Doppler Echocardiography in Adults With Symptomatic Aortic Stenosis

Diagnostic Utility and Cost-effectiveness

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• To evaluate the diagnostic utility and cost-effectiveness of Doppler echocardiography in adults with symptomatic aortic stenosis, we performed a prospective study in which the need for aortic valve replacement (AVR) was the outcome event. The total sample consisted of 103 adults (mean age, 69 years) undergoing cardiac catheterization for suspected aortic stenosis. Twenty-six patients (25%) were used as a training set to develop a clinical prediction rule. (1) If maximum aortic jet velocity (V_{max}) was more than 4.0 m/s, AVR was recommended. (2) If V_{max} was less than 3.0 m/s, AVR was not needed. (3) If V_{max} was 3.0 to 4.0 m/s *and* (*a*) Doppler aortic valve area (AVA) was 1.0 cm^2 or less, AVR was recommended, while (*b*) if Doppler AVA was 1.7 cm^2 or greater, AVR was not needed, and (*c*) if Doppler AVA was 1.1 to 1.6 cm^2, consideration of the degree of coexisting aortic insufficiency was necessary. When this rule was applied to the test set (n=77), the sensitivity was 98%, with a specificity of 89% and a total error rate of 3.9%. The approach could have resulted in cost savings between 24% and 34% compared with an invasive diagnostic approach.

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Evaluation of the adult with symptoms of aortic stenosis is an important clinical problem, since valve replacement is indicated when obstruction is severe.[1,2] Physical examination[3,4] and several noninvasive techniques, including systolic time intervals,[5] frequency analysis of the murmur,[6] echocardiographic imaging of the valve,[7,8] and the response of the left ventricle to pressure overload,[9] have been proposed as diagnostic tests. However, none has been consistently reliable in distinguishing severe obstruction from mild or moderate disease. Thus, the diagnostic method of choice has been cardiac catheterization, which allows measurement of transaortic pressure gradient, calculation of aortic valve area, and evaluation of coexisting aortic insufficiency.

Recently, a number of investigators[10-22] have used Doppler echocardiography and a modification of Bernoulli's theorem to determine transaortic pressure gradients noninvasively. However, pressure gradients depend on transaortic volume flow as well as aortic valve area. Conditions that alter transaortic volume flow (and thus pressure gradient), such as left ventricular dysfunction or coexisting aortic insufficiency, are common in adults with aortic stenosis.[23,24] Therefore, quantitative evaluation of the severity of aortic stenosis requires consideration of the volume of flow, in addition to the pressure gradient, across the stenotic valve in systole.

Recent work has documented that aortic valve area can be calculated by means of ultrasonic techniques, based on the concept that systolic volume flow in the narrowed valve orifice equals systolic volume flow just proximal to the aortic valve.[24-27] Studies using this method demonstrate good agreement between noninvasive aortic valve areas and results at catheterization. Nonetheless, two important clinical questions remain: Can noninvasive data be substituted for invasive measures of severity in making clinical decisions about aortic valve replacement? Are Doppler and two-dimensional echocardiographic measures cost-effective as compared with conventional invasive techniques?

To help answer these questions, we conducted a prospective cohort study of 103 adults undergoing cardiac catheterization for suspected aortic stenosis. A clinical prediction rule was developed by means of the split-sample technique,[28] with the first[26] (25%) of the patients being used to develop the rule, which then was tested on the subsequent 77 patients (75%). In addition, we analyzed the cost-effectiveness of the proposed clinical prediction rule.

PATIENTS AND METHODS

Patient Population

We prospectively evaluated all adult patients undergoing cardiac catheterization at University Hospital, Seattle, for suspected aortic stenosis over a consecutive 22-month period. Of a total of 116 patients, 13 were not included in this study: five refused to participate, two were medically unstable, two had technically inadequate Doppler studies, and four had inadequate catheteriza-

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tion data (no measurement of transaortic pressure gradient). The remaining 103 patients gave informed consent and formed the study population. No patient was excluded because of coexisting valvular lesions, congenital heart disease, coronary artery disease, or left ventricular dysfunction. A comparison of hemodynamic and Doppler data has been reported previously on the first 48 of these patients.[24]

Our catheterization laboratory is used by several groups of physicians, so that 77 (75%) of these 103 patients represent a community-based population (56 patients from two health maintenance organizations and 21 patients from community cardiologists), while only 26 patients (25%) were referred from the university itself. Patients ranged in age from 33 to 87 years (mean, 69 years), with 97 (94%) of 103 being over 50 years of age. There were 67 men and 36 women. The cause of aortic stenosis was a congenitally bicuspid valve in 26, rheumatic in six, and degenerative calcific stenosis in 71 patients. All patients had symptoms of angina (n = 59), congestive heart failure (n = 55), and/or syncope (n = 22), and all had physical findings consistent with aortic stenosis.

Cardiac Catheterization

Cardiac catheterization was performed for clinical indications. Transaortic pressure gradients were measured with the use of fluid-filled catheters. Forward cardiac output was measured by the thermodilution technique. Left ventricular angiography (right anterior oblique projection) was performed in 91 patients. Mitral regurgitation could be evaluated on a 0 to 4+ scale[29] in 73 studies. Angiography was technically adequate for calculation of left ventricular volumes[30] and total stroke volume in 73 patients. Angiographic assessment of aortic insufficiency[29] by means of supravalvular aortography was performed in 27 patients. Coronary angiography was done in 100 patients, with significant coronary stenosis defined as luminal diameter narrowing of 50% or more.

Mean transaortic pressure gradients were averaged from three to five beats. Aortic valve areas were calculated by the formula of Gorlin and Gorlin[31] with the use of angiographic cardiac output for transaortic volume flow when appropriate.

Doppler Echocardiography

Doppler studies were performed and interpreted without knowledge of catheterization results. The Doppler study was done on the day of catheterization in 100 patients, two days earlier in one patient, and two weeks before catheterization in two patients.

Parasternal, long-axis, two-dimensional echocardiographic images (ATL-600, Advanced Technology Laboratories, Bothell, Wash) were recorded on videotape for measurement of left ventricular outflow tract diameter. Care was taken to adjust the transducer orientation and instrument settings for optimal definition of the septal endocardium and anterior mitral valve leaflet just below the aortic valve, in midsystole.[24]

Flow velocity in the outflow tract was recorded from an apical approach by means of pulsed Doppler with a sample volume 9 mm in length. With the midportion of the sample volume positioned about 1.0 cm below the valve, flow was examined across the outflow tract to determine if it was spatially uniform. Then the sample volume position was adjusted, using the audible signal and spectral output as a guide, to obtain a smooth waveform spatially representative of flow velocities just below the region of flow acceleration into the aortic jet. Velocity records assumed an intercept angle of 0°. Spectral outputs were recorded on paper at 50 mm/s, and both audible and spectral outputs were recorded on videotape.

Aortic jet velocity was recorded with continuous-wave Doppler (Irex III-B, Irex Medical Systems, Ramsey, NJ) on paper at 50 mm/s. In each patient, multiple ultrasound windows were used with careful angulation of the transducer to obtain a tonal, high-pitched audible signal with a well-demarcated time-velocity curve. The highest peak flow velocity obtained without angle correction was assumed to have been recorded at a near-parallel intercept angle and used for subsequent analysis. The highest-velocity aortic jet was recorded from the apex in 92 patients and from a suprasternal or high right parasternal position in 11 patients.

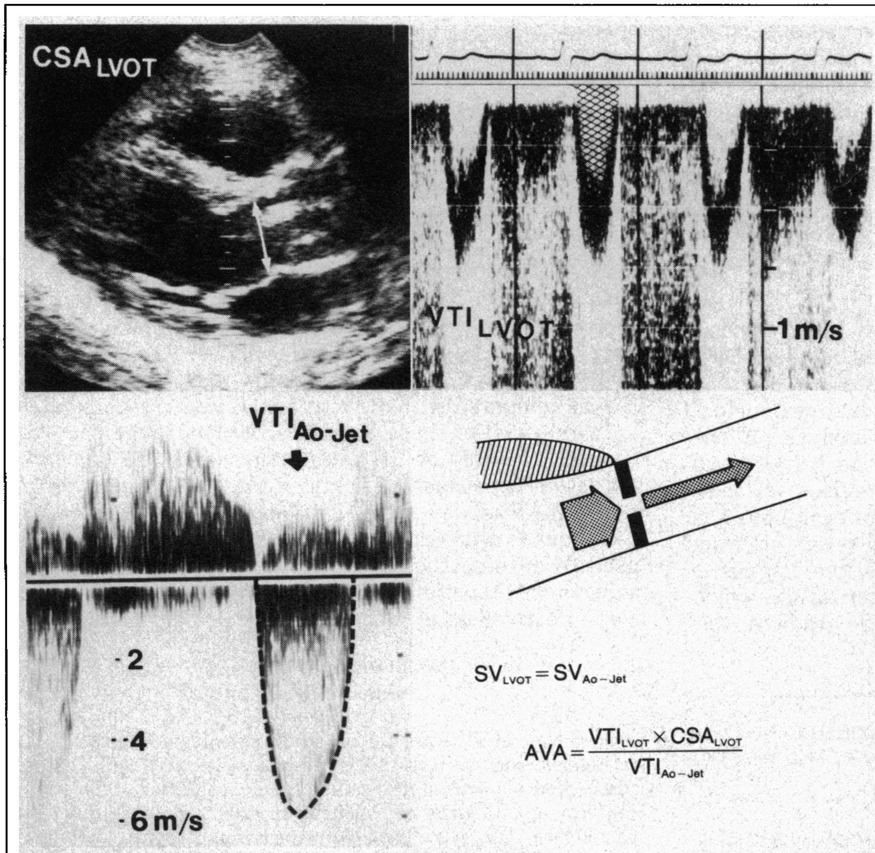

Fig 1.—Calculation of aortic valve area. Top left, Left ventricular outflow tract diameter is measured (arrows) from parasternal long-axis view and cross-sectional area (CSA_{LVOT}) calculated as $\pi(D/2)^2$. Top right, Velocity time integral in outflow tract (VTI_{LVOT}) is recorded from apical view, shown by crosshatching. Bottom left, Velocity time integral in aortic jet (VTI_{Ao-Jet}) is measured from approach giving highest velocity, in this case apical. Bottom right, Since stroke volume (SV) in LVOT equals stroke volume in aortic jet, aortic valve area (AVA) can be determined.

Aortic insufficiency was graded as 0 (absent), 1+ (turbulence localized adjacent to the aortic leaflets), 2+ (turbulence extending to the mitral valve leaflet tips), or 3+ (turbulence extending past the mitral leaflet tips) by means of flow mapping[32] with pulsed Doppler (1.5-mm sample volume length) guided by two-dimensional imaging from parasternal and apical views.

Analysis of Doppler Data

Quantitative measures were made with the use of one of two systems (Insight 2000, Franklin Inc, Woodinville, Wash, or DataVue, MicroSonics, Indianapolis). Left ventricular outflow tract diameter (D) was averaged from 5 to 10 midsystolic images, and cross-sectional area was calculated as $\pi(D/2)^2$. Peak velocities and systolic flow velocity integrals in the aortic jet and in the left ventricular outflow tract were averaged from three to five beats. Intraobserver and interobserver mean coefficients of variation for these measurements ranged from 2.2% to 7.9%, as reported previously.[24]

Transaortic pressure gradient was determined with the modified Bernoulli equation from the Doppler velocity waveform, with maximum aortic jet velocity used to calculate maximum pressure gradient, and instantaneous pressure gradients measured at 10-ms intervals to compute mean pressure gradient.

Aortic valve area was calculated with the continuity equation,[24] as shown in Fig 1.

Clinical Outcome

Each patient's own cardiologist used the clinical presentation and catheterization data to decide whether or not to recommend aortic valve replacement for relief of aortic stenosis. This decision, used as the *initial* end point for evaluation of Doppler data, was made without reference to the proposed predictive findings; clinicians had no knowledge of the Doppler data, and the proposed noninvasive diagnostic approach was never available to them.

Since this decision potentially is related to behavioral and social factors as well as a strictly biologic diagnosis, we further evaluated outcome in the test set by surgical findings in those who underwent valve replacement and by one-year cardiac mortality in those who did not. In the test set, the outcome event used to evaluate the predictive utility of noninvasive stenosis severity measures was defined as positive (aortic valve replacement needed) if valve replacement was performed with confirmation of severe stenosis at surgery *or* if valve replacement was not performed but cardiac

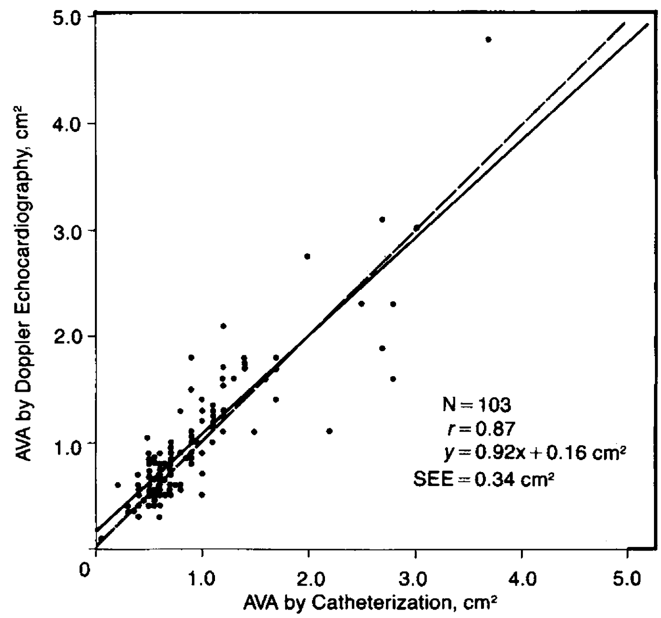

Fig 2.—Aortic valve area (AVA) calculated with Doppler echocardiography (*y*-axis) are compared with aortic valve areas calculated with Gorlin and Gorlin formula at catheterization (*x*-axis). SEE indicates standard error of the estimate.

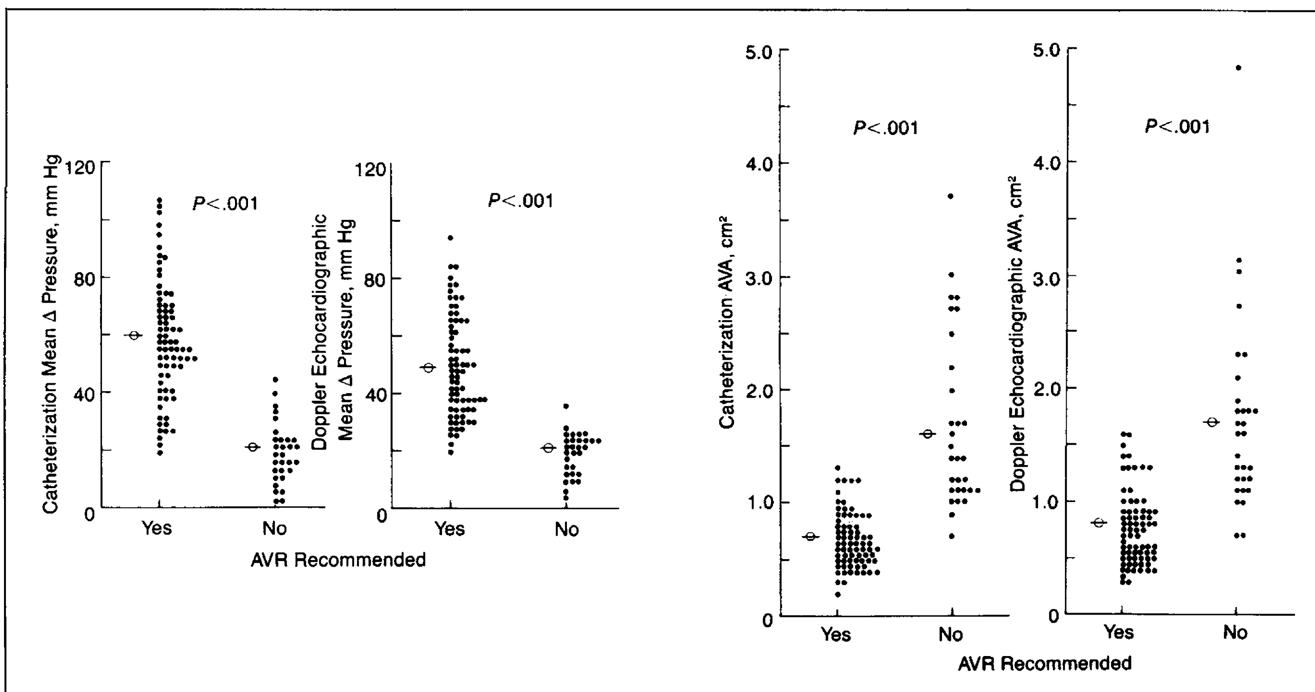

Fig 3.—Catheterization and Doppler measures of stenosis severity plotted for those in whom aortic valve replacement (AVR) was and was not recommended for relief of aortic stenosis. Far left, Catheterization mean transaortic pressure gradient (ΔPressure). Left center, Doppler mean transaortic aortic pressure gradient. Right center, Catheterization Gorlin and Gorlin formula aortic valve area (AVA). Far right, Doppler continuity equation aortic valve area. For each patient group, mean values are indicated by open circle with horizontal line across it.

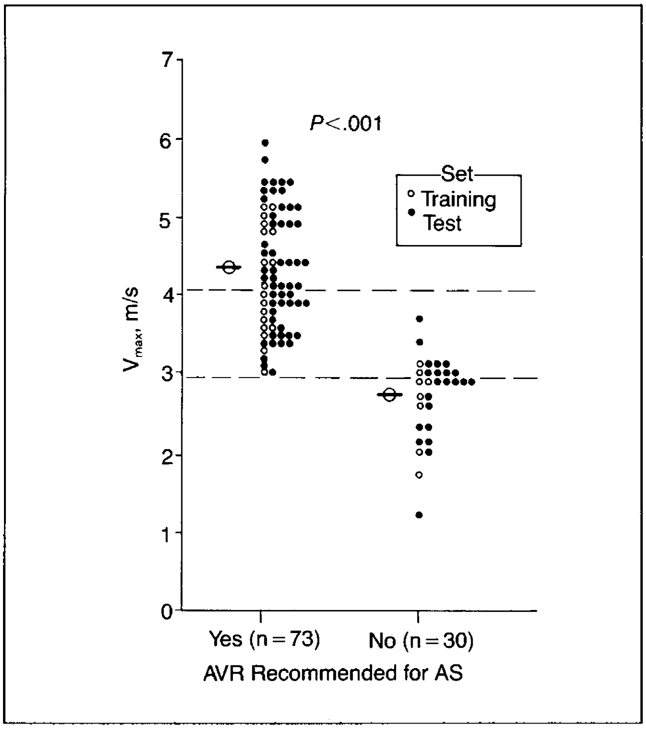

Fig 4.—Maximum aortic jet velocity (V_{max}) plotted for those in whom aortic valve replacement (AVR) was and was not recommended for relief of significant aortic stenosis (AS). Dashed lines at less than 3.0 and more than 4.0 m/s are empirically derived break points, as discussed in text. Open circles indicate training set from which empiric break points were derived.

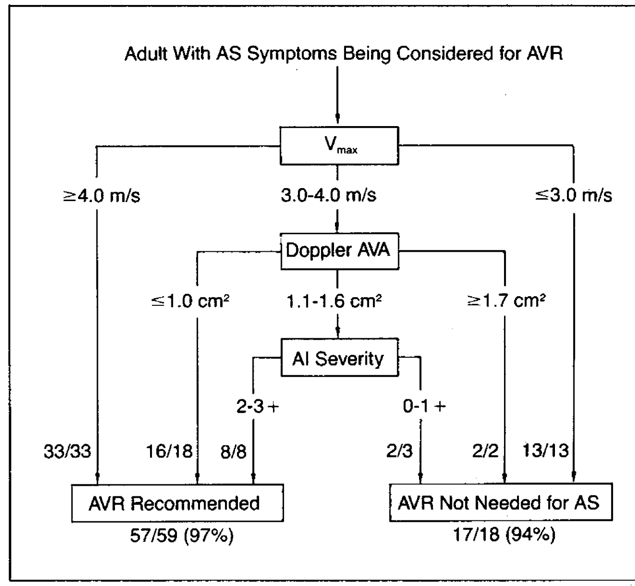

Fig 5.—Proposed approach to adults with symptoms of aortic stenosis. For test set, numbers indicate total number of patients in each subset (denominator) and number who actually had outcome event (numerator), defined as valve replacement plus one-year follow-up. AI indicates aortic insufficiency; AS, aortic stenosis; AVA, aortic valve area; AVR, aortic valve replacement; and V_{max}, maximum aortic jet velocity.

death occurred within one year. The outcome event was defined as negative (valve replacement not needed) if the subject was alive without valve replacement one year after evaluation *or* if surgery failed to confirm severe stenosis.

Statistical Analysis

Data from all three sources—Doppler echocardiography, cardiac catheterization, and clinical outcome—were recorded and analyzed independently. Linear regression was used to compare Doppler data with catheterization results. The unpaired Student's *t* test was used to compare group means.

The cost analysis was based on total charges for diagnostic tests at our hospital (including hospital and professional fees). Approximate charges were $400 for a complete echocardiogram (M-mode, two-dimensional, and Doppler), $1500 for coronary angiography alone, and $2500 for complete right and left heart catheterization (ventricular angiography, coronary angiography, cardiac output determination, and measurement of transaortic pressure gradient).

RESULTS

Aortic Stenosis Severity

At cardiac catheterization, mean transaortic pressure gradient ranged from 2 to 107 mm Hg (mean, 47 mm Hg), and aortic valve area ranged from 0.2 to 3.7 cm² (mean, 0.97 cm²), with valve area 1.0 cm² or less in 72 patients (70% of the total group). Mean pressure gradient was less than 30 mm Hg in 22 (31%) of these 72 patients with significant stenosis. Cardiac index ranged from 1.6 to 7.8 L/min/m² (mean, ±2.9 L/min/m²) and was less than 2.5 L/min/m² in 35 patients (34% of total).

In the 27 patients with a supravalvular aortogram, aortic insufficiency was absent in three, 1+ in nine, 2+ in five, and 3+ in ten patients. In the 73 patients with adequate left ventricular angiograms, mitral regurgitation was absent in 27, 1+ in 33, 2+ in nine, 3+ in two, and 4+ in two patients. Coronary angiography (n=100) showed no significant lesions in 50 patients, one-vessel disease in 19, two-vessel disease in 14, three-vessel disease in 14, and left main disease in three patients.

Doppler aortic jet velocity ranged from 1.2 to 5.9 m/s (mean, 3.8 m/s). Maximum transaortic pressure gradient (ΔP) ranged from 6 to 140 mm Hg (mean, 61 mm Hg), and mean gradient ranged from 4 to 93 mm Hg (mean, 40 mm Hg). Of note, Doppler maximum and mean gradients showed excellent linear correlation ($r=.99$, maximum $\Delta P = 1.45$ [mean ΔP] + 2.2 mm Hg, standard error of the estimate [SEE] = 3.8 mm Hg). Left ventricular outflow tract velocity ranged from 0.5 to 1.8 m/s (mean, 0.9 m/s). Outflow tract diameter ranged from 1.4 to 3.5 cm (mean, 2.3 cm). It was unrelated to body surface area but was smaller in women (mean ± 1 SD, 2.0 ± 0.3 cm) than in men (2.5 ± 0.3 cm) ($P<.01$).

Continuity equation aortic valve area ranged from 0.3 to 4.8 cm² (mean, 1.06 cm²). Aortic insufficiency was present by Doppler flow mapping in 88 patients (85% of total) and was 1+ in 25, 2+ in 48, and 3+ in 15 patients. Thus, 63 patients (61%) had more than 1+ coexisting aortic insufficiency.

In the total group (N=103), Doppler and catheterization data compared well for both mean transaortic pressure gradients ($r=.88$; Doppler = 0.71[catheterization] + 7.1 mm Hg) and aortic valve areas ($r=.87$; Doppler = 0.92[catheterization] + 0.16 cm²) (Fig 2).

Clinical Outcome: Relation to Doppler Measures

On the basis of clinical and catheterization findings, aortic valve replacement was recommended in 73 patients. This group includes five patients in whom valve replacement was recommended but not performed: two died of noncardiac causes before valve replacement, two did not undergo surgery because of coexisting medical problems

Table 1.—Misclassification Rate of Proposed Noninvasive Diagnostic Approach for Symptomatic AS in Test Set*

Actual Outcome	Predicted Outcome AVR	No AVR	Total
AVR needed	57	1	**58**
AVR not needed	2	17	**19**
Total	**59**	**18**	**77**

*AVR indicates aortic valve replacement; AS, aortic stenosis. Sensitivity of proposed approach = 57/58 = 98%; specificity of proposed approach = 17/19 = 89%; positive predictive value = 57/59 = 97%; negative predictive value = 17/18 = 94%; total error rate = (2 + 1)/103 = 3%.

Table 2.—Cost Analysis

Diagnostic Approach (N = 103)	Cost/Patient, $	Total Cost, $
Echocardiogram + complete catheterization	2900	298 700
Complete catheterization (no echocardiogram)	2500	257 500
Echocardiogram + coronary angiogram	1900	195 700*

*Reduction of 34% from echocardiogram + complete catheterization and 24% from complete catheterization without echocardiogram.

(both had cardiac death by one-year follow-up), and one refused surgery. Severe aortic stenosis was confirmed by direct inspection at surgery in the remaining 68 patients.

Aortic valve replacement for relief of aortic stenosis was not recommended in 30 patients. Two of these patients had valve replacement for predominant aortic insufficiency; this diagnosis, and the absence of significant stenosis, was confirmed at surgery.

For the entire study group, there was substantial overlap between the subgroups who were and were not referred for aortic valve replacement for Doppler maximum aortic jet velocity, Doppler mean transaortic pressure gradient, and Doppler valve area, even though there were significant differences between subgroup means. Similar overlap between these subgroups also was noted for catheterization mean pressure gradients and valve areas (Fig 3).

Using the split-sample technique to develop a clinical prediction rule, we examined a "training set" consisting of the first 25% (n = 26) of the study population. This sample size was chosen to allow at least five patients in the smallest outcome group.[28] There were significant differences (all $P<.01$) between subgroup means for those in whom valve replacement was (n = 18) and was not (n = 8) recommended, for maximum aortic jet velocity (4.2 vs 2.6 m/s), mean pressure gradient (45 vs 16 mm Hg), and aortic valve area (0.8 vs 2.0 cm^2). However, there was substantial overlap for the range of each variable, so that no single value could be used to separate the two subgroups.

The overlap between subgroups was no greater for the more easily measured maximum velocity than for mean pressure gradient or valve area, suggesting that aortic jet velocity might be a useful *initial* step in assessing aortic stenosis severity. Therefore, we chose two maximum velocity break points that distinguished three subgroups: one in which valve replacement was indicated, one in which valve replacement was not indicated, and an intermediate subgroup in whom further diagnostic data were needed. The lower break point was chosen empirically at 3.0 m/s, since no patient with a velocity of less than 3.0 m/s (n = 6) required valve replacement (Fig 4). An upper break point of 4.0 m/s (corresponding to a mean pressure gradient of about 45 mm Hg) was chosen on theoretical grounds to ensure that an aortic jet velocity exceeding this value indicated the need for valve replacement with a high predictive value.

For patients with jet velocities of 3.0 to 4.0 m/s, the relatively low corresponding pressure gradients may indicate either severe aortic stenosis with low transaortic volume flow or only moderate stenosis. Of the 11 such patients, all seven with Doppler valve area of 1.0 cm^2 or less underwent valve replacement, while the one patient with a valve area of 1.7 cm^2 or greater did not. Of the three patients with maximum jet velocity of 3.0 to 4.0 m/s and valve area of 1.1 to 1.6 cm^2, two had valve replacement for combined moderate stenosis and insufficiency.

Proposed Diagnostic Approach

The above results suggested the following diagnostic approach (Fig 5) to the adult with symptomatic aortic stenosis being considered for valve replacement: (1) When maximum aortic jet velocity is more than 4.0 m/s, aortic valve replacement can be recommended. (2) When maximum jet velocity is less than 3.0 m/s, aortic valve replacement is not needed. (3) When maximum jet velocity is 3.0 to 4.0 m/s, Doppler determination of aortic valve area is needed; (*a*) if valve area is 1.0 cm^2 or less, valve replacement can be recommended; (*b*) if valve area is 1.7 cm^2 or more, valve replacement is not needed; and (*c*) if valve area is between 1.1 and 1.6 cm^2, the degree of coexisting aortic insufficiency should be assessed.

Validation of Proposed Approach

This noninvasive diagnostic approach was then applied to our "test set," consisting of the remaining 75% of the study population (n = 77) (Fig 5). The proposed noninvasive diagnostic approach suggested that valve replacement was indicated in 59 patients. In 53 of these patients (90%), valve replacement actually was recommended. Of the six patients in whom the need for valve replacement was suggested by the noninvasive data but not actually recommended, two patients had valve areas between 1.1 and 1.6 cm^2 and 2 to 3+ coexistent aortic insufficiency by both Doppler and catheterization; during the following year, one of these patients died suddenly and one underwent valve replacement. The other four patients had Doppler valve areas of 1.0 cm^2 or less, there was close agreement between Doppler and invasive pressure gradients and valve areas, and two died during follow-up. Thus, based on clinical follow-up in addition to actual clinical management and surgical findings, only two (2.6%) of the 77 patients represent false-positive results for the proposed noninvasive approach. These two patients were alive with stable symptoms one year after cardiac catheterization.

In the remaining 18 patients, the noninvasive diagnostic approach suggested that valve replacement was not needed. In 16 (89%) of these patients, the actual clinical decision was that valve replacement was not indicated for relief of aortic stenosis. At one year of follow-up, all but one of these patients were alive, and this single death was noncardiac (autopsy confirmed). For the two patients in whom valve replacement was performed even though the noninvasive approach suggested that it was not needed, Doppler measures of mean pressure gradient and valve area underestimated the degree of stenosis in one patient. The other patient underwent coronary artery bypass surgery for angina refractory to medical therapy; moderate aortic stenosis, suggested by Doppler and confirmed at

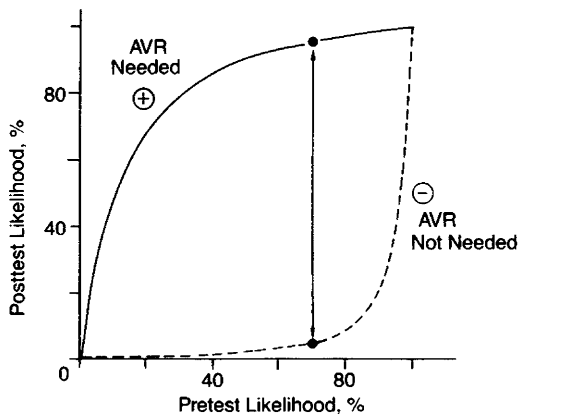

Fig 6.—With bayesian analysis, posttest likelihood of need for aortic valve replacement (AVR) (vertical axis) was calculated for each hypothetical pretest likelihood (horizontal axis). Pretest and corresponding posttest likelihoods for study population are indicated by arrow. AS indicates aortic stenosis.

catheterization, was reconfirmed at surgery, at which time valve replacement was performed electively. Had coronary surgery not been needed, valve replacement surgery would not have been done in this patient. Thus, only one (1.3%) of the 77 patients represents a false-negative result for the proposed approach.

Of note, all 33 patients with maximum aortic jet velocity greater than 4.0 m/s were referred for valve replacement, while none of the 13 with jet velocity less than 3.0 m/s needed valve replacement. Thus, the predictive value of maximum aortic jet velocity greater than 4.0 m/s or less than 3.0 m/s was 100%. The sensitivity, specificity, predictive value, and total error rate for the proposed approach in the test set are shown in Table 1.

Cost Analysis

The total cost of this noninvasive diagnostic approach was compared with that of "conventional" diagnostic evaluation. The diagnostic testing that constitutes "conventional" laboratory evaluation for symptomatic aortic stenosis differs from institution to institution. Many physicians would perform echocardiographic studies as a guide to subsequent right and left heart catheterization (approach A); others might consider noninvasive studies to be superfluous and proceed directly to complete catheterization (approach B). With the use of the noninvasive approach outlined above, all patients would have undergone echocardiography plus coronary angiography, which we assumed was needed in all these symptomatic patients (approach C). The cost of these approaches is compared in Table 2.

On the basis of this analysis, the relative total cost of "conventional" diagnostic testing ranges from 1.3 to 1.5 times the cost of noninvasive testing. Assuming coronary angiography is necessary in all patients, potential cost savings are 24% to 34% if the noninvasive approach had been used for decision making.

COMMENT

In this prospective cohort study, we developed and validated a noninvasive approach to adults with symptomatic aortic stenosis with the use of Doppler measures as predictive findings compared with blinded assessment of clinical outcome.[28] Our goals were to improve patient care by decreasing costs while maintaining clinical accuracy. If validated by others, the proposed clinical prediction rule could be widely applicable, since Doppler measures of stenosis severity are feasible and the study group largely represented a community-based population.

Doppler Measures of Aortic Stenosis Severity

Transvalvular pressure gradient is an important indicator of aortic stenosis severity. Doppler pressure gradients show good agreement with invasive measures, as found not only in this study, but also in flow and animal models of stenosis[33-36] and in other clinical studies of children and adults.[10-22] It should be emphasized that optimal Doppler velocity recordings require substantial technical expertise, and underestimation of pressure gradients can result from misalignment of the ultrasound beam and aortic jet. Furthermore, it is noteworthy that because of left ventricular dysfunction, an intermediate pressure gradient (mean ΔP, 25 to 45 mm Hg) was present *despite severe stenosis* in one third of our patients.

Aortic valve area itself can be determined by means of the Doppler continuity equation[24-27] or other noninvasive methods.[37-41] The Doppler approach makes several assumptions about fluid dynamics below and in the narrowed orifice,[42] and, again, technical mistakes in recording Doppler velocities and outflow tract diameters can lead to erroneous valve areas. On the other hand, measurement of transaortic pressure gradient[43] and transaortic volume flow[30] at catheterization, and the Gorlin and Gorlin formula[44-46] itself, also have potential sources of error.

While measures of the severity of aortic stenosis can be determined accurately (at experienced centers) with Doppler echocardiography, the utility of these data for managing individual patients has not, to our knowledge, been evaluated previously.

Diagnostic Utility

In this study, we developed a multifactor noninvasive approach for evaluating the adult with symptomatic aortic stenosis. The simple measurement of maximum aortic jet velocity provided a useful *initial* diagnostic step, since all patients with high jet velocity (>4.0 m/s) had valve replacement recommended for relief of aortic stenosis, while no patient with low jet velocity (<3.0 m/s) required valve replacement. The utility of this simple measurement is not surprising. Symptomatic patients with high aortic jet velocity usually have significant isolated stenosis; occasionally they have moderate stenosis combined with moderate regurgitation but still are candidates for valve replacement. At the other end of the spectrum, patients with low jet velocities do not have significant aortic stenosis or regurgitation and do not need valve replacement.

Patients with jet velocities between 3.0 and 4.0 m/s (41% of the study population) require further evaluation. These velocities indicate a maximum instantaneous pressure gradient of 36 to 64 mm Hg, corresponding to a mean pressure gradient of about 25 to 45 mm Hg. This group includes not only patients with moderate aortic stenosis and normal cardiac output, but also those with severe stenosis and low pressure gradient (due to low transaortic volume flow) and those with moderate stenosis and coexisting moderate insufficiency. Determination of aortic valve area is important in these patients. Those with Doppler valve areas of 1.0 cm^2 or less have severe stenosis (with small gradients due to low transaortic volume flow), and valve replacement can be recommended. Those with valve area of 1.7 cm^2 or more do not have significant stenosis.

Symptomatic adults with maximum velocity between 3.0 and 4.0 m/s but with a valve area between 1.1 and 1.6 cm^2 represent a more difficult problem. Evaluation of the degree of coexisting aortic insufficiency may be helpful, since patients with mixed moderate stenosis and moderate insufficiency may benefit from valve replacement. However, other factors must be considered in these patients, including the presence and degree of left ventricular dilation, duration of symptoms, and degree of symptomatic limitation. In some cases, cardiac catheterization may be needed, not only to confirm the severity of aortic valve disease but also to evaluate for coronary artery disease as another potential cause of symptoms.

Cost-effectiveness

In this study population, the proposed noninvasive approach could have accrued savings between 24% and 34%. Although the actual costs used for this analysis will vary between institutions and may change over time, the *relative* costs of these diagnostic procedures should be less variable. Similarly, although patient charges may not always accurately reflect actual costs, they should reflect the relative costs of these procedures. Some patients may not need coronary angiography if severe aortic stenosis has been excluded, so that cost savings potentially may be greater than predicted by this analysis. Since the proposed approach results in cost savings with an equal clinical outcome compared with a conventional diagnostic approach, use of the term "cost-effective" is appropriate.[47]

Limitations of Proposed Approach

A potential shortcoming of this analysis is that the validity of the proposed diagnostic approach is judged by comparison with actual clinical decisions. Thus, there was no objective gold standard. Nonetheless, these decisions were made without knowledge of the Doppler data and thereby avoid test review bias. They also were made by each patient's cardiologist rather than by a single individual; thus, differing standards for "significant" stenosis may have been used in each case, and the "correct" decision may not always have been made. The validity of our definition of a true-positive result is supported by anatomic confirmation of severe stenosis in patients undergoing valve replacement.

It is more difficult to define what represents "correct" management for patients in whom surgery was not recommended. Thus, we used cardiac mortality at one year as an additional end point for definition of the true-negative results. Follow-up was assessed at only one year, since a longer duration of clinical follow-up without subsequent evaluation of aortic stenosis severity may be misleading due to disease progression. In addition, most of these patients had comorbid cardiac disease (especially coronary artery disease), and it was not always possible to separate death due to aortic stenosis from that due to other cardiac causes.

Despite these potential limitations, the total error rate of the proposed approach was only 4%. Even if valve replacement alone were considered the outcome event, the total "error rate" would increase to only 8%.

It should be emphasized that our noninvasive approach applies only to patients with signs, symptoms, and two-dimensional echocardiographic findings of native valvular aortic stenosis who are being considered for valve replacement. In an asymptomatic patient, many physicians would choose to defer valve replacement, even if stenosis were severe. In our population, in which the pretest likelihood of the need for valve replacement was 70%, the proposed approach increased the posttest likelihood[48] to 95% with a positive result or decreased it to 5% with a negative result (Fig 6).

Further evaluation of the proposed approach is needed in a larger population of patients with aortic stenosis with both clinical and hemodynamic follow-up before this approach is widely applied. Follow-up in particular may help resolve the issue of apparent "misdiagnosis." Ideally, the strategy should be tested in both the academic and community medical settings.

Conclusions

A simple triage approach to adults with symptomatic aortic stenosis, based on noninvasive measures of aortic maximum jet velocity and valve area, has utility in diagnosis and patient management and offers potential cost savings. The high prevalence of left ventricular dysfunction in elderly patients with aortic stenosis is noteworthy, and the significance of moderate pressure gradients must be interpreted cautiously. In these patients, aortic valve area determination is particularly useful. The proposed noninvasive approach to adults with symptomatic aortic stenosis appears to be clinically accurate and cost-effective. Extrapolation of these Doppler techniques to the larger population of mildly symptomatic or asymptomatic patients with a systolic murmur may be possible.

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