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STATE-OF-THE-ART PAPER

Valvular Aortic Stenosis
Disease Severity and Timing of Intervention

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Standard echocardiographic evaluation of aortic stenosis (AS) severity includes measurement of aortic velocity, mean transaortic pressure gradient, and continuity equation valve area. Although these measures are adequate for decision making in most patients, there is no single value that defines severe stenosis. Aortic stenosis affects not just the valve, but the entire vascular system, including the left ventricle (LV) and systemic vasculature. More sophisticated measures of disease severity might explain the apparent overlap in hemodynamic severity between symptomatic and asymptomatic patients and might better predict the optimal timing of valve replacement. There have been several approaches to evaluation of stenosis severity based on valve hemodynamics, the ventricular response to increased afterload, ventricular-vascular coupling, or the systemic functional consequences of valve obstruction, such as exercise testing and serum brain natriuretic peptide levels. Aortic valve replacement is indicated when symptoms due to severe AS are present. In most asymptomatic patients, the risk of surgery is greater than the risk of watchful waiting so that management includes patient education, periodic echocardiography, and cardiac risk factor modification. Many adults with AS have comorbid conditions that affect both the diagnosis and management of the valve disease, including aortic regurgitation, aortic root dilation, hypertension, coronary artery disease, LV dysfunction, and atrial fibrillation. Comorbid conditions should be evaluated and treated based on established guidelines, although awareness of the potential effects of therapy in the presence of valve obstruction is needed. (J Am Coll Cardiol 2006; 47:2141–51) © 2006 by the American College of Cardiology Foundation

Aortic stenosis (AS) most often is due to calcification of a congenitally bicuspid or normal trileaflet valve. Calcific changes are due to an active disease process characterized by lipid accumulation, inflammation, and calcification (1). Once initiated, progressive leaflet calcification and fibrosis eventually result in reduced leaflet motion with obstruction to left ventricular (LV) outflow (2–4). Aortic stenosis often is first diagnosed by the finding of a murmur on auscultation. However, while a soft murmur with a physiologic split S2 reliably excludes severe stenosis and a grade 4 murmur with diminished carotid upstrokes confirms severe obstruction, between these extremes physical examination is not accurate for evaluation of disease severity.

EVALUATION OF DISEASE SEVERITY

Standard approach. Echocardiography is the clinical standard for evaluation of adults with suspected or known valvular AS. Anatomic images show the etiology of AS, level of obstruction, valve calcification, leaflet motion, and aortic root anatomy. The LV response to chronic pressure overload, and other hemodynamic consequences of AS, also can be evaluated. Basic hemodynamic parameters include maximum aortic velocity, mean transvalvular gradient, and continuity equation valve area. All of these measures have been well validated compared with invasive data and, more importantly, as predictors of clinical outcome.

Of these measures, aortic velocity is the most reproducible and is the strongest predictor of clinical outcome. Aortic velocity allows classification of stenosis as mild (2.6 to 3.0 m/s), moderate (3 to 4 m/s), or severe (>4 m/s). Leaflet thickening and calcification with adequate leaflet motion and a velocity ≤2.5 m/s is called aortic sclerosis. Maximum transaortic pressure gradient (ΔP) is calculated from velocity (V) based on the simplified Bernoulli equation:

$$\Delta P_{max} = 4V_{max}^2$$

Mean gradient is determined by tracing the continuous-wave Doppler curve to average the instantaneous gradients over the ejection period.

Aortic valve area (AVA) is calculated based on the principle that volume flow proximal to the valve equals volume flow through the narrowed orifice (Fig. 1). Volume flow is calculated as the cross-sectional area (CSA) of flow times the velocity-time integral (VTI) of flow at that site. In the left ventricular outflow tract (LVOT), flow just proximal to the stenotic valve is relatively laminar with a flat velocity profile. Thus:

Abbreviations and Acronyms

AR	=	aortic regurgitation
AS	=	aortic stenosis
AVA	=	aortic valve area
AVR	=	aortic valve replacement
CSA	=	cross-sectional area
LV	=	left ventricle/ventricular
LVOT	=	left ventricular outflow tract
VTI	=	velocity-time integral
Z_{va}	=	valvulo-ventricular impedance
ΔP	=	pressure gradient

$$AVA \times VTI_{AS} = CSA_{LVOT} \times VTI_{LVOT}$$

or

$$AVA = (CSA_{LVOT} \times VTI_{LVOT}) / VTI_{AS}$$

In clinical practice, maximum velocities often are substituted for VTIs, in the simplified continuity equation:

$$AVA = (CSA_{LVOT} \times V_{LVOT}) / V_{AS}$$

A further simplification of the continuity equation is the dimensionless ratio of outflow tract to aortic velocity:

$$Velocity\ ratio = (V_{LVOT})/V_{AS}$$

This ratio reflects the relative valve size compared with the area of the patient's outflow track (i.e., is effectively indexed for body size) and is particularly useful when images of outflow tract diameter are suboptimal. This ratio approaches 1 with a normal valve. A ratio <0.25 indicates a valve area 25% of expected, corresponding to severe stenosis. The accuracy of all these Doppler measures of stenosis severity is highly dependent on meticulous attention to technical details and a comprehensive examination by an experienced echocardiographer.

Why measure stenosis severity? The clinical utility of measuring stenosis severity is two-fold: to reliably predict the optimal timing of valve replacement and to ensure that valve disease is the cause of the patient's symptoms. Despite our reliance on conventional measures of hemodynamic
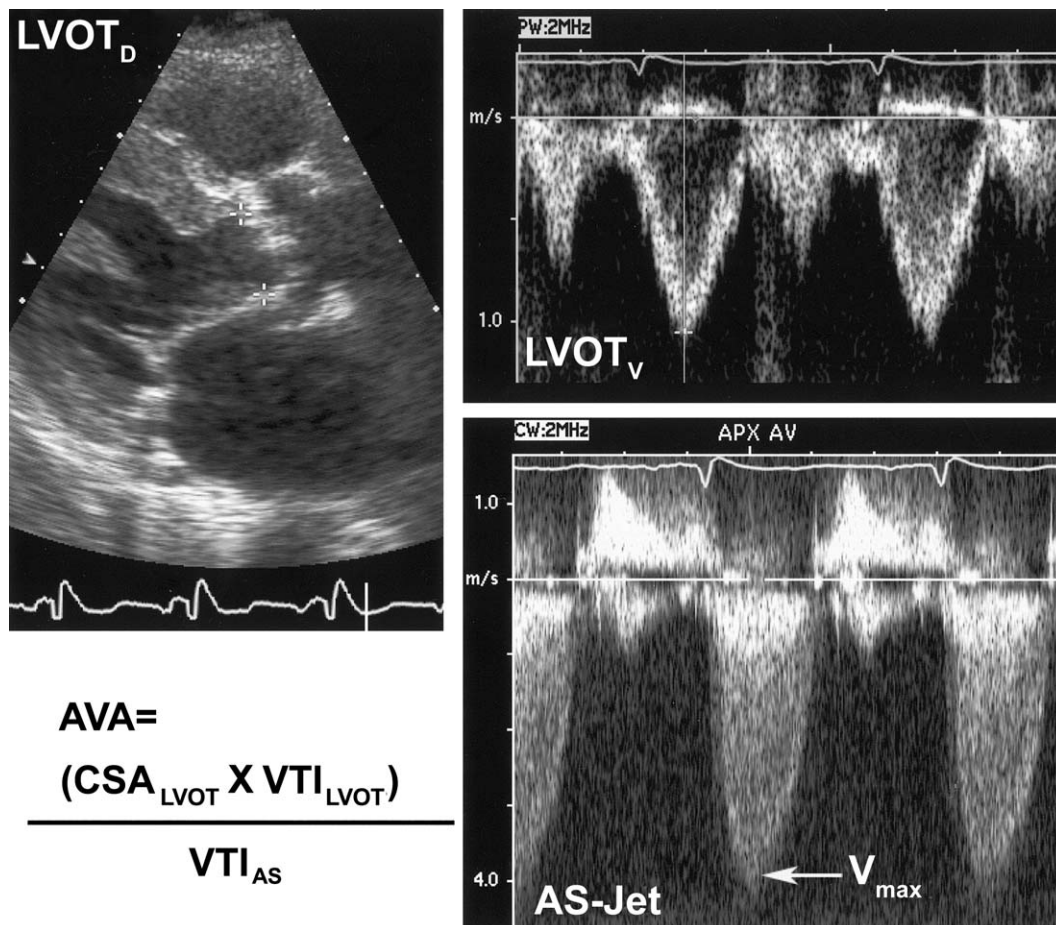

Figure 1. Standard evaluation of aortic stenosis (AS) severity is based on measurement of left ventricular outflow tract (LVOT) diameter (D) in a parasternal long-axis view for calculation of a circular cross-sectional area (CSA), outflow tract velocity (V) from an apical approach using pulsed Doppler, and the maximum aortic jet (AS-Jet, V_{max}) from the continuous-wave Doppler recording. Either velocity-time integrals (VTIs) or maximum velocities can be used in the continuity equation for aortic valve area (AVA).

severity for clinical decision making, it is clear that there is no single value for velocity, gradient, or valve area that defines symptom onset in an individual patient. In prospective studies, there is a marked overlap in measures of hemodynamic severity between asymptomatic and symptomatic patients (2,3,5). This overlap persists using valve area (which corrects for cardiac output) and using indexed valve area (corrected for body size). This apparent paradox suggests that current measures of severity are too simplistic and do not take into account the interaction between the valve, LV, and peripheral vasculature. There are three basic approaches to defining an ideal measure of stenosis severity that would reliably predict symptom onset and clinical outcome: evaluation of the valve, the ventricle, or the ventricular-vascular coupling.

Stenosis severity defined by valve hemodynamics. Even when velocities and calculated ΔPs are measured correctly, this data may not accurately classify disease severity. Velocity reflects the conversion of potential (or pressure) energy into kinetic energy as the high-velocity jet passes through the narrowed orifice. Downstream from the orifice, the flow stream expands and decelerates with a corresponding decrease in kinetic and increase in potential energy, a phenomenon called "pressure recovery" (6,7). Thus, the net ΔP between the LV and the mid-ascending aorta is lower than the pressure drop immediately adjacent to the valve. Doppler measures velocity at the narrowest orifice, thus Doppler ΔPs are higher than the net ΔP (Fig. 2). The clinical impact of pressure recovery usually is small but can

be significant with mild stenosis and a small aortic root (8) or with a doming congenitally stenotic valve (9).

Approaches to more accurate measurement of overall ventricular workload include correction of ΔP based on aortic valve and root areas, calculation of stroke work loss, or measurement of the energy loss index (10,11). Stroke work loss—the ratio of the mean transaortic ΔP to mean LV pressure—is a strong predictor of clinical outcome (11). The energy loss index (ELI) is calculated from AVA and the area of the aorta at the level of the sinotubular junction (A_a) as (12):

$$ELI = [(AVA \times A_a)/(A_a - AVA)]/BSA$$

Both stroke work loss and the energy loss index avoid errors due to pressure recovery, but these ratios only reflect the steady component of potential energy loss and do not account for kinetic energy, pulsatile flow, or downstream vascular compliance.

Although valve area seems like the most straightforward way to evaluate disease severity, the actual extent of leaflet opening is an elusive measurement in patients with calcific AS where the primary process is increased leaflet stiffness without commisural fusion (13). Early in the disease process, the valve leaflets are flexible so that AVA increases as the force of ventricular contraction increases, resulting in an increase in stroke volume with only a modest increase in velocity. With disease progression, the stiff leaflets become
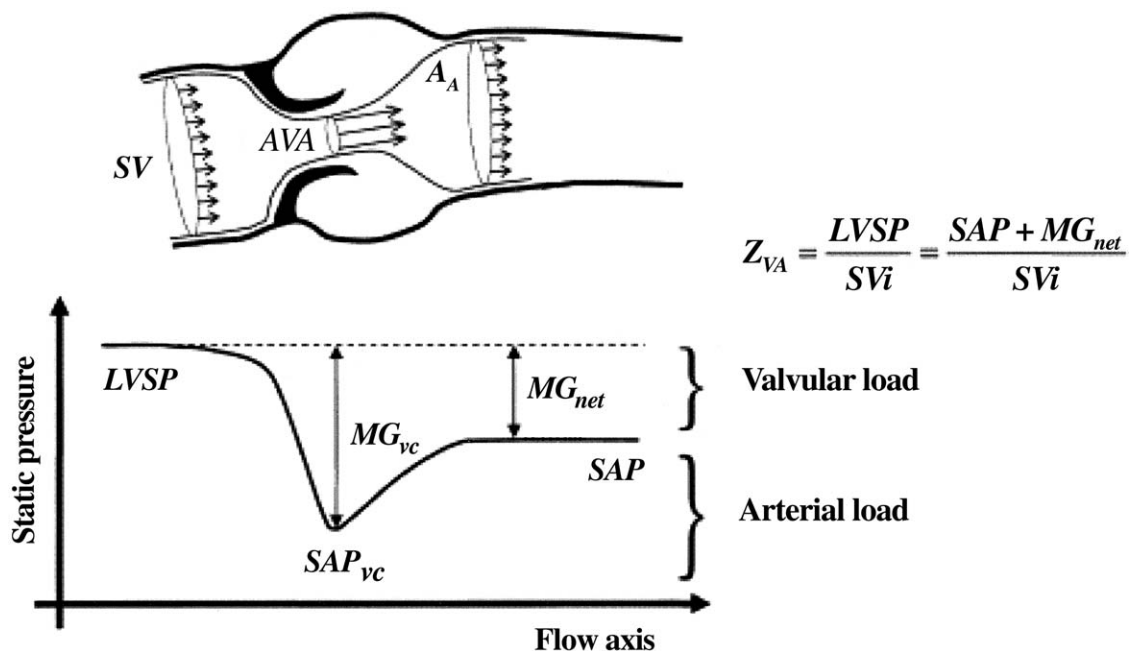

$$Z_{VA} = \frac{LVSP}{SVi} = \frac{SAP + MG_{net}}{SVi}$$

Figure 2. Schematic representation of the flow and static pressure across the left ventricular (LV) outflow tract, aortic valve, and ascending aorta during systole. A_A = aortic cross-sectional area; AVA = effective aortic valve area (i.e., the cross-sectional area of the vena contracta); LVSP = left ventricular systolic pressure; MG_{net} = transvalvular pressure gradient after pressure recovery (i.e., net MG); MG_{vc} = transvalvular pressure gradient at the vena contracta; SAP = systolic aortic pressure; SAP_{vc} = systolic aortic pressure at the vena contracta; SV = stroke volume; SVi = stroke volume index; Z_{VA} = valvulo-arterial impedance. From Briand et al. (12), with permission.

fixed so that valve area fails to increase, despite an increase in volume flow across the valve.

However, measurement of the dynamic change in AVA is challenging because it requires precise measurements at two flow rates, and the observed changes are close to the limits of measurement variability. Valve flexibility also can be estimated from the variability in valve opening during a single systolic ejection period (14). Again, although conceptually sound, clinical utility is problematic due to measurement variability. More sophisticated approaches to evaluation of instantaneous AVA, flow rate, and ΔP have provided insight into the dynamics of calcific valve disease but are not clinically applicable (Fig. 3) (15). Compared with valve area, there is no clear advantage to the concept of valve resistance, and there are some concerns with the assumptions underlying this calculation (15).

Direct imaging of valve area is helpful only in an occasional individual because reverberations and shadowing due to valve calcification limit accuracy. Even with optimal images, effective orifice area is not identical to anatomic orifice area, due to contraction of the flow stream as it passes through the orifice, particularly when the three-dimensional valve shape is flat, as seen with calcific valve disease (9).

LV response to chronic pressure overload. The second approach to defining stenosis severity focuses on the effects of outflow obstruction on the LV. This approach is based on the recognition that LV dysfunction is the main adverse consequence of AS, with initial symptoms often due to diastolic dysfunction. Earlier detection of myocardial diastolic or systolic dysfunction might identify the optimal timing of valve replacement (16).

Total LV load is complex and includes the effects of wall stress, ventricular geometry, and mitral valve competency in addition to the degree of outflow obstruction. Mid-wall meridional wall stress is the most appropriate measure of ventricular afterload. However, calculation requires echocardiographic epicardial and endocardial border tracing along with noninvasive calculation of LV systolic pressure as the sum of transvalvular ΔP and systemic blood pressure (17). Thus, if wall stress is determined, it typically is calculated only at end-systole, rather than instantaneously over the cardiac cycle. There is little recent outcome data on wall stress as a predictor of clinical outcome. However, the concept of ventricular load as the optimal measure of disease remains theoretically appealing. Perhaps if newer imaging techniques allow accurate noninvasive phasic measurement of ventricular load, the utility of this parameter in predicting clinical outcome can be studied further.

Ventricular-vascular coupling. The third approach to evaluation of stenosis severity is to develop an index that includes the degree of valve obstruction, ventricular response, and systemic vasculature impedance. This approach is a variant of the ventricular-vascular coupling concept with the stenotic valve added to the system. This unified ap-
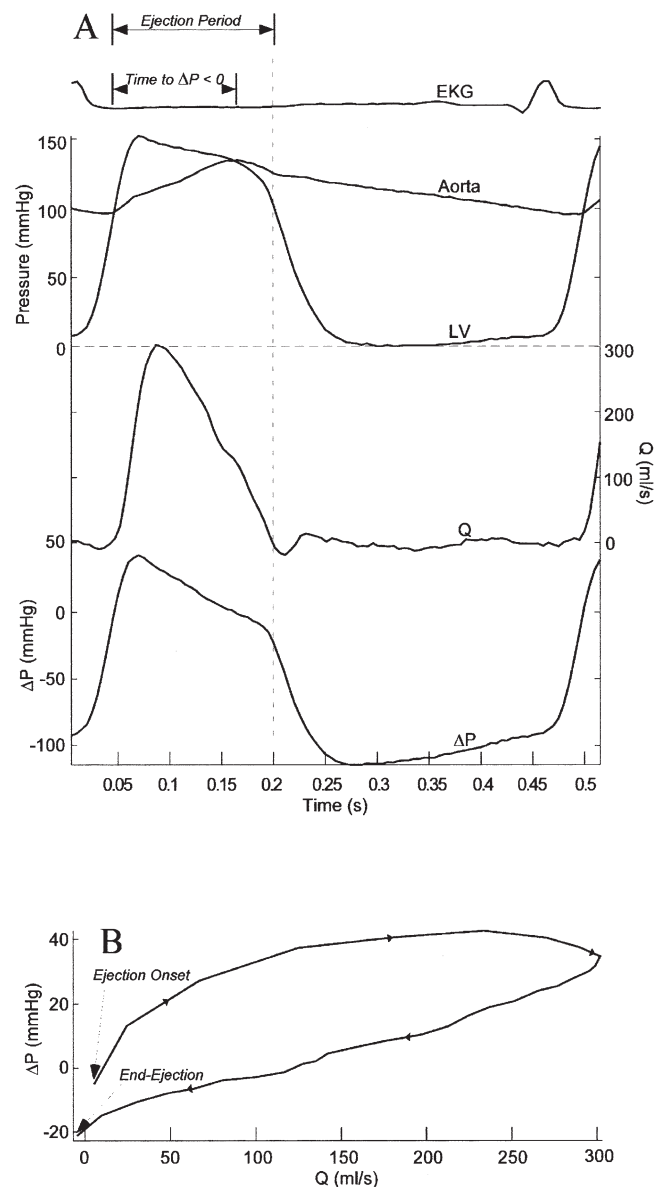

Figure 3. Hemodynamic data in a model of aortic stenosis were obtained using a dual micromanometer catheter and a transit time flow probe. **(A)** The simultaneous instantaneous electrocardiogram, aortic and left ventricular (LV) pressures, transaortic volume flow (Q), and aortic pressure gradient (ΔP) are shown. During late ejection P is negative. **(B)** The phase diagram of ΔP-Q for this cardiac cycle demonstrates the nonlinearity and time dependence of the ΔP-Q relationship. EKG = electrocardiogram. From Bermejo et al. (15), with permission.

proach has the potential advantage that it should apply to patients with concurrent conditions that affect the ventricle or vasculature. In clinical practice, few patients have "isolated AS"; most have some degree of aortic regurgitation (AR) and many have hypertension and/or coronary artery disease. Challenges in applying the ventricular vascular coupling concept to AS are that complete analysis requires recording high-fidelity instantaneous pressure and flow data with complex frequency analysis of the data (18). In addition, previous models of ventricular vascular coupling were initially developed to be applied in patients with systemic

hypertension. These models, therefore, assumed that the contribution of the aortic valve was negligible.

The research group in Quebec (12,19) has proposed a modified ventricular-vascular coupling approach based on "valvulo-arterial impedance" (Z_{va}), which incorporates the degree of valve stenosis and the systemic arterial compliance (Fig. 2). This calculation is based on the net mean gradient (ΔP_{net}), the systolic arterial pressure (SAP), and the indexed stroke volume (SVi) as:

$$Z_{va} = (SAP + \Delta P_{net})/SVi$$

The ΔP_{net} takes into account post-stenotic pressure recovery, based on measurement of the aortic CSA at the sinotubular junction (AoA):

$$\Delta P_{net} = \text{Doppler } \Delta P_{mean} - \{4v^2 \times [2(AVA/AoA) \times (1 - AVA/AoA)]\}$$

In a series of 208 adults with AS, Z_{va} was the strongest predictor of LV dysfunction, even when the energy loss index and systemic arterial compliance were included in the analysis (12). A $Z_{va} \geq 5.0$ mm Hg/ml/m^2 is suggested as indicating excessive total ventricular load. Further studies are needed to determine if this approach reliably predicts clinical outcome.

Other diagnostic modalities. Cardiac catheterization now is rarely used for evaluation of AS and is reserved for cases where echocardiographic data are nondiagnostic (<1% of cases in experienced centers) or when clinical and echocardiographic data are discrepant. When catheterization is performed, care is needed to obtain an accurate transaortic ΔP and volume flow rate.

Newer imaging approaches, including multi-slice computed tomography and cardiac magnetic resonance imaging can provide anatomic and hemodynamic evaluation of stenotic valves. These approaches are not yet widely available, and the role of these approaches for evaluation of AS is unclear.

TIMING OF VALVE SURGERY

Symptomatic patients. Aortic valve replacement is indicated for severe symptomatic AS (20,21). The classical symptoms of AS are angina, syncope, and heart failure. However, most prospectively followed patients present with more subtle symptoms, typically decreased exercise tolerance, or dyspnea on exertion (2). It is not uncommon for patients to decrease their activity level below their symptom threshold—a careful history comparing current and last year's activity levels is needed to recognize that these patients, in fact, are symptomatic. The risk of sudden death is high once any symptom is present, so that valve surgery is appropriate with even mild symptoms (Fig. 4) (21,22–26).

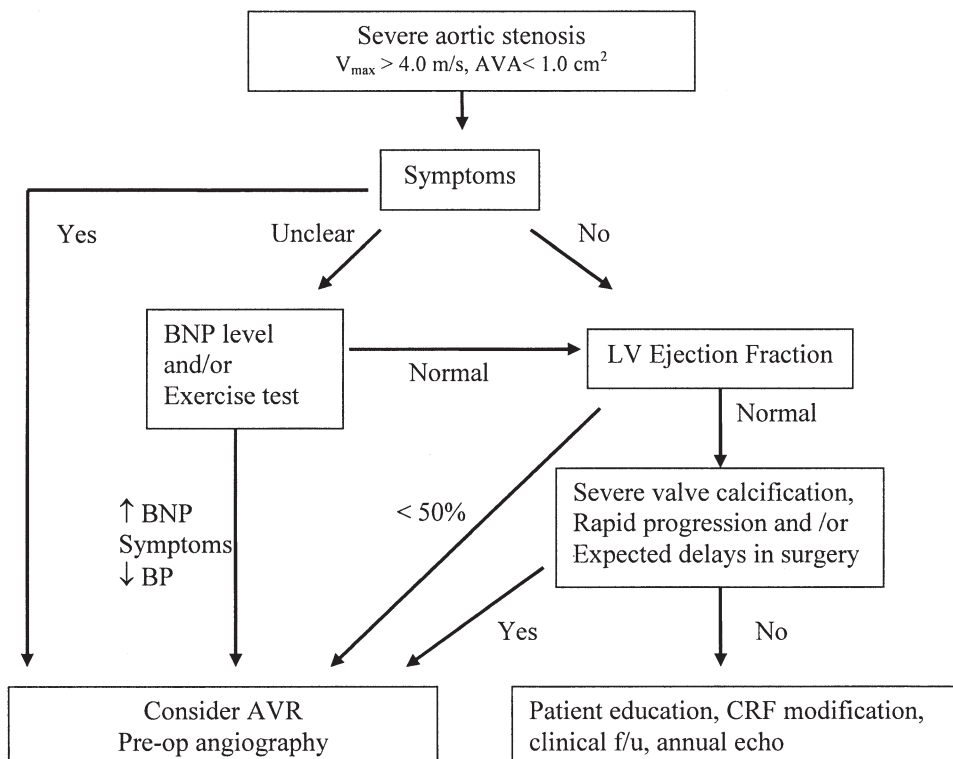When symptoms are present, valve area is <1 cm^2, and Doppler velocity is >4 m/s, the decision to proceed with

Figure 4. Suggested approach to evaluation of adults with severe aortic stenosis. Additional considerations include comorbidities and patient preferences. AVA = aortic valve area; AVR = aortic valve replacement; BNP = brain natriuretic peptide; BP = blood pressure; CRF = cardiac risk factors; f/u = follow-up; LV = left ventricular; V$_{max}$ = maximum velocity.
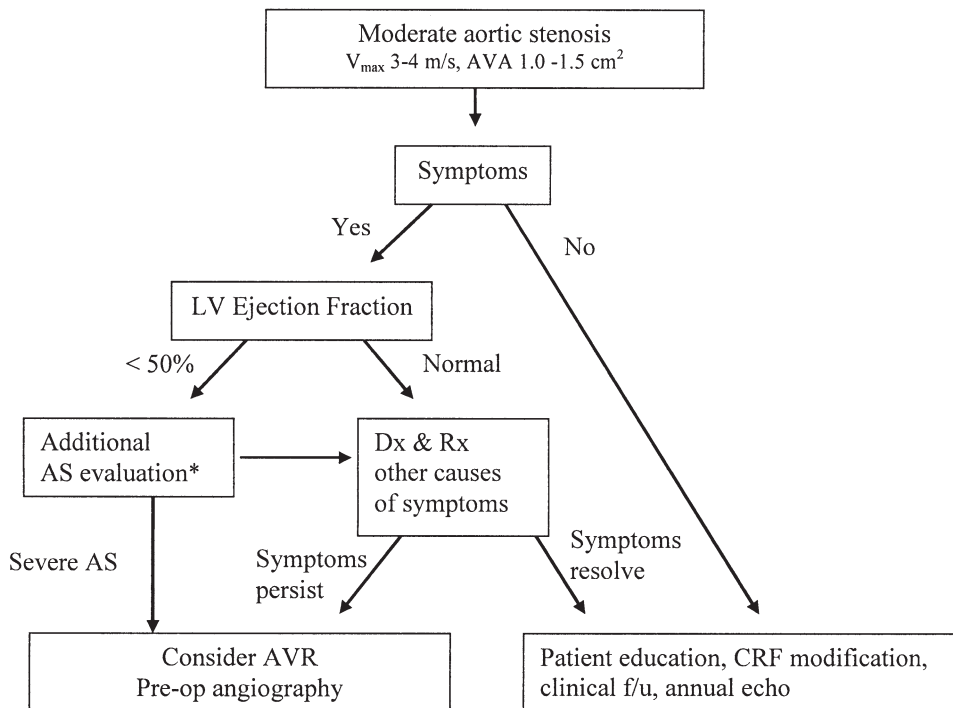
Figure 5. Suggested approach to evaluation of adults with moderate aortic stenosis (AS). *Additional evaluation of AS severity may include measurement of newer parameters discussed in the text, evaluation of the extent of leaflet calcification, cardiac catheterization, and/or dobutamine stress echocardiography. Dx = diagnosis; Rx = therapy; other abbreviations as in Figure 4.

valve replacement is straightforward. However, some patients have symptoms with a valve area between 1 and 1.5 cm^2 or with a velocity between 3 and 4 m/s (Fig. 5). In these patients, careful evaluation, including coronary angiography, for other causes of the symptoms is needed. It also is appropriate to seek objective evidence of clinical decompensation, such as pulmonary congestion on chest radiography, an elevated serum brain natriuretic peptide level, or reduced exercise tolerance, to ensure that symptoms are truly present. With clear symptoms that have no other explanation, valve replacement surgery should be considered if the valve shows significant calcification, even with only "moderate" stenosis.

Asymptomatic patients. In asymptomatic patients, the risks of valve surgery are weighed against the risk of an adverse outcome without surgical intervention. Aortic valve repair is not an option, so that the long-term durability and risks of a prosthetic valve also must be considered. In addition, the severity of native valve stenosis should exceed the functional stenosis of the prosthetic valve that would be implanted.

If symptom status is unclear, exercise testing may be helpful to determine exercise duration and the hemodynamic changes. Patients with reduced exercise tolerance, a blunted blood pressure rise (<20 mm Hg), or abnormal symptoms with exertion should be considered symptomatic and referred for valve surgery (22–24). Exercise-induced ST-segment depression is frequently present and is not predictive of symptom onset or the presence of coronary disease (22). Exercise testing should be performed cau-

tiously in patients with severe AS and is reserved for the <6% of cases where symptom status is unclear (21).

Serum brain natriuretic peptide levels may be helpful when symptom status is unclear, although caution is needed as brain natriuretic peptide levels also are elevated with other cardiac conditions and in response to some medications (25). Brain natriuretic peptide levels are higher in patients with symptomatic AS compared with those with asymptomatic severe disease and correlate with symptom severity (26).

Even with severe valve obstruction, the risk of sudden death is low (<1%) in the asymptomatic patient. In theory, earlier surgery might prevent ventricular systolic or diastolic dysfunction, but outcome data addressing this issue are not available. Although the risk of surgery is <1% in a 55-year-old man with no other medical conditions, predicted operative mortality rises to 7% for an 85-year-old woman with hypertension and coronary disease and exceeds 24% for an 80-year-old man with coronary disease, prior cardiac surgery, and renal dysfunction (27). Taken together, in the patient with asymptomatic AS, the balance is shifted towards watchful waiting until symptoms supervene. Appropriate management includes patient education about symptoms and the importance of promptly seeking medical attention once symptoms are present, periodic echocardiography, and cardiovascular risk factor reduction.

There are some exceptions. In patients with asymptomatic moderate-to-severe AS who are undergoing other cardiac surgery, valve replacement should be considered. In a small subset of AS patients, LV systolic dysfunction
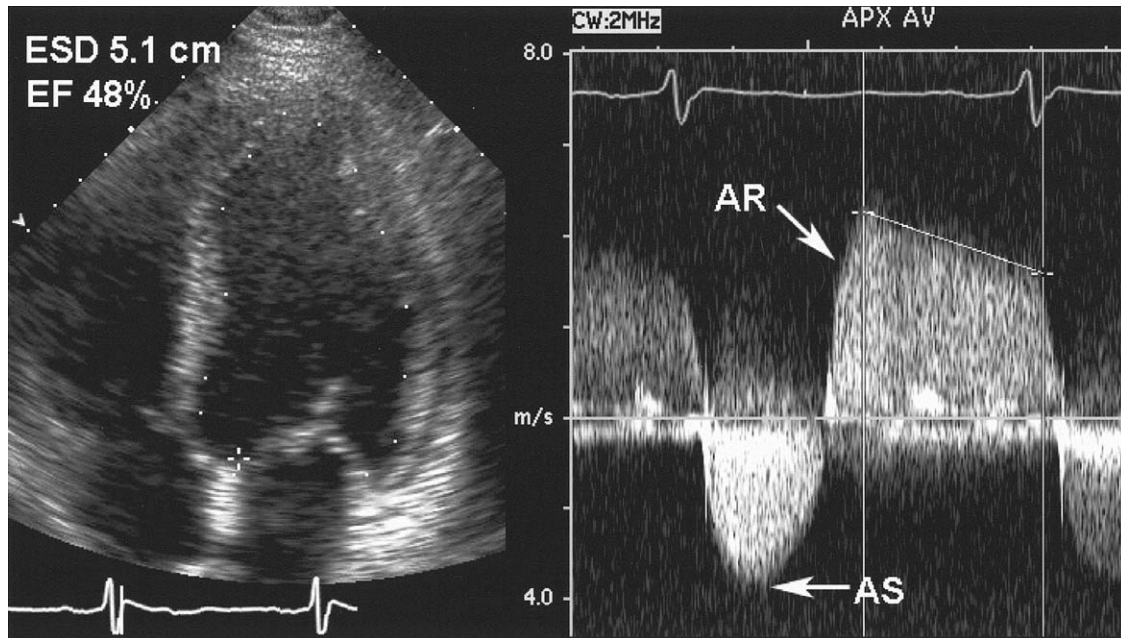
Figure 6. Example of decision making with moderate aortic stenosis (AS) and aortic regurgitation (AR). This 59-year-old man has a markedly calcified aortic valve, but aortic velocity is only 3.7 m/s, mean gradient 34 mm Hg, and valve area is 1.3 cm². Moderate regurgitation also is present with a vena contract of 5 mm, and holodiastolic flow reversal in the descending aorta. However, significant left ventricular dilation and systolic dysfunction are present, so that aortic valve replacement is appropriate. EF = ejection fraction; ESD = end-systolic dimension.

(ejection fraction <50%) develops in the absence of symptoms (20). Because ventricular function may improve after relief of the increased afterload due to AS, valve replacement is appropriate. Some guidelines suggest that valve surgery is reasonable with severe stenosis and evidence of rapid progression or severe calcification (21). Valve surgery also may be considered in patients with severe stenosis when there is an expected delay in surgical intervention once symptoms occur, for example a patient living in a remote area. Some centers advocate exercise testing in patients with severe AS to detect subclinical symptoms. The value of this approach likely is related to the patient's understanding of the disease process, personal awareness of symptoms, and the physician's ability to obtain an accurate history. In asymptomatic patients, brain natriuretic peptide levels predict symptom onset, as well as post-operative survival and ventricular function, but data do not yet support using brain natriuretic peptide levels to recommend surgery in an asymptomatic patient (25,28,29).

PROBLEMATIC CLINICAL SITUATIONS

Combined stenosis and regurgitation. Most patients with AS have at least mild coexisting AR. These patients can be evaluated and managed using standard diagnostic approaches. Echocardiographic measures of stenosis severity remain accurate even with combined AS and AR. In these patients, the issue is that symptom onset or ventricular dysfunction may occur with only "moderate" AS due to the combined effects of ventricular pressure and volume overload. There are no established guidelines for timing of intervention in patients with mixed AS/AR, but general

principles for isolated AS or AR are still applicable. It also is helpful to quantitate the degree of AR, in addition to the severity of stenosis. Surgical intervention is appropriate in patients with combined moderate AS/AR when symptoms are present, LV systolic function is reduced, or at the time of other cardiac surgery (Fig. 6).

Aortic root disease. The underlying etiology of AS is a bicuspid valve in over 50% of adults including about 60% of those presenting at age 50 to 70 years and about 40% of those >70 years of age (30). Patients with a bicuspid aortic valve have an abnormal aorta with an increased risk for aortic dilation and dissection (31). After aortic valve replacement, the strongest risk factor for aortic dissection is a bicuspid aortic valve.

Evaluation of aortic root anatomy and dimensions should be standard in all patients with aortic valve disease. In some cases, the timing of surgery will be driven by progressive root dilation, even when valve dysfunction is not severe. When valve disease is the primary indication for surgical intervention, concurrent aortic root replacement should be considered if significant aortic dilation is present.

Hypertension. Aortic valve disease and hypertension are both prevalent in older adults and occur together in 35% to 45% of AS patients (2–5). The presence of hypertension affects decision making in patients with AS in two reciprocal ways: hypertension may mask the severity of stenosis, and the presence of stenosis may affect the optimal treatment of hypertension. In addition, the combination of AS and hypertension, in effect, "double-loads" the ventricle; total afterload includes both the valve obstruction and the elevated systemic vascular resistance (19).
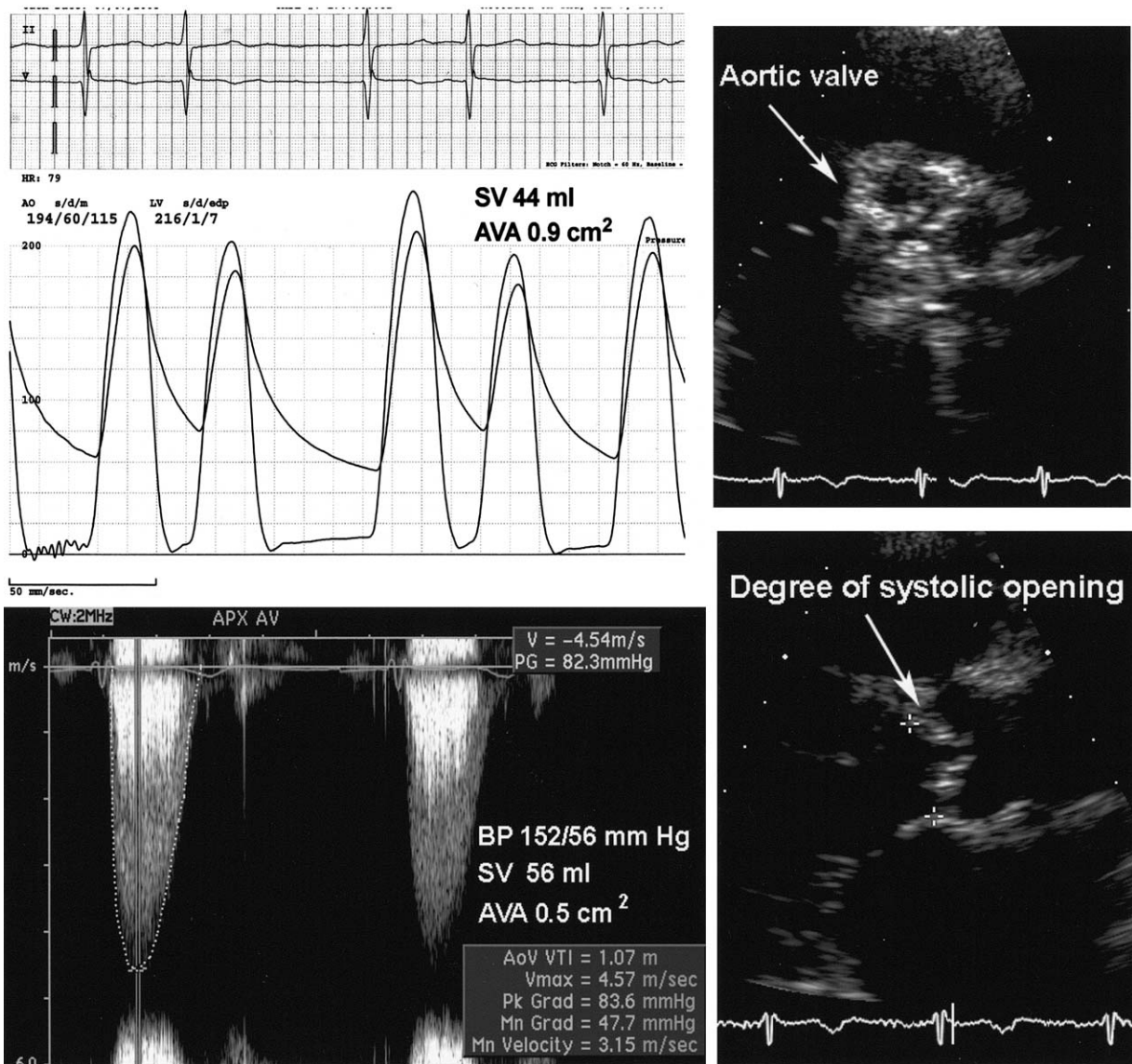
Figure 7. This 82-year-old woman underwent echocardiography for evaluation of a systolic murmur. The valve was heavily calcified as seen the short-axis view **(top)** with reduced systolic opening in the long-axis view **(bottom)**, with Doppler data consistent with severe stenosis. At cardiac catheterization several days later, a lower pressure gradient and lower stroke volume were recorded. The apparent discrepancy in the catheterization data most likely is related to pressure recovery and severe hypertension (blood pressure [BP] 194 systolic during catheterization). AoV = aortic valve; AVA = aortic valve area; Grad = gradient; Mn = mean; Pk = peak; SV = stroke volume; V_{max} = maximum velocity; VTI = velocity time integral.

The complex changes that occur with AS plus hypertension remain incompletely understood. However, recent studies suggest that, for a given valve area, transaortic ΔP and velocity are reduced when systemic vascular compliance is decreased. In this situation, stenosis severity may be underestimated, particularly at catheterization where "recovered" pressure, rather than vena contracta pressure, is recorded. Although AVA better reflects the degree of valve narrowing, data still may be inaccurate (Fig. 7). To avoid these errors, evaluation of AS severity should be performed after treatment to reduce blood pressure to a normotensive state (19).

Traditionally, treatment of hypertension in patients with AS has been controversial due to the possible hypotensive effect of peripheral vasodilation with fixed valve obstruction.

Current data suggest that valve opening and stroke volume can increase in response to a decrease in total afterload, except with very severe disease, suggesting that medical therapy of hypertension in patients with asymptomatic AS is reasonable and may decrease overall LV load (32–34). However, caution is needed. Antihypertensive medications should be started at very low doses and slowly titrated to a therapeutic level. It is unclear if specific medications, such as angiotensin-converting enzyme inhibitors, which might both treat hypertension and prevent ventricular remodeling, are preferable in patients with valve disease (35).

Coronary artery disease. Although angina is one of the typical symptoms of AS, it can be a diagnostic challenge to decide whether angina is due to valve obstruction or coronary disease, when both are present. In prospective

studies, about 30% of patients with mild-to-moderate AS have clinical evidence of coronary disease; at pre-operative catheterization, significant coronary disease is present in about 50% (2,3,5). In a patient with severe AS and angina, valve replacement is indicated with pre-operative coronary angiography to evaluate for possible bypass grafting at the time of surgery. In patients with angina but only mild stenosis, evaluation and treatment of coronary disease, using standard approaches, is appropriate. Decision making is more difficult when angina is present in a patient with moderate AS. One approach is coronary angiography followed by percutaneous revascularization to see if symptoms resolve. Persistent angina without flow-limiting coronary lesions suggests the cause may be valve obstruction. Functional studies to evaluate for regional ischemia are sometimes helpful but are limited by lower diagnostic accuracy in the presence of AS.

LV dysfunction. In prospective studies, LV systolic dysfunction is an uncommon consequence of AS (about 5% of patients). However, patients may first present with heart failure and be found to have an abnormal aortic valve. In these patients, a low antegrade velocity and ΔP may be seen, even when severe stenosis is present. Although Doppler AVA calculations accurately reflect the extent of valve opening, leaflet motion may be reduced due to a low volume flow rate across the valve, even when stenosis is not severe.

Conversely, LV dysfunction may be due to the high afterload imposed by severe valve obstruction. It is important to identify which patients have severe stenosis as these patients will benefit from valve replacement with an acceptable operative mortality, an improved long-term survival, and an increase in ejection fraction (36). In contrast, patients with primary myocardial dysfunction and concurrent mild or moderate AS benefit less from surgical intervention (37).

The diagnostic approach starts with conventional measures of AS severity, evaluation for other causes of LV dysfunction (such as coronary disease), and assessment of valve calcification. If it remains unclear whether the primary process is severe stenosis versus primary ventricular dysfunction, dobutamine stress echocardiography may be helpful (37,38). Pressure gradient, valve area, and ejection fraction are measured at rest and with incremental doses of dobutamine (up to a maximum of 20 μg/kg/min). With flexible valve leaflets, AVA and ejection fraction increase in conjunction with the increase in cardiac output, indicating that stenosis is not severe. Therapy for primary ventricular dysfunction is appropriate in these patients. With severe stenosis, AVA does not increase despite an increase in ejection fraction because the leaflets are rigid and cannot open any further (Fig. 8). These patients are likely to benefit from valve replacement. In patients with no improvement in
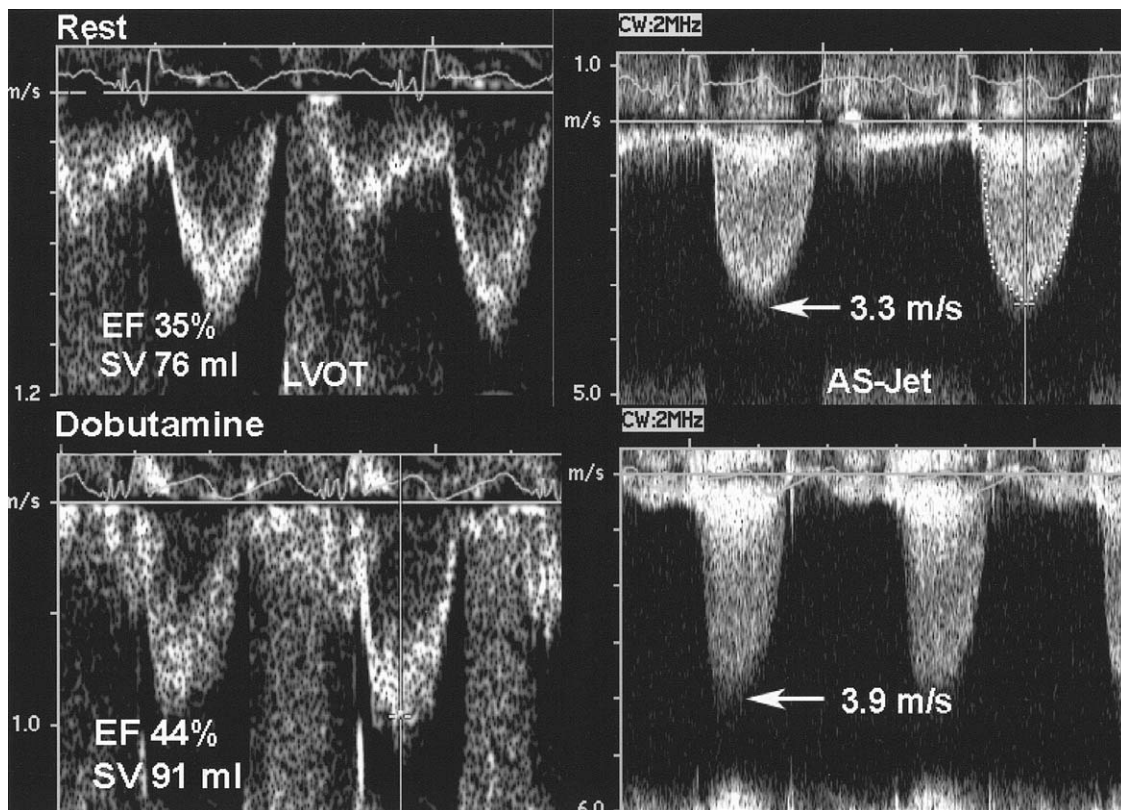

Figure 8. Dobutamine stress echocardiography was requested in this 52-year-old man with a history of radiation therapy with heart failure symptoms, left ventricular dysfunction, and a calcified aortic valve. With dobutamine, ejection fraction (EF) and stroke volume (SV) increased, indicating contractile reserve. Outflow tract peak velocity increased from 0.9 to 1.0 cm/s (left ventricular outflow tract [LVOT] diameter 2.2 cm), so calculated aortic valve area was unchanged at 1.0 cm² at rest and at peak dose dobutamine consistent with stiff inflexible leaflets. AS-Jet = aortic jet.

ejection fraction or cardiac output with dobutamine—a condition called "lack of contractile reserve"—outcomes are poor with either medical or surgical therapy.

Atrial fibrillation. Atrial fibrillation occurs in only 5% of adults with AS, but management is challenging. Evaluation of AS may be misleading if there is a short R-R interval due to a rapid ventricular response. Ideally, Doppler evaluation averages several beats when heart rate is controlled. In patients with mild-to-moderate AS, management of atrial fibrillation is based on established clinical guidelines with awareness of the possible hemodynamic effects of medications in the presence of AS. In patients with severe stenosis, atrial fibrillation may be the first sign of clinical decompensation; symptoms often persist despite rate control, prompting valve surgery.

FUTURE DIRECTIONS

Currently, standard noninvasive measures of AS severity—jet velocity, mean gradient, and valve area—suffice in most patients. In the future, complex measures that integrate the ventricular, valvular, and vascular components of the disease may allow optimal timing of intervention. The clearest indication for valve replacement is symptoms due to outflow obstruction. However, if better valve substitutes can be implanted at low risk, the balance might shift toward earlier intervention to prevent adverse effects on the myocardium and ventricular geometry.

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