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CLINICAL STUDIES

Hemodynamic Progression of Aortic Stenosis in Adults Assessed by Doppler Echocardiography

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Doppler echocardiography was used to follow the hemodynamic severity of aortic stenosis. First, the reproducibility of repeat recordings (mean interval 28 ± 36 days) of aortic jet velocity, made by two independent observers, was tested in 38 adults with aortic stenosis and unchanged clinical status. The two recordings of maximal velocity correlated well (r = 0.96, y = 0.88x + 0.46m/s, SEE = 0.21 m/s) with a mean coefficient of variation of 3.2%. Repeat recording of left ventricular outflow tract velocity by two independent observers in 10 other patients with aortic stenosis also correlated well (r = 0.94, y = 1.06x + 0.0 m/s, SEE = 0.06 m/s) with a mean coefficient of variation of 4.6%.

Next, Doppler echocardiography was used to study 42 patients with aortic stenosis (mean age 66 years) over a follow-up interval of 6 to 43 months (mean 20). Maximal aortic jet velocity increased by 0.36 m/s per year (range −0.3 to +1.0 m/s per year). Mean transaortic pressure gradient changed by −7 to +23 (mean 8) mm Hg/year. Aortic valve area by the continuity equation (n = 25) decreased by 0 to 0.5 cm^2/year (mean decrease 0.1 cm^2/year). Some patients had a worsening of stenosis (decrease in valve area) even though they had no change or a decrease in pressure gradient, because of concurrent decreases in transaortic volume flow.

Twenty-one patients (50%) developed new or progressive symptoms of aortic stenosis necessitating valve replacement. These patients had a higher maximal aortic jet velocity at follow-up (4.5 versus 3.9 m/s, $p < 0.01$) and a greater rate of increase in mean pressure gradient (15 versus 7 mm Hg/year, $p < 0.01$) than did those who remained asymptomatic; however, there were no significant differences in age, follow-up interval or maximal aortic jet velocity at entry.

It is concluded that Doppler echocardiographic measures of aortic stenosis severity are reproducible. The rate of change of transaortic pressure gradient varies among patients and the gradient may not increase even when stenosis severity worsens. Although stenosis severity progresses more rapidly in patients who develop symptoms requiring valve replacement, these patients cannot be identified at the initial study.

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Early studies of the natural history of aortic stenosis described the symptoms, physical findings and outcome in patients with a clinical (1,2) or autopsy (3,4) diagnosis of valvular aortic stenosis. Hemodynamic data are not available in these series. Many subsequent studies (5–8) have concentrated on clinical outcome after an initial assessment of stenosis severity. Historically, the development of diagnostic cardiac catheterization coincided with the ability to perform valve replacement. Therefore, studies that specifically evaluated the rate of hemodynamic progression of aortic stenosis are based on repeat cardiac catheterization in small groups of selected patients (9–13).

Until recently, there were no alternatives to cardiac catheterization for evaluating the hemodynamic severity of aortic stenosis. Now, noninvasive evaluation is feasible with the use of Doppler echocardiographic measures of intracardiac flow velocities to calculate transaortic pressure gradient (14–18) and valve area (18–21). This approach is well suited to study the rate of progression of aortic stenosis severity in adults.

Methods

Study patients. We prospectively followed up 42 adults with valvular aortic stenosis, with informed consent of all subjects (institutional review board approved December 21, 1983). On the basis of two-dimensional echocardiographic

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findings, the origin of aortic stenosis was congenital in 5, rheumatic in 6 and calcific in 31 patients. The group with calcific stenosis included patients in whom the valve was originally bicuspid as well as those with a trileaflet valve, because these conditions cannot always be distinguished echocardiographically once heavy calcification has supervened. Patients ranged in age from 38 to 85 years (mean age 66.4) with 28 of 42 (62%) >65 years of age. There were 12 women with 30 men. In all patients, initial echocardiograms showed thickened aortic valve leaflets with reduced systolic opening (<15 mm), and a maximal transaortic jet velocity ≥2.6 m/s. At entry, 27 patients had no cardiac symptoms and 15 had mild symptoms that were not thought to be due to aortic stenosis: 7 with angina, 4 with dyspnea on exertion, 1 with syncope and 4 with dizziness. Each patient was followed up for 6 to 43 months (mean 20); two to five (mean 2.4) echocardiograms per patient were performed during follow-up. Patients were classified into two subgroups—those who did and those who did not have progressive symptoms requiring valve replacement during follow-up.

Doppler echocardiography. Maximal transaortic jet velocity was recorded with the use of continuous wave Doppler ultrasound (Irex IIIB or VingMed SD-100) from the examining window that gave the highest velocity signal. Maximal and mean transaortic pressure gradients were calculated with use of the modified Bernoulli equation (10–14). Aortic valve area was calculated with use of the simplified continuity equation, with measurement of left ventricular outflow tract diameter from two-dimensional parasternal long-axis images and with pulsed Doppler recording of outflow tract velocity from an apical approach (ATL-600 or UM-8 instrument, Advanced Technology Laboratories) as previously described (22). Echocardiographic data were analyzed by a single observer who was unaware of findings from other studies in the same patient. In some of the earliest studies, complete data for calculation of valve area were not recorded. Coexisting aortic insufficiency was graded on a 0 to 3+ scale with used conventional pulsed Doppler flow mapping (23).

Reproducibility of Doppler data. Intra- and interobserver variability when the same Doppler data are *measured* repeatedly has been reported previously, with mean coefficients of variation of 3.2% and 3.1% for maximal aortic jet velocity, 3.0% and 3.9% for outflow tract velocity and 5.1% and 7.9% for outflow tract diameter, respectively (18).

To assess variability when Doppler data are recorded by two different observers, two sonographers independently recorded maximal aortic jet velocity in 38 adults (mean age 69 years) with aortic stenosis. Echocardiograms were performed on each subject at a mean interval of 28 (±36) days with no intervening change in clinical status. Performing both recordings on the same day would have lengthened the examination to an unacceptable extent. In a separate group of 10 patients with aortic stenosis (mean age 68 years), recording of outflow tract velocity (which is technically easier) was performed by two independent sonographers within 15 min of each other.

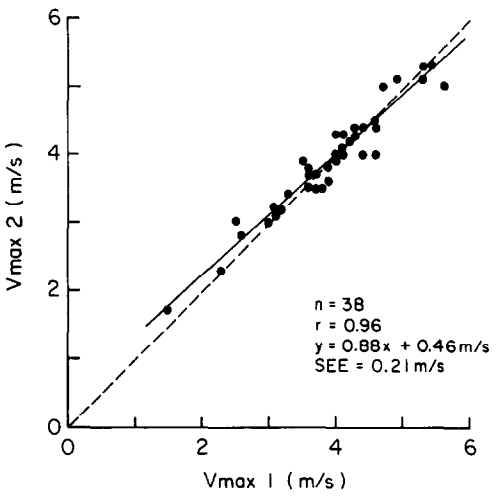


Figure 1. Reproducibility of recording maximal aortic jet velocity in 38 patients is shown with maximal velocity from the initial study (V_{max} 1) on the horizontal axis and from the second study (V_{max} 2) on the vertical axis.

Statistical analysis. Reproducibility data were analyzed by linear regression with calculation of Pearson's correlation coefficient. In addition, mean coefficients of variation were determined.

Rates of increase in measures of aortic stenosis severity were corrected for follow-up duration and expressed as units per year. A paired *t* test was used to compare continuous data, including changes in measures of stenosis severity during follow-up. An unpaired *t* test was used to assess differences between groups of patients who subsequently did or did not undergo valve replacement. Discrete data, such as the prevalence of aortic insufficiency at presentation versus follow-up, were compared with use of the chi-square analysis with the Yates correction.

Results

Reproducibility of Doppler recordings (Fig. 1). Maximal aortic jet velocity ranged from 1.5 to 5.3 (mean 3.9) m/s; there was close agreement between the two recordings (n = 38, r = 0.96, y = 0.88x + 0.46 m/s, SEE = 0.21 m/s); and the mean coefficient of variation was 3.2%. Left ventricular outflow tract maximal velocity ranged from 0.5 to 1.0 m/s, and again the two recordings showed close agreement (n = 10, r = 0.94, y = 1.06x + 0 m/s, SEE = 0.06 m/s) with a mean coefficient of variation of 4.6%.

Stenosis severity at initial study. Maximal aortic jet velocity at entry into the study ranged from 2.6 to 5.2 m/s (mean 3.7), corresponding to a maximal transaortic pressure gradient of 27 to 108 mm Hg (average 54) and a mean transaortic

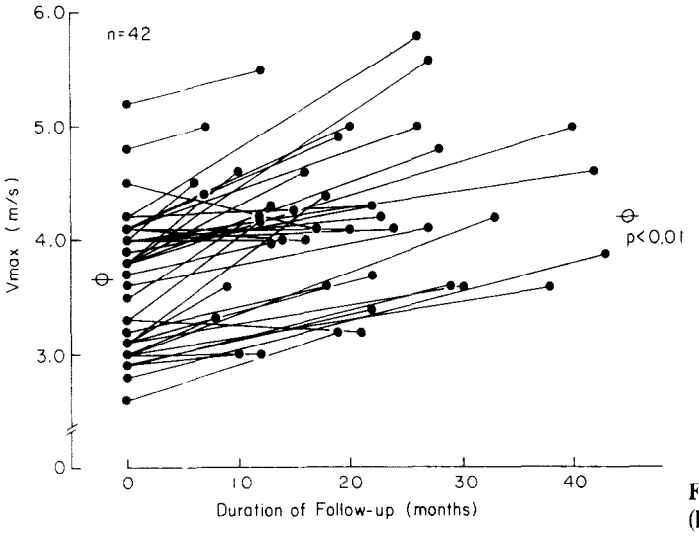


Figure 2. Maximal aortic jet velocity (V_{max}) is plotted for the initial and final Doppler studies in 42 patients. Group means are indicated by the symbol ⊖.

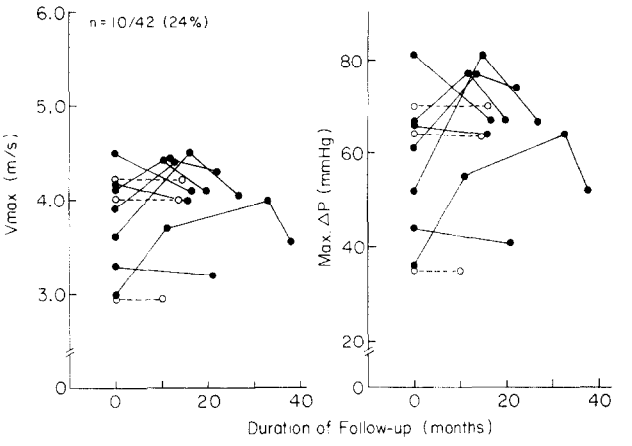


Figure 3. Sequential changes in maximal aortic jet velocity (V_{max}) (**left**) and maximal transaortic pressure gradient (Max. ΔP) (**right**) are shown for the subgroup of 10 patients with no change (**open circles**) or a decrease (**closed circles**) in maximal aortic jet velocity during follow-up. Group mean aortic jet velocity decreased from a high point of 4.04 to 3.86 m/s at final follow-up ($p < 0.01$), whereas group mean maximal pressure gradient decreased from a peak of 66 to 59 mm Hg ($p = 0.03$).

pressure gradient of 16 to 72 mm Hg (average 35). Coexisting aortic insufficiency was present in 36 (86%) of 42 patients and was 1+ in 17, 2+ in 16 and 3+ in 3.

Rate of progression of aortic stenosis severity (Fig. 2 to 4). Maximal aortic jet velocity changed by −0.3 to +1.0 m/s per year (average +0.36 m/s per year; Fig. 2). The maximal transaortic pressure gradient changed by −10 to +34 mm Hg/year (average +12 mm Hg/year); the mean gradient changed by −7 to +23 mm Hg/year (average +8 mm Hg/year).

Coexisting aortic insufficiency was present at follow-up in 37 patients (88%), a proportion not different from that at entry. Regurgitant severity was 1+ in 20 patients, 2+ in 13 and 3+ in 4.

Data for calculation of aortic valve area were available in 25 of the 42 patients. The decrease in valve area was variable (range 0.0 to 0.5 cm^2/year [mean 0.1 cm^2/year]). Mean outflow tract diameter was 2.4 ± 0.36 cm at entry and was unchanged at follow-up (2.4 ± 0.34 cm). In individual patients, there were no changes in outflow tract diameter outside the confidence limits for intraobserver measurement variability.

Consistent increases in maximal jet velocity (and pressure gradient) were seen in 32 patients at sequential follow-up, but 10 (24%) of the 42 patients demonstrated either no change in maximal aortic jet velocity during the entire study or a decrease in velocity between two of the follow-up studies (Fig. 3). Data for calculation of aortic valve area were available in 9 of the 10 patients in this subgroup. Four of these patients had no change in valve area, four had a decrease in valve area despite a decrease in maximal velocity and one had a decrease in valve area with no change in maximal velocity (Fig. 4). Group mean valve area decreased from 0.96 to 0.85 cm^2 ($p = 0.03$).

Relation between hemodynamic stenosis progression and clinical outcome. At follow-up, 21 (50%) of the 42 patients had developed new symptoms of aortic stenosis (angina in 11, congestive heart failure in 7 and syncope in 3) and subsequently underwent valve replacement. To identify factors that might predict symptom progression, this group was compared with the 21 patients who remained asymptomatic (Table 1). Both the maximal jet velocity on the last echocardiogram and the rate of change in pressure gradient during the follow-up period were significantly higher in those who became symptomatic. However, there were no differences

Figure 4. Change in aortic valve area (AVA) during follow-up in the subgroup of 10 patients with no change (**open circles**) or a decrease (**closed circles**) in maximal aortic jet velocity during follow-up.

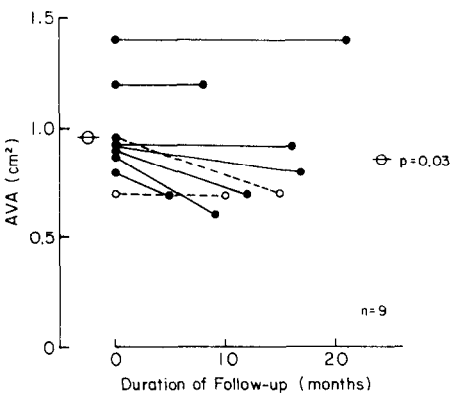


Table 1. Clinical and Doppler Measures Versus Subsequent Aortic Valve Replacement in 42 Patients

	Valve Replacement		
	Performed (n = 21)	Not Required (n = 21)	
Change in maximal ΔP (mm Hg/yr)	15.2 + 10.4	7.3 + 8.2	$p < 0.01$
Final V_{max} at F/U (m/s)	4.5 + 0.7	3.9 + 0.6	$p < 0.01$
V_{max} at entry (m/s)	3.8 + 0.5	3.5 + 0.6	p = NS
Age (yr)	66 + 12	66 + 12	p = NS
F/U interval (months)	21 + 10	20 + 10	p = NS

Values shown are group means ± 1 SD. F/U = follow-up; V_{max} = maximal aortic jet velocity; ΔP = pressure gradient.

between group means for age, follow-up duration or maximal aortic jet velocity at the initial study (all $p > 0.05$). In addition, there was no difference between groups in the prevalence or severity of coexisting aortic insufficiency or in the etiology of aortic stenosis ($p > 0.05$). The group undergoing valve replacement included one patient with a maximal jet velocity of only 3.0 m/s (this patient had a valve area of 0.7 cm^2 and the low aortic jet velocity was due to associated severe left ventricular systolic dysfunction), whereas the asymptomatic group included patients with a maximal velocity as high as 5 m/s and a valve area as small as 0.7 cm^2.

Discussion

In this prospective study of 42 adults with valvular aortic stenosis, we used Doppler echocardiography to follow hemodynamic indicators of disease progression. Our data highlight the importance of measuring valve area, not just pressure gradient, in sequential studies of stenosis severity.

Reproducibility of Doppler data. In previous studies (14–21), Doppler measures have been shown to be comparable with invasive measures of stenosis severity, with an intra- and interobserver variability for *measuring* the data (18) similar to the variability reported for other cardiac diagnostic tests (24–27). However, to be useful in following disease progression in individual patients, it must also be possible to *record* the data reproducibly. This factor is of particular concern with Doppler echocardiography because it is technically demanding. Accurate and reproducible recording of aortic jet velocity requires a meticulous continuous wave Doppler examination, with careful transducer angulation from several windows to obtain a near parallel intercept angle between the direction of blood flow and the ultrasound beam. Recording outflow tract velocity requires careful placement of the pulsed Doppler sample volume just proximal to the region of flow acceleration into the jet.

In this study, recording of aortic jet and outflow tract velocities by two independent observers showed that in our laboratory these data can be recorded reproducibly. Thus, Doppler measures of aortic stenosis severity are well suited for monitoring hemodynamic progression. Measurement variability is best expressed as a percentage (the mean coefficient of variation) because the absolute value of the variability will differ over the range of the measurement. In an individual patient with measurements at the mid-range of our sample, a change in aortic jet velocity of approximately 0.2 m/s (corresponding to ±2 mean coefficients of variation) or a change in outflow tract velocity of 0.1 m/s would be outside the range of test variability. Given that outflow tract diameter is relatively constant in each patient, the variability in aortic valve area measurement is expected to be approximately 8% (a change of ±0.15 cm^2).

In fact, variability in valve area may be less than this value because intertest variability includes not only technical factors in recording the data and intraobserver variability in measuring the data, but also temporal variability of flow velocities in these patients. Even when valve area remains constant, changes in transaortic volume flow (and therefore outflow tract velocity) and transaortic pressure gradient (and therefore aortic jet velocity) may occur because of physiologic changes between examinations.

Rate of disease progression. Previous studies of hemodynamic progression of aortic stenosis (9–13) have utilized invasive measures of pressure gradient and valve area. When changes in hemodynamic measurements are standardized for follow-up intervals, each of these studies demonstrates a variable rate of increase in stenosis severity from patient to patient, with transaortic pressure gradient increasing by 0 to 45 mm Hg/year and valve area decreasing by 0 to 0.6 cm^2/year. Normalized rates of progression (in those studies that report data allowing these calculations) are shown in Table 2. Data in the current study also showed a variable rate of stenosis progression among patients with similar directional changes in pressure gradient and valve area.

Because pressure gradient depends on transaortic volume flow as well as valve area, an increase in the severity of stenosis often occurs despite no change or a decrease in

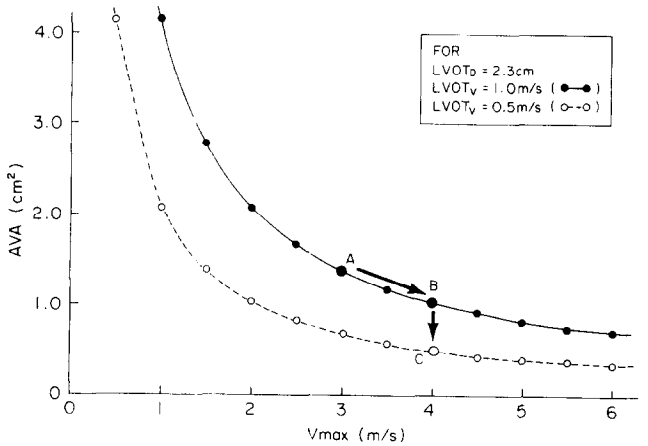
Table 2. Comparison With Previous Reports on Hemodynamic Progression of Aortic Stenosis Severity

Reference	n	Change in Mean ΔP (mm Hg/yr)	Change in AVA (cm^2/yr)
Bogart et al. (9)	11	1.2 to 24 (11.6)	0.02 to 0.6 (0.2)
Cheitlin et al. (10)	29	−12 to 45 (8.4)*	NA
Nestico et al. (11)	29	−8 to 10.4 (0.8)	0 to 0.5 (0.05)
Wagner et al. (12)	50	Group I = "rapid" (n = 21);	0.3 ± 0.2
		Group II = "slow" (n = 29)	0.02 ± 0.08
Current series	42	−7 to 23 (8)	0 to 0.5 (0.1)

*Peak instead of mean systolic pressure gradient reported. for each study the number of patients enrolled (n), the range and mean (in parentheses) of the change in pressure gradient (ΔP) and the range and mean (in parentheses) of the change in aortic value area (AVA) are shown. The first four studies were performed with use of invasive hemodynamics. NA = not available.

transaortic pressure gradient as a result of a decline in transaortic volume flow, as is illustrated for a hypothetical case in Figure 5. Clinically, increased stenosis severity without an increase in transaortic pressure gradient is most likely to occur when left ventricular dysfunction develops, secondary either to the aortic obstruction itself or to coexisting cardiac disease (especially coronary artery disease). An increase in stenosis severity without an increase in transaortic pressure gradient occurred in 25% of our patients. In this situation, noninvasive calculation of aortic valve area with use of the continuity equation is essential for identifying progression of severity.

Figure 5. Relation between aortic valve area (AVA) calculated with the continuity equation and maximal aortic jet velocity (V_{max}) is shown for a constant left ventricular outflow tract diameter ($LVOT_D$) and two hypothetical outflow tract maximal velocities ($LVOT_V$). If valve area decreases while volume flow remains constant, a patient may initially progress from A to B with a corresponding decrease in maximal aortic jet velocity. However, if volume flow also has decreased, a decrease in valve area can occur (B to C) with *no* change in maximal aortic jet velocity.



Although several investigators (9,11,12) suggest that patients with aortic stenosis can be classified into those with rapid or slow progression, these observers differ in whether rapid progression is related to decreased cardiac output (9), milder degree of stenosis at entry (11) or etiology of valve disease (12). In the current study, those patients who subsequently required valve replacement because of progressive symptoms had a more rapid rate of progression than those who remained asymptomatic. However, we were unable to identify factors that distinguished these patients at the initial study, including age, etiology of valve disease, severity of valve disease at entry or coexisting aortic insufficiency. The relatively small number of patients limits subgroup analysis, and identification of factors that predict the rate of disease progression in an individual patient may be possible in a larger study. In addition, a longer follow-up and inclusion of more patients with mild disease may be instructive.

Conclusions. Doppler echocardiography has several advantages over invasive techniques in following the hemodynamic progression of aortic stenosis. It is noninvasive and relatively inexpensive, as well as accurate and reproducible. It should be ideal for prospective cohort studies on the hemodynamic progression of aortic stenosis in adults with a wide range of initial disease severity, with multiple assessments of hemodynamic severity made over longer follow-up intervals.

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