrow, depressed. Reproduced from Carabello,<sup>57</sup> with the permission of the publisher.

of the left ventricle by the large volume of blood stored in the left atrium in diastole. Echocardiography confirms enlargement of the chamber, and color-flow examination of the mitral valve establishes the pattern of disturbed flow caused by regurgitation across the mitral valve.

Although a variety of methods of quantifying the severity of regurgitation have been used, none have met with universal success. Currently, echocardiography provides only a semiquantitative estimate of the severity of mitral regurgitation. Left ventriculography

performed during cardiac catheterization provides an additional but also imperfect estimate of the severity of mitral regurgitation. However, catheterization is used only when surgery is being contemplated, and it is not suitable for longitudinal follow-up.

**Timing of Surgery**

Unlike the stenotic lesions, regurgitant lesions may progress insidiously, causing left ventricular damage before symptoms have developed.<sup>58</sup> Thus, although the presence of symptoms in chronic mitral regurgi-

tation usually indicates disordered physiology and the need for valve surgery, surgery should also be performed if asymptomatic left ventricular dysfunction has begun to develop. The loading conditions in mitral regurgitation are favorable to left ventricular ejection; preload is increased whereas afterload is normal or occasionally decreased, and thus the lesion itself facilitates left ventricular emptying.<sup>57</sup> Therefore, in the presence of normal muscle function, the ejection fraction should be supernormal in the patient with mitral regurgitation.<sup>59</sup> Once the ejection fraction falls below 60 percent, the prognosis worsens.<sup>60</sup>

Left ventricular performance can also be gauged in mitral regurgitation by assessing the diameter to which the left ventricle can contract at the end of systole. End-systolic dimension is less dependent on preload than is ejection fraction and can be used as another measure of left ventricular contractile function.<sup>61</sup> When the end-systolic dimension exceeds 45 mm, the prognosis worsens.<sup>62-64</sup> Thus, patients should be referred for surgery if more than mild symptoms develop, or if the ejection fraction falls toward 60 percent or the end-systolic dimension approaches 45 mm, even in the absence of symptoms.

Hochreiter et al.<sup>65</sup> demonstrated a worsened prognosis if right ventricular function is reduced, emphasizing the prognostic role of pulmonary hypertension in this disease. Patients with a right ventricular ejection fraction of less than 30 percent are at especially high risk.

#### Importance of the Mitral-Valve Apparatus

Although the importance of the mitral-valve apparatus was described decades ago,<sup>66</sup> its role in sustaining left ventricular function has become almost universally recognized only recently. Mitral-valve repair has a lower operative mortality and a better late outcome<sup>67</sup> than mitral-valve replacement. Thus, mitral-valve repair rather than replacement should be performed whenever possible.<sup>68-70</sup> Even when the mitral valve must be replaced because of extensive degeneration of the valve, an attempt should be made to conserve the chordal structures and their connections. In the past, when standard replacement of the mitral valve involved destruction of the chordal apparatus, the ejection fraction almost always fell after the operation. Currently, however, the ejection fraction is usually maintained at its preoperative level when the chordal apparatus is preserved in either repair or replacement of the mitral valve.<sup>69,71,72</sup> Repair rather than replacement also obviates the need for anticoagulant therapy in patients in sinus rhythm and avoids possible failure of the prosthetic valve.

With these improved surgical techniques, postoperative survival after well-timed mitral-valve surgery now approaches that of the general population, as it does for patients with aortic or mitral stenosis.<sup>60</sup> It

should be noted, however, that whereas in aortic stenosis, age alone is not a contraindication to surgery, in mitral stenosis patients more than 75 years of age have a worse prognosis after surgery than younger patients, especially if mitral-valve replacement rather than repair has been performed or if coronary disease is present.<sup>73</sup>

#### Medical Therapy

Although vasodilators are successfully used to increase forward output and decrease left ventricular filling pressure in patients with acute mitral regurgitation, there is currently no apparent benefit to long-term use, especially in asymptomatic patients.<sup>74</sup> Although such benefit might be possible, no long-term, large studies have demonstrated that the use of vasodilators safely reduces or delays the need for surgery or improves outcome.

### AORTIC REGURGITATION

Aortic regurgitation results from disease of either the aortic leaflets or the aortic root that distorts the leaflets to prevent their coaptation. Common causes of leaflet abnormalities that result in aortic regurgitation include infective endocarditis and rheumatic fever. Aortic-root causes of aortic regurgitation include annuloaortic ectasia (idiopathic root dilatation associated with hypertension and aging), Marfan's syndrome, aortic dissection, collagen vascular disease, and syphilis.

In chronic aortic regurgitation, left ventricular enlargement produces a large total stroke volume that is entirely ejected into the aorta. In contrast, in mitral regurgitation the regurgitant volume enters the left atrium. Increased stroke volume increases pulse pressure, causing systolic hypertension, which imposes increased afterload on the left ventricle. Indeed, afterload can be as high in aortic regurgitation as it is in aortic stenosis.<sup>75,76</sup>

#### Recognition and Assessment of Severity

The large total stroke volume in aortic regurgitation increases pulse pressure, which produces a myriad of clinical signs. Although the typical diastolic blowing murmur heard along the left sternal border is the usual sign of aortic regurgitation, the peripheral signs of a hyperdynamic circulation often indicate that the disease is severe. A partial list of these signs includes Quincke's pulse (systolic plethora and diastolic blanching in the nail bed when gentle pressure is placed on it), Corrigan's pulse (a bounding, full carotid pulse with a rapid downstroke), Musset's sign (head bobbing), and Hill's sign (systolic blood pressure in the leg at least 30 mm Hg higher than that in the arm).

In addition to the typical murmur of aortic insufficiency, a diastolic rumble (Austin Flint murmur) may also be heard over the cardiac apex. Although

its origin is debatable, the Austin Flint murmur is probably produced as the aortic jet impinges on the mitral valve, causing it to vibrate; also, simultaneous diastolic filling of the left ventricle from the left atrium and aorta tends to close the mitral valve in diastole, producing physiologic stenosis.

Once aortic regurgitation is suspected on physical examination, echocardiography with Doppler examination of the aortic valve can help estimate its severity. Aortography during catheterization helps confirm the severity of the disease.

## Therapy

### Surgical Correction

As with mitral regurgitation, symptoms may not appear until left ventricular dysfunction in aortic insufficiency is well advanced. The symptoms are usually those of left-sided heart failure (dyspnea, orthopnea, and fatigue). Angina may also occur in patients with aortic insufficiency without coronary disease, but less frequently than in patients with aortic stenosis.<sup>13</sup> Although aortic insufficiency should be corrected when more than mild symptoms develop, there is compelling evidence that aortic regurgitation should be corrected before the onset of permanent left ventricular damage, even in asymptomatic patients.<sup>77-81</sup> As noted above, aortic insufficiency increases left ventricular afterload, in part because the high stroke volume produces a wide pulse pressure and systolic hypertension. After aortic-valve replacement, afterload is reduced and ejection fraction improves. Thus, it is not surprising that patients with aortic insufficiency can have a greater decrease in ejection performance and a larger end-systolic dimension than patients with mitral insufficiency, while still having a good postoperative outcome.

In general, the "55 rule" has been useful in gauging the timing of surgery for this disease.<sup>77-81</sup> Aortic-valve surgery should be performed before the ejection fraction falls below 55 percent or the end-systolic dimension exceeds 55 mm. The markers for the timing of surgery in mitral regurgitation and aortic insufficiency are shown in Table 1. Although replacement of the aortic valve with a tissue or mechanical prosthesis has been the definitive therapy

for severe aortic regurgitation, experience with the pulmonary autograft (Ross procedure) and aortic-valve reconstruction is rapidly increasing.<sup>82-85</sup>

### Medical Therapy

Because aortic regurgitation represents a state of excess afterload, it could be anticipated that reduction of afterload with vasodilators would improve left ventricular performance while simultaneously decreasing the amount of aortic regurgitation, thus reducing or delaying the need for surgery. The most compelling evidence supporting this concept is from a study showing that the use of nifedipine in asymptomatic patients with severe aortic regurgitation and normal left ventricular function can delay the need for surgery by two to three years.<sup>86</sup> It is likely that other vasodilators will also be efficacious in safely forestalling surgery.<sup>87</sup>

### Acute Aortic Insufficiency

#### Assessment of Severity and Timing of Surgery

Acute severe aortic insufficiency is usually a surgical emergency. The large regurgitant volume suddenly entering the left ventricle, before adaptation to the volume load has developed, increases left ventricular filling pressure, causing acute pulmonary congestion. Severe regurgitation impairs forward cardiac output, thus reducing organ perfusion. Reduced output, in concert with elevated left ventricular filling pressure, probably reduces coronary blood flow, possibly potentiating myocardial ischemia and further left ventricular deterioration. A fact of diagnostic importance is that the large left ventricular stroke volume present in compensated chronic aortic insufficiency is absent in acute aortic insufficiency, because left ventricular enlargement has not yet occurred. Therefore, many of the signs of severe aortic regurgitation discussed above are absent, and the diagnosis is easy to miss.<sup>88</sup>

Important clues during physical examination include the diastolic blowing murmur of aortic insufficiency and a soft first heart sound. A soft first heart sound occurs because rapid ventricular filling due to aortic insufficiency closes the mitral valve before the onset of systole, and thus S<sub>1</sub> is constituted only by the closure sound of the tricuspid valve. Preclosure of the mitral valve, suspected on physical examination and confirmed by echocardiography, is an ominous development, usually indicating the need for urgent surgery.<sup>89</sup>

Because acute aortic insufficiency is usually caused by infective endocarditis, there is always concern about aortic-valve replacement in the presence of infection. However, in most cases the risk of sudden death from cardiac causes outweighs the relatively small risk (less than 10 percent) of prosthetic-valve infection.<sup>90</sup> Most consider the aortic homograft the

**TABLE 1.** ECHOCARDIOGRAPHIC PREDICTORS OF GOOD OUTCOME IN AORTIC AND MITRAL REGURGITATION.

TYPE OF REGURGITATION	END-DIASTOLIC DIMENSION	EJECTION FRACTION	SHORTENING FRACTION
Aortic	≤55	≥0.55	>0.27
Mitral	≤45	≥0.60	>0.32

valve of choice in this situation. Thus, aortic-valve replacement should be contemplated in any patient with acute aortic insufficiency who has evidence of even mild congestive heart failure or mitral-valve preclosure.

### CORONARY ARTERY DISEASE

The presence of coronary disease in patients with either mitral or aortic valve disease worsens the long-term prognosis.<sup>73,91,92</sup> Although the operative risk may not be increased,<sup>93</sup> the long-term prognosis in combined coronary and valvular heart disease is not as good as that in valvular disease alone, even when coronary bypass surgery is performed at the time of valve replacement. This is presumably a result of the progressive nature of coronary disease. Ischemic mitral regurgitation carries the worst prognosis: operative mortality is 10 to 20 percent, and long-term survival is substantially lower than with nonischemic mitral regurgitation.<sup>94,95</sup>

An unresolved issue is the approach to the aortic valve in patients who have mild-to-moderate aortic stenosis and who are undergoing coronary bypass grafting. Although some centers report that patients who undergo later reoperation because of progression to severe aortic stenosis do not have an increased risk of morbidity and mortality,<sup>96</sup> others suggest a very high mortality rate.<sup>97</sup> Because progression to severe aortic stenosis may occur rapidly,<sup>98</sup> it has been suggested that serious consideration should be given to elective valve replacement at the time of the initial bypass operation.<sup>97</sup>

### SUMMARY

The prognosis for patients with valvular heart disease has improved substantially over the past 15 years. A better understanding of the proper timing of surgery is one of the key reasons. In general, surgery for stenotic valvular disease can be delayed until symptoms appear. Conversely, in regurgitant valvular heart disease, prognostically important left ventricular dysfunction may develop in the absence of symptoms, and thus valve surgery for some asymptomatic patients is entirely appropriate.

It is likely that in the future there will be progress toward increasing conservation of the patient's native valve. This will be beneficial because even modern prosthetic valves have inherent risks.<sup>99</sup> Acquired aortic stenosis will often continue to require prosthetic aortic-valve replacement. However, valvular disease will increasingly be treated by procedures that conserve native valves. These include pulmonary autografts for aortic stenosis, balloon commissurotomy for mitral stenosis, mitral-valve repair for mitral regurgitation, and aortic-valve repair for aortic regurgitation. These procedures will make surgery more attractive by eliminating the risks associated with prostheses. Thus, continuing advances in noninva-

sive assessment of the aortic and mitral valves, appropriate timing of referral for surgery, improved surgical techniques for valve replacement and reconstruction, and very recent advances in less invasive surgical approaches should combine to improve the outlook for patients with valvular heart disease.

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