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Aortic Regurgitation ■ ■ETIOLOGY (Table 273-1) Aortic regurgitation (AR) may be caused by primary valve disease, aortic root disease, or their combination. Primary Valve Disease Rheumatic disease results in thicken ing, deformity, and shortening of the individual aortic valve cusps, changes that prevent their proper opening during systole and closure during diastole. A rheumatic origin is much less common in patients with isolated AR who do not have associated rheumatic mitral valve disease. Patients with congenital bicuspid aortic valve (BAV) disease may develop predominant AR, and ~20% of these patients will require aortic valve surgery between 10 and 40 years of age. Congenital fenes trations of the aortic valve occasionally produce mild AR. Membranous subaortic stenosis results in a high-velocity systolic jet that often leads to thickening and scarring of the aortic valve leaflets and secondary AR. Prolapse of an aortic cusp, resulting in progressive chronic AR, occurs in ~15% of patients with ventricular septal defect (Chap. 280), but may also occur as an isolated phenomenon or as a consequence of myxomatous degeneration sometimes associated with mitral and/or tricuspid valve involvement. AR may result from infective endocarditis (IE), which can develop on a valve previously affected by rheumatic disease, a congenitally deformed valve, or on a normal aortic valve, and may lead to perfora tion or destruction of one or more leaflets. The aortic valve leaflets may become scarred and retracted during the course of syphilis or ankylos ing spondylitis and contribute further to the AR that derives primarily from associated root dilation. Although traumatic rupture or avulsion of an aortic cusp is an uncommon cause of acute AR, it represents the most frequent serious lesion in patients surviving nonpenetrat ing cardiac injuries. The coexistence of hemodynamically significant aortic stenosis (AS) with AR usually excludes all the rarer forms of AR because it occurs almost exclusively in patients with rheumatic or congenital AR. In patients with AR due to primary valvular disease, dilation of the aortic annulus may occur secondarily and lead to wors ening regurgitation. Primary Aortic Root Disease AR also may be due entirely to marked aortic annular dilation, i.e., aortic root disease, without pri mary involvement of the valve leaflets; widening of the aortic annulus and lack of diastolic coaptation of the aortic leaflets are responsible for the AR (Chap. 291). Medial degeneration of the ascending aorta, TABLE 273-1 Major Causes of Aortic Regurgitation VALVE LESION ETIOLOGIES Aortic regurgitation Valvular Congenital (bicuspid) Endocarditis Rheumatic fever Myxomatous (prolapse) Radiation Trauma Syphilis Ankylosing spondylitis Aortic root disease Aortic dissection Medial degeneration Marfan syndrome Bicuspid aortic valve Nonsyndromic familial aneurysm Aortitis Hypertension

which may or may not be associated with other manifestations of Marfan’s syndrome; idiopathic dilation of the aorta; annuloaortic ectasia; osteogenesis imperfecta; and severe, chronic

hypertension may all widen the aortic annulus and lead to progressive AR. Occasionally AR is caused by retrograde dissection of the aorta involving the aortic annulus. Syphilis and ankylosing spondylitis, both of which may also affect the aortic leaflets, may be associated with cellular infiltration and scarring of the media of the thoracic aorta, leading to aortic dilation, aneurysm formation, and severe regurgitation. In syphilis of the aorta (Chap. 187), now a very rare condition, the involvement of the intima may narrow the coronary ostia, which in turn may be responsible for myocardial ischemia. Takayasu's aortitis and giant cell aortitis can also result in aneurysm formation and secondary AR.

CHAPTER 273 Aortic Regurgitation ■ ■PATHOPHYSIOLOGY The total stroke volume ejected by the left ventricle (LV) (i.e., the sum of the effective forward stroke volume and the volume of blood that regurgitates back into the LV) is increased in patients with AR. In patients with severe AR, the volume of regurgitant flow may equal the effective forward stroke volume. In contrast to MR, in which a portion of the LV stroke volume is delivered into the low-pressure left atrium (LA), in AR, the entire LV stroke volume is ejected into a high-pressure zone, the aorta. An increase in the LV end-diastolic volume (increased preload) constitutes the major hemodynamic compensation for AR. The dilation and eccentric hypertrophy of the LV allow this chamber to eject a larger stroke volume without requiring any increase in the relative shortening of each myofibril. Therefore, severe AR may occur with a normal effective forward stroke volume and a normal LV ejec tion fraction (LVEF, total [forward plus regurgitant] stroke volume/ end-diastolic volume), together with an elevated LV end-diastolic pressure and volume. However, through the operation of Laplace's law, LV dilation increases the LV systolic tension required to develop any given level of systolic pressure. Chronic AR is, thus, a state in which LV preload and afterload are both increased. Ultimately, these adaptive measures fail. As LV function deteriorates, the end-diastolic volume rises further and the forward stroke volume and ejection fraction (EF) decline. Deterioration of LV function often precedes the development of symptoms. Considerable thickening of the LV wall also occurs with chronic AR, and at autopsy, the hearts of these patients may be among the largest encountered, sometimes weighing >1000 g. The reverse diastolic pressure gradient from aorta to LV, which drives the AR flow, decreases progressively during diastole, accounting for the typical decrescendo nature of the diastolic murmur. Equilibration between aortic and LV pressures may occur toward the end of diastole in patients with chronic severe AR, particularly when the heart rate is slow. In patients with acute severe AR, the LV is unprepared for the regurgi tant volume load. LV compliance is normal or reduced, and LV diastolic pressures rise rapidly, occasionally to levels >40 mmHg. The LV pressure may exceed the LA pressure toward the end of diastole, and this reversed pressure gradient closes the mitral valve prematurely. In patients with chronic severe AR, the effective forward cardiac output (CO) usually is normal or only slightly reduced at rest, but often it fails to rise normally during exercise. An early sign of LV dysfunction is a reduction in the EF. In advanced stages, there may be considerable elevation of the LA, pulmonary artery (PA) wedge, PA, and right ven tricular (RV) pressures and reduced forward CO at rest. Myocardial ischemia may occur in patients with AR because myo cardial oxygen requirements are elevated by LV dilation, hypertrophy, and elevated LV systolic tension, and coronary blood flow may be compromised. A large fraction (the majority) of coronary blood flow occurs during diastole, when aortic pressure is low, thereby reducing coronary perfusion or driving pressure. This combination of increased oxygen demand and reduced supply may cause myocardial ischemia, particularly of the subendocardium, even in the absence of epicardial coronary artery disease (CAD). ■ ■HISTORY Approximately three-fourths of patients with pure or predominant val vular AR are men; women predominate among patients with primary

valvular AR who have associated rheumatic mitral valve disease. A his tory compatible with IE may sometimes be elicited from patients with rheumatic or congenital involvement of the aortic valve, and the infec tion often precipitates or seriously aggravates preexisting symptoms.

In patients with acute severe AR, as may occur in IE, aortic dissec tion, or trauma, the LV cannot dilate sufficiently to maintain stroke volume, and LV diastolic pressure rises rapidly with associated marked elevations of LA and PA wedge pressures. Pulmonary edema and/or cardiogenic shock may develop rapidly. PART 6 Disorders of the Cardiovascular System Chronic severe AR may have a long latent period, and patients may remain relatively asymptomatic for as long as 10–15 years. Uncomfort able awareness of the heartbeat, especially on lying down, may be an early complaint. Sinus tachycardia, during exertion or with emotion, or premature ventricular contractions may produce particularly uncom fortable palpitations as well as head pounding. These complaints may persist for many years before the development of exertional dyspnea, usually the first symptom of diminished cardiac reserve. The dyspnea is followed by orthopnea, paroxysmal nocturnal dyspnea, and excessive diaphoresis. Anginal chest pain even in the absence of CAD may occur in patients with severe AR, even in younger patients. Anginal pain may develop at rest as well as during exertion. Nocturnal angina may be a particularly troublesome symptom, and it may be accompanied by marked diaphoresis. The anginal episodes can be prolonged and often do not respond satisfactorily to sublingual nitroglycerin. Systemic fluid accumulation, including congestive hepatomegaly and ankle edema, may develop late in the course of the disease. ■ ■PHYSICAL FINDINGS In chronic severe AR, the jarring of the entire body and the bobbing motion of the head with each systole can be appreciated, and the abrupt distention and collapse of the larger arteries are easily visible. The examination should be directed toward the detection of conditions predisposing to AR, such as bicuspid valve, IE, Marfan’s syndrome, or ankylosing spondylitis. Arterial Pulse A rapidly rising “water-hammer” pulse, which col lapses suddenly as arterial pressure falls rapidly during late systole and diastole (Corrigan’s pulse), and capillary pulsations, an alternate flushing and paling of the skin at the root of the nail while pressure is applied to the tip of the nail (Quincke’s pulse), are characteristic of chronic severe AR. A booming “pistol-shot” sound can be heard over the femoral arter ies (Traube’s sign), and a to-and-fro murmur (Duroziez’s sign) is audible if the femoral artery is lightly compressed with a stethoscope. The arterial pulse pressure is widened as a result of both systolic hypertension and a lowering of the diastolic pressure. The measure ment of arterial diastolic pressure with a sphygmomanometer may be complicated by the fact that systolic sounds are frequently heard with the cuff completely deflated. However, the level of cuff pressure at the time of muffling of the Korotkoff sounds (phase IV) generally corre sponds fairly closely to the true intra-arterial diastolic pressure. As the disease progresses and the LV end-diastolic pressure rises, the arterial diastolic pressure may actually rise as well, because the aortic diastolic pressure cannot fall below the LV end-diastolic pressure. For the same reason, acute severe AR may also be accompanied by only a slight wid ening of the pulse pressure. Such patients are invariably tachycardic as the heart rate increases in an attempt to preserve the CO. Palpation In patients with chronic severe AR, the LV impulse is heaving and displaced laterally and inferiorly. The systolic expansion and diastolic retraction of the apex are prominent. A diastolic thrill may be palpable along the left sternal border in thin-chested individu als, and a prominent systolic thrill may be palpable in the suprasternal notch and transmitted upward along the carotid arteries. This systolic thrill and the accompanying murmur do not necessarily signify the coexistence of AS. In some patients with AR or with combined AS and AR, the carotid arterial pulse may be bisferiens, i.e., with two systolic waves separated by a trough (see Fig. 246-2C). Auscultation In patients with

severe AR, the aortic valve closure sound (A2) is usually absent. A systolic ejection sound is audible in

patients with BAV disease, and occasionally an S4 also may be heard. The murmur of chronic AR is typically a high-pitched, blowing, decre scendo diastolic murmur, heard best in the third intercostal space along the left sternal border (see Fig. 246-5B). In patients with mild AR, this murmur is brief, but as the severity increases, it generally becomes louder and longer, indeed holodiastolic. When the murmur is soft, it can be heard best with the diaphragm of the stethoscope and with the patient sitting up, leaning forward, and with the breath held in forced expiration. In patients in whom the AR is caused by primary valvular disease, the diastolic murmur is usually louder along the left than the right sternal border. However, when the murmur is louder along the right sternal border, it suggests that the AR is caused by aneurysmal dilation of the aortic root. “Cooing” or musical diastolic murmurs suggest eversion of an aortic cusp vibrating in the regurgitant stream. A mid-systolic ejection murmur is frequently audible in isolated AR. It is generally heard best at the base of the heart and is transmitted along the carotid arteries. This murmur may be quite loud without sig nifying aortic valve obstruction. A third murmur sometimes heard in patients with severe AR is the Austin Flint murmur, a soft, low-pitched, rumbling mid-to-late diastolic murmur. It is probably produced by the diastolic displacement of the anterior leaflet of the mitral valve by the AR stream and is not associated with hemodynamically significant mitral valve obstruction. The auscultatory features of AR are intensi fied by strenuous and sustained handgrip, which augments systemic vascular resistance and increases LV afterload. In acute severe AR, the elevation of LV end-diastolic pressure may lead to early closure of the mitral valve, a soft S1, a pulse pressure that is not particularly wide, and a soft, short, early diastolic murmur of AR. ■ ■LABORATORY EXAMINATION ECG In patients with chronic severe AR, ECG signs of LV hyper trophy are common (Chap. 247). In addition, these patients frequently exhibit ST-segment depression and T-wave inversion in leads I, aVL, V5, and V6 (“LV strain”). Left axis deviation and/or QRS prolongation may also be present. Echocardiogram (Fig. 273-1) LV size is increased in chronic AR, and systolic function is normal or even supernormal until myocar dial contractility declines, as signaled by a decrease in EF or increase in the end-systolic dimension. A rapid, high-frequency diastolic fluttering of the anterior mitral leaflet produced by the impact of the regurgi tant jet is a characteristic finding. The echocardiogram is also useful in determining the cause of AR, by detecting dilation of the aortic annulus and root, aortic dissection or primary leaflet pathology. With severe AR, the central jet width assessed by color flow Doppler imag ing exceeds 65% of the width of the LV outflow tract, the regurgitant volume is ≥60 mL/beat, the regurgitant fraction is ≥50%, and there is diastolic flow reversal in the proximal portion of the descending tho racic aorta. The continuous-wave Doppler profile of the AR jet shows a rapid deceleration time in patients with acute severe AR, due to the rapid increase in LV diastolic pressure. Surveillance transthoracic echocardiography (TTE) forms the cornerstone of longitudinal followup and allows for the early detection of changes in LV size and/or function. Assessment of LV global longitudinal strain (GLS; a measure of myocardial thickening in systole) with speckle track imaging may demonstrate changes in LV systolic function that precede a fall in EF. There is increasing experience with the use of three-dimensional echo cardiography to measure LV volumes. Transesophageal echocardiogra phy (TEE) can provide detailed anatomic assessment of the valve, root, and portions of the aorta. For patients in whom TTE is limited by poor acoustical windows or inadequate characterization of LV function or the cause or severity of the regurgitation, cardiac magnetic resonance (CMR) imaging can be performed. This modality also allows for accu rate assessment of LV volumes, as well as aortic size

and contour. It can also be utilized to screen for increased LV interstitial (extracellular volume fraction) and replacement fibrosis (late gadolinium enhance ment). Both CMR imaging and cardiac computed tomography (CT) can also provide detailed assessment of aortic valve, root, and thoracic aortic anatomy.

A B FIGURE 273-1 Echocardiographic and Doppler depiction of severe aortic regurgitation. (A) Color flow transesophageal echocardiographic long axis image in diastole shows a broad jet of severe aortic regurgitation (AR, yellow arrow) directed into the left ventricle. ECG rhythm strip below. Ao, aorta; BPM, beats per minute; HR, heart rate; LV, left ventricle. (B) Continuous wave Doppler tracing (middle image) obtained from the suprasternal window (top image) during transthoracic echocardiography shows dense, holodiastolic flow reversal in the descending thoracic aorta (yellow arrow) indicative of severe AR. ECG rhythm strip below. Chest X-Ray In chronic severe AR, the apex is displaced down ward and to the left in the frontal projection. In the left anterior oblique and lateral projections, the LV is displaced posteriorly and encroaches on the spine. When AR is caused by primary disease of the aortic root, aneurysmal dilation of the aorta may be noted, and the aorta may fill the retrosternal space in the lateral view. Echocar diography, CMR imaging, and chest CT angiography are more sensi tive than a chest x-ray for the detection of root and ascending aortic enlargement. Cardiac Catheterization and Angiography When needed, right and left heart catheterization with contrast aortography can pro vide confirmation of the magnitude of regurgitation and the status of LV function. Coronary angiography is performed routinely in patients at risk of coronary artery disease prior to surgery, although this ana tomic information can also be obtained in many patients with coronary CT angiography. TREATMENT Aortic Regurgitation ACUTE AORTIC REGURGITATION (FIG. 273-2) Patients with acute severe AR may respond to intravenous diuretics and vasodilators (such as sodium nitroprusside), but stabilization is usually short-lived and operation is indicated urgently. Intra-aortic balloon counterpulsation is contraindicated. Beta blockers are best avoided so as not to reduce the CO further or slow the heart rate, thus allowing more time for diastolic filling of the LV. Surgery is the treatment of choice and is usually necessary within 24 h of diagnosis. CHRONIC AORTIC REGURGITATION The onset of symptoms, or LV systolic dysfunction, is an indica tion for surgery. Medical treatment with diuretics and vasodilators (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers [ARBs], dihydropyridine calcium channel blockers, or hydralazine) may be useful as a temporizing measure. Surgery

CHAPTER 273 Aortic Regurgitation can then be performed in a more controlled setting. The use of vasodilators to extend the compensated phase of chronic severe AR in asymptomatic patients before the onset of symptoms or the development of LV dysfunction is not useful, although these agents should be employed to treat hypertension (systolic blood pressure

> 140 mmHg). It is often difficult to achieve adequate blood pres sure control because of the increased stroke volume and enhanced LV ejection that accompany severe AR. Cardiac arrhythmias and systemic infections are poorly tolerated in patients with severe AR and must be treated promptly and vigorously. Although nitroglyc erin and long-acting nitrates are not as helpful in relieving anginal pain as they are in patients with coronary heart disease, they

> are worth a trial. Patients with syphilitic aortitis should receive a full course of penicillin therapy (Chap. 187). Beta blockers and the ARB losartan may be useful to retard the rate of aortic root enlarge ment in young patients with Marfan's syndrome and aortic root dilation. A randomized controlled trial showed no difference in efficacy between atenolol and losartan for this indication. Whether beta blockers or ARBs are useful in retarding the rate of growth of aortic aneurysms in other patient subsets (e.g., BAV disease with aortopathy, Takayasu's disease) has not been demonstrated. Beta blockers in patients with valvular AR were previously considered relatively contraindicated due to concern that slowing of the heart rate would allow more time for diastolic regurgitation and LV filling. Observational reports, however, have suggested that beta blockers may provide functional benefit in some patients with chronic AR. Beta blockers can sometimes provide incremental blood pressure lowering in patients with chronic AR and hypertension. They can also lessen the sense of forceful heart action that many patients find uncomfortable. Patients with severe AR, particularly those with an associated aortopathy, should avoid isometric exercises. SURGICAL TREATMENT In deciding on the advisability and proper timing of surgical treat ment, two points should be kept in mind: (1) patients with chronic severe AR usually do not become symptomatic until after the devel opment of myocardial dysfunction; and (2) when delayed too long

PART 6 Disorders of the Cardiovascular System Severe AR (VC >0.6 cm, holodiastolic aortic flow reversal, RVol ≥60 mL, RF ≥50%, ERO ≥0.3 cm2) Symptomatic (Stage D) Asymptomatic (Stage C) Other cardiac surgery EF ≤55% (Stage C2) EF ≥55% LVESD >50 mm and LVESD >25 mm/m2 AVR (1) AVR (2a) AVR (2a) AVR (2b) FIGURE 273-2 Management of patients with aortic regurgitation. See legend for Fig. 272-4 for explanation of treatment recommendations (Class I, IIa, and IIb) and disease stages (B, C1, C2, and D). Preoperative coronary angiography should be performed routinely as determined by age, symptoms, and coronary risk factors. Cardiac catheterization and angiography may also be helpful when there is a discrepancy between clinical and noninvasive findings. Surgery is indicated for patients with severe AR and symptoms, LV dysfunction, or other indications for operation (e.g., aneurysm disease). Surgery is also reasonable once the LV indexed end-systolic dimension reaches or exceeds 25 mm/m2. Patients who do not meet criteria for intervention should be monitored periodically with clinical and echocardiographic follow-up. AR, aortic regurgitation; AVR, aortic valve replacement (valve repair may be appropriate in selected patients); EDD, end-diastolic dimension; EF, ejection fraction; ERO, effective regurgitant orifice; LV, left ventricular; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; RF, regurgitant fraction; RVol, regurgitant volume; VC, vena contracta. (Reproduced with permission from CM Otto et al: 2020 AHA/ACC Guideline for management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2021;143(5):e72.) (defined as >1 year from onset of symptoms or LV dysfunction), surgical treatment often does not restore normal LV size and func tion. Therefore, in patients with chronic severe AR, careful clinical follow-up and noninvasive testing with echocardiography at ~6- to 12-month intervals are necessary if operation is to be undertaken at the optimal time, i.e., coincident

with or after the onset of LV dysfunction but prior to the development of symptoms. Exercise testing may be helpful to assess effort tolerance more objectively and should be employed whenever questions about symptoms arise. Operation can be deferred as long as the patient both remains asymptomatic and retains normal LV function without severe or progressive chamber dilation. Aortic valve replacement (AVR) is indicated for the treatment of severe AR in symptomatic patients irrespective of LV function. In general, the operation should be carried out in asymptomatic patients with severe AR and progressive LV dysfunction defined by an LVEF <55% on serial studies, an LV end-systolic dimension

> 50 mm (>25 mm/m2), or an LV diastolic dimension >65 mm. Smaller dimensions may be appropriate thresholds in individuals of smaller stature or when there is evidence of progressively decreasing LV function or increasing LV size on serial studies and the anticipated risks for surgical morbidity and mortality are low. Two case series

Aortic regurgitation Moderate AR Other cardiac surgery Progressive changes (≥3 studies) EF 55–60% EDD >65 mm Low surgical risk from surgical referral centers have suggested that surgery should be performed at an even lower threshold for LV end-systolic dimension index (≥20 mm/m2), but data from randomized con trolled trials are lacking. Abnormal LV GLS (≥ –18%) has been associated with an excess hazard for death in single-center studies. Observational studies using either three-dimensional echocar diography or CMR imaging have also suggested that event-free survival is reduced in asymptomatic patients with an LV endsystolic volume index ≥45 mL/m2, compared with patients with an LV end-systolic volume index <45 mL/m2. Patients with severe AR without indications for operation should be followed by clinical and echocardiographic examination every 6–12 months. Trans catheter aortic valve implantation (TAVI) is not recommended for patients with severe AR who are surgical candidates. Technical success with TAVI in patients with chronic AR is limited by the degree of aortic annular dilation and the relative paucity of valvu lar and annular calcium. Surgical options for management of aortic valve and root disease have expanded considerably over the past decade. AVR with a suit able mechanical or tissue (biological) prosthesis is generally necessary in patients with rheumatic AR and in many patients with other causes of valvular AR. Rarely, when a leaflet has been perforated during IE

B A D FIGURE 273-3 Valve-sparing aortic root reconstruction (David procedure). Aortic root and proximal ascending aorta (A) are resected (B) with sinuses of Valsalva and mobilized coronary artery buttons remaining. Subannular sutures (C) are placed, commissural posts are drawn up inside the valve, and the annular sutures are passed through the proximal end of the graft. The annular sutures are tied (D), the valve is reimplanted inside the graft, aortic continuity is reestablished with another graft of appropriate size, and the coronary buttons are attached to the side of the graft. (From P Steltzer et al [eds]: Valvular Heart Disease: A Companion to Braunwald’s Heart Disease, 3rd ed, Fig. 12-27, p. 200.) or torn from its attachments to the aortic annulus by thoracic trauma, primary surgical repair may be possible. When AR is due to aneurys mal dilation of the root or proximal ascending aorta rather than to primary valve involvement, it may be possible to reduce or eliminate the regurgitation by narrowing the annulus or by excising a portion of the aortic root without replacing the valve. Elective, valve-sparing aortic root reconstruction

generally involves reimplantation of the valve in a contoured graft with reattachment of the coronary artery buttons into the side of the graft and is best undertaken in specialized surgical centers by experienced operators (Fig. 273-3). Resuspension of the native aortic valve leaflets is possible in ~50% of patients with acute AR in the setting of type A aortic dissection. In other condi tions, however, AR can be effectively eliminated only by replacing the aortic valve, as well as the dilated or aneurysmal ascending aorta responsible for the regurgitation, often using a composite prosthetic valve-graft conduit. Pure AR is not by itself a contraindication to the Ross procedure, although the presence of aortic annular dilation and/ or an associated aortopathy would eliminate this option. As is true in patients with other valvular heart disease, both operative and late mortality risks are largely dependent on the stage of the disease and myocardial function at the time of operation. The overall operative mortality rate for isolated AVR performed for pure AR is ~1–2%. The mortality risk doubles when aortic surgery is added to the operation. Patients with AR, marked cardiac enlarge ment, and established LV dysfunction experience an operative mortality rate of ~5–10% and a late mortality rate of ~3–5% per

 C year due to LV failure despite a technically satisfactory operation. Nonetheless, because of the very poor prognosis with medical management, even patients with advanced LV systolic dysfunction should be considered for operation. Patients with acute severe AR require prompt (24–48 h) surgical treatment, which may be lifesaving. ■ ■FURTHER READING Hashimoto G et al: Association of left ventricular remodeling assess ment by cardiac magnetic resonance with outcomes in patients with chronic aortic regurgitation. JAMA Cardiol 7:924, 2022. Lacro RV et al: Atenolol versus losartan in children and young adults with Marfan’s syndrome. N Engl J Med 371:2061, 2014. Malaisrie SC, McCarthy PM: Surgical approach to disease of the aortic valve and the aortic root, in Valvular Heart Disease: A Compan ion to Braunwald’s Heart Disease, 5th ed. CM Otto, RO Bonow (eds). Philadelphia, Elsevier Saunders, 2020, pp 267–288. Otto CM et al: 2020 ACC/AHA guideline for the management of patients with valvular heart disease: A report of the American Col lege of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 143:e72, 2021. Yang L-T et al: Association of echocardiographic left ventricular endsystolic volume and volume-derived ejection fraction with outcome in asymptomatic chronic aortic regurgitation. JAMA Cardiol 6:189, 2021.

Revision #1
Created 2026-01-06 16:33:52 UTC by Omar Ayman
Updated 2026-01-06 16:33:52 UTC by Omar Ayman