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Physiologic Changes With Maximal Exercise in Asymptomatic Valvular Aortic Stenosis Assessed by Doppler Echocardiography

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Objectives. We hypothesized that the physiologic response to exercise in valvular aortic stenosis could be measured by Doppler echocardiography.

Background. Data on exercise hemodynamics in patients with aortic stenosis are limited, yet Doppler echocardiography provides accurate, noninvasive measures of stenosis severity.

Methods. In 28 asymptomatic subjects with aortic stenosis maximal treadmill exercise testing was performed with Doppler recordings of left ventricular outflow tract and aortic jet velocities immediately before and after exercise. Maximal and mean volume flow rate (Q_{max} and Q_{mean}), stroke volume, cardiac output, maximal and mean aortic jet velocity (V_{max}, V_{mean}), mean pressure gradient (ΔP) and continuity equation aortic valve area were calculated at rest and after exercise.

The actual change from rest to exercise in Q_{max} and V_{max} was compared with the predicted relation between these variables for a given orifice area. Subjects were classified into two groups: Group I (rest-exercise V_{max}/Q_{max} slope >0, n = 19) and Group II (slope ≤ 0, n = 9).

Results. Mean exercise duration was 6.7 ± 4.3 min. With exercise, V_{max} increased from 3.99 ± 0.93 to 4.61 ± 1.12 m/s ($p < 0.0001$) and mean ΔP increased from 39 ± 20 to 52 ± 26 mm Hg ($p < 0.0001$). Q_{max} rose with exercise (422 ± 117 to 523 ± 209 ml/s, $p < 0.0001$), but the systolic ejection period decreased (0.33 ± 0.04 to 0.24 ± 0.04, $p < 0.0001$), so that stroke volume decreased slightly (98 ± 29 to 89 ± 32 ml, $p = 0.01$). The increase in cardiac output with exercise (6.5 ± 1.7 to 10.2 ± 4.4 liters/min, $p < 0.0001$) was mediated by increased heart rate (71 ± 17 to 147 ± 28 beats/min, $p < 0.0001$). There was no significant change in the mean aortic valve area with exercise (1.17 ± 0.45 to 1.28 ± 0.65, $p = 0.06$).

Compared with Group I patients, patients with a rest-exercise slope ≤ 0 (Group II) tended to be older (69 ± 12 vs. 58 ± 19 years, $p = 0.07$) and had a trend toward a shorter exercise duration (5.3 ± 2.9 vs. 7.3 ± 4.9 min, $p = 0.20$). There was no difference between groups for heart rate at rest, blood pressure, stroke volume, cardiac output, V_{max}, mean ΔP or aortic valve area. With exercise, Group II subjects had a lower cardiac output (7.4 ± 2.4 vs. 11.5 ± 4.6 liters/min, $p = 0.005$) and a smaller percent increase in V_{max} (3 ± 9% vs. 22 ± 14%, $p < 0.0001$).

Conclusions. Doppler echocardiography allows assessment of physiologic changes with exercise in adults with asymptomatic aortic stenosis. A majority of subjects show a rest-exercise response that closely parallels the predicted relation between V_{max} and Q_{max} for a given orifice area. The potential utility of this approach for elucidating the relation between hemodynamic severity and clinical symptoms deserves further study.

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Doppler echocardiography allows accurate assessment of the severity of both valvular aortic stenosis (pressure gradient and valve area) (1–5) and transaortic volume flow (stroke volume and cardiac output) (6) at rest. The purpose of the current study was to evaluate the feasibility of using Doppler echocardiography to assess exercise physiology and to explore the rest-exercise hemodynamic response in adults with asymptomatic valvular aortic stenosis.

Methods

Patient group. The study group was derived from 34 consecutive asymptomatic subjects being followed in the prospective Progression of Aortic Stenosis Study (PASS). Entry criteria for this study are age >18 years, abnormal aortic valve by two-dimensional echocardiography (leaflet separation <15 mm), maximal aortic jet velocity ≥2.5 m/s and absence of symptoms due to aortic valve stenosis. Potential subjects were not excluded for other coexisting cardiac or noncardiac diseases. Four potential subjects were unable or unwilling to undergo exercise testing, one had asymptomatic ventricular bigeminy for 5 min after exercise and in one subject, the videorecorder malfunctioned. The remaining 28 subjects formed the basis of this report. The protocol was approved by our Institutional Review Board and written informed consent was obtained from each subject.

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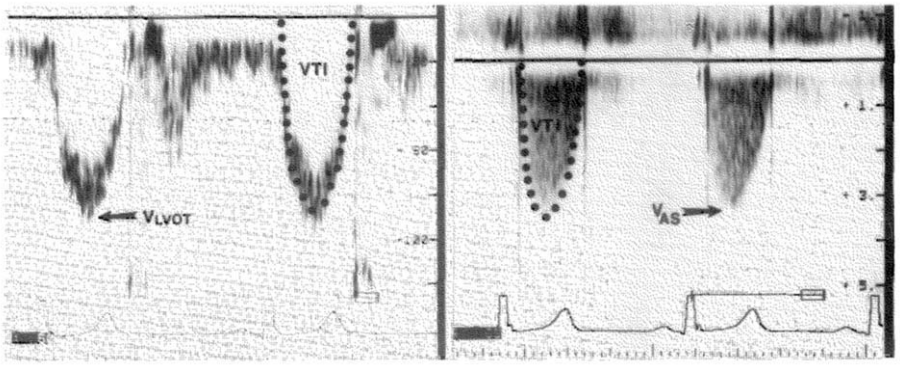

Figure 1. Recordings of left ventricular outflow tract (LVOT) velocity measured with pulsed Doppler echocardiography (**left**) and aortic stenosis (AS) jet velocity measured with continuous wave ultrasound (**right**). In both curves, maximal velocity (V_{LVOT} and V_{AS}, respectively) and the velocity-time integral (VTI) are labeled.

The age range was 22 to 84 years (mean 61 ± 18); 10 patients (36%) were women and 18 (64%) were men. The etiology of aortic stenosis was congenital (unicuspid or bicuspid) in 8 subjects and secondary to valve leaflet calcification in 20.

Study protocol. At rest, a Doppler and two-dimensional echocardiographic examination was performed with the subject in the left lateral decubitus position. Parasternal long-axis, two-dimensional images were used to measure left ventricular outflow tract diameter in mid-systole, parallel to the valve plane and just proximal to the aortic leaflet insertion into the anulus. Left ventricular outflow tract velocity was recorded from an apical approach using pulsed Doppler echocardiography with a 5- to 10-mm sample volume length. Care was taken to position the sample volume just proximal to the aortic valve (identified by the valve closing click) but not in the jet or proximal flow convergence region (identified by acceleration and spectral broadening of the Doppler velocity curve). The aortic stenosis jet was recorded with continuous wave Doppler ultrasound (VingMed SD-100 instrument) from that window yielding the highest velocity signal. Multiple transducer positions and angulations with appropriate patient positioning were used to record the highest jet velocity. The best windows for outflow tract and aortic jet velocities were marked on the subject's chest to facilitate data acquisition after exercise.

Rest images of the left ventricle from parasternal and apical windows were recorded for quantitative evaluation of left ventricular mass and systolic function obtained with the apical biplane method (7). Coexisting aortic regurgitation was assessed with Doppler color flow imaging and graded as absent, mild, moderate or severe (8).

Next, the subject underwent maximal Bruce protocol treadmill exercise testing with continuous monitoring of the 12-lead electrocardiogram (ECG) (Marquette Instruments) and intermittent auscultatory measurement of cuff arm blood pressures. Immediately after exercise, the subject returned to the left lateral decubitus position on the echocardiographic examination stretcher (with an apical cutout) located next to the treadmill. Repeat recordings, in sequence, of aortic stenosis jet velocity with continuous wave Doppler echocardiography, followed by pulsed Doppler recordings of outflow tract velocity, were made within 2 min of stopping exercise. Signal loss during inspiration was prominent, so that velocity measures were made only from high quality Doppler signals obtained between breaths. Electrocardiographic and blood pressure monitoring were continued for 5 min after exercise or until all exercise-induced changes had resolved.

Doppler calculations. Rest and immediate postexercise maximal aortic jet velocities (V_{max} in m/s) and outflow tract velocities (V_{LVOT} in cm/s) were averaged from three high quality signals (Fig. 1). The systolic velocity-time integrals (VTI in cm) from the aortic jet and outflow tract were determined by integrating the respective velocity curves during the period of flow. Rest outflow tract diameter was used to calculate a circular cross-sectional area (CSA_{LVOT} in cm^2). Maximal volume flow rate (Q_{max} in cm^3/s) was calculated as:

$$Q_{max} = V_{LVOT} \times CSA_{LVOT}. \quad [1]$$

Stroke volume (SV in cm^3) was calculated as (10):

$$SV = VTI_{LVOT} \times CSA_{LVOT}, \quad [2]$$

where VTI_{LVOT} = velocity-time integral of the left ventricular outflow tract. Cardiac output was then computed as heart rate times stroke volume. Aortic valve area (AVA in cm^2) was calculated with the continuity equation (3–5):

$$AVA = \frac{VTI_{LVOT}}{VTI_{AS}} \times CSA_{LVOT}, \quad [3]$$

where VTI_{AS} = velocity-time integral of the aortic stenosis jet. Maximal transaortic pressure gradient (ΔP_{max} in mm Hg) was calculated with the simplified Bernoulli equation (1–5):

$$\Delta P_{max} = 4V_{max}^2. \quad [4]$$

Mean gradient was determined by averaging the instantaneous pressure gradients over the period of flow.

The ratio of maximal velocity in the outflow tract (V_{LVOT}) to that in the aortic jet (V_{max}) was calculated at rest and after exercise as:

$$\text{Velocity ratio} = V_{LVOT}/V_{max}. \quad [5]$$

Predicted exercise response. The relation between maximal volume flow rate and maximal jet velocity is predictable

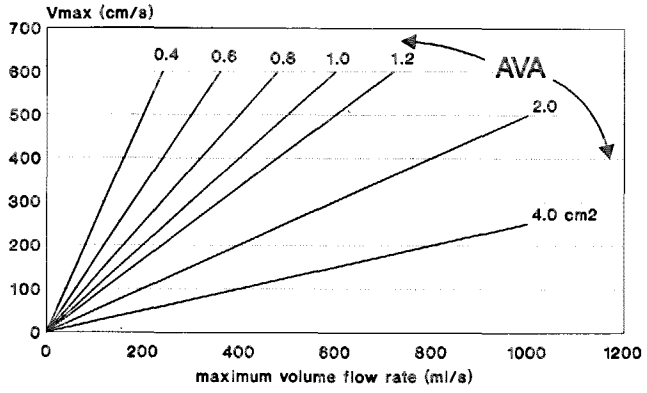

Figure 2. Graph of the predicted relation between maximal aortic jet velocity (V_{max}, y axis) and maximal volume flow rate (Q_{max}, x axis) and for a given aortic valve area (AVA), as indicated by the individual lines.

for a given orifice area. Stroke volume through the narrowed orifice equals the cross-sectional area of flow (in this case, aortic valve area) multiplied by mean flow velocity times the systolic ejection period (SEP):

$$SV = AVA \times \text{Mean velocity} \times SEP. \quad [6]$$

At maximal ejection, assuming simultaneous maximal flow rate and jet velocity, the maximal volume flow rate will equal valve area times jet velocity:

$$Q_{max} = AVA \times V_{max}. \quad [7]$$

For mean flow rate (Q_{mean}) and jet velocity (V_{mean}):

$$Q_{mean} = AVA \times V_{mean}. \quad [8]$$

Stated differently, for a fixed degree of valve stenosis, the expected maximal and mean jet velocity can be determined for each maximal and mean volume flow rate, respectively. Thus, as volume flow rate increases with exercise, a predictable increase in aortic jet velocity should occur. This predicted relation is graphed for several valve areas in Figure 2.

There are two important assumptions underlying this predicted relation, which must be considered in data analysis:

1. Maximal volume flow rate and jet velocity (or pressure gradient) occur simultaneously in the presence of valvular aortic stenosis. Although it is clear that these two events are *not* simultaneous with a normal aortic valve or in the presence of dynamic subaortic obstruction, data from in vitro models and clinical observation (9,10) suggest that this assumption is warranted in the setting of valve stenosis.

2. This predicted relation applies to a *fixed* physiologic orifice area (11). Some investigators (12,13) have suggested that the discharge coefficient for a stenotic orifice varies with volume flow rate (especially at low flow rates) so that effective flow area may vary for a given anatomic orifice. However, other investigators have shown no significant change in the discharge coefficient with flow rate (although it was influenced by orifice size and shape) (14). Thus, the importance of potential variations in the orifice discharge coefficient remains unclear in the clinical setting of aortic stenosis. In addition, if actual changes in the degree of leaflet opening were to occur in some patients with changing volume flow rates, the rest-exercise slope would deviate from the predicted relation. Of note, the continuity equation measures the effective flow area (the physiologic orifice) rather than the anatomic valve area.

Table 1. Intraobserver and Interobserver Variability for Doppler-Echocardiographic Data (n = 14)

	Intraobserver		Interobserver	
Measurement	Mean Diff ± 1 SD	r Value	Mean Diff ± 1 SD	r Value
LVOT velocity (m/s)				
Rest	−0.06 ± 0.08	0.91	0.09 ± 0.10	0.84
Postexercise	−0.03 ± 0.12	0.90	0.09 ± 0.14	0.85
AS jet velocity (m/s)				
Rest	−0.15 ± 0.18	0.98	0.17 ± 0.22	0.97
Postexercise	−0.03 ± 0.10	0.99	0.07 ± 0.18	0.99
LVOT diameter (cm)	0 ± 0.08	0.98	0 ± 0.10	0.96

AS = aortic stenosis; Diff = difference; LVOT = left ventricular outflow tract.

Measurement variability. Intraobserver and interobserver variability for measurement of rest and exercise aortic jet velocity and outflow tract velocity and for rest outflow tract diameter were assessed in 14 (50%) subjects in the study group (Table 1) by calculation of the mean difference (and SD of the difference) between the two measurements and by calculation of Pearson's correlation coefficient.

In 19 subjects, repeat recordings of outflow tract diameter at rest and after exercise were obtained at a subsequent exercise test. The rest and exercise diameters correlated closely (r = 0.97) with little difference between the measurements (0 ± 0.06 cm).

Statistical analysis. Values were expressed as mean value ± 1 SD. Differences between rest and exercise data were compared using the paired *t* test. Group means were compared by using the unpaired *t* test. A p value ≤ 0.05 was considered significant. The rest and exercise values of aortic jet velocity (y axis) and maximal volume flow rate (x axis) were plotted for each subject and the slope of the straight line between these points defined as the actual rest-exercise slope. The predicted slope was calculated from the expected V_{max} or V_{mean} using the *actual* Q_{max} or Q_{mean} and rest aortic valve area in equations 7 and 8.

Subgroup analysis. Based on the observed relation between actual versus predicted rest-exercise slope, subjects were subgrouped as follows:

Group I: V_{max}/Q_{max} slope >0 (n = 19) with:
(Group IA) Actual slope ≤ predicted slope (n = 12), or
(Group IB) Actual slope > predicted slope (n = 7);
Group II: V_{max}/Q_{max} slope ≤ 0 (flat or negative) (n = 9).

Analogous groups were defined on the basis of V_{mean}/Q_{mean} slope.

Results

Exercise testing. Exercise duration ranged from 1 to 16.8 min (mean 6.7 ± 4.3). In 25 of the 28 subjects, maximal exercise was limited by fatigue (54%), leg discomfort (21%) or shortness of breath (14%). In the remaining three subjects (11%), an asymptomatic decrease in systolic blood pressure (≥10 mm Hg) occurred; the exercise test was stopped at that time. No subject complained of chest discomfort. In 21 subjects (75%) >1 mm flat or downsloping ST depression was observed. In 8 of these 21 subjects, the rest ECG was consistent with left ventricular hypertrophy with strain. In three subjects ST depression persisted up to 20 min after exercise. Occasional premature ventricular beats were common (11 [39%] of 28); one subject had an asymptomatic, three-beat run of ventricular tachycardia. There were no major complications.

Baseline Doppler and echocardiographic findings. At rest, maximal aortic jet velocity ranged from 2.5 to 6.1 m/s (mean 3.99 ± 0.93), maximal transaortic pressure gradient from 25 to 149 mm Hg (mean 67 ± 31), mean transaortic pressure gradient from 12 to 94 mm Hg (mean 39 ± 20) and valve area from 0.5 to 2.1 cm^2 (mean 1.2 ± 0.4 cm^2). Coexisting aortic regurgitation was present in 22 (79%) of 28 subjects; it was mild (1+) in 13 and moderate (2+) in 9; no subject had severe aortic regurgitation.

Left ventricular systolic function by qualitative evaluation was normal in 27 (96%) of 28 subjects and mildly reduced in the remaining subject. Quantitative two-dimensional echocardiographic ejection fraction ranged from 49% to 82% (mean 67 ± 9%). Left ventricular mass index ranged from 39 to 137 g/m^2 (mean 87 ± 24) with 4 (14%) of 28 having a mass index >120 g/m^2.

Physiologic changes with exercise (Table 2). Heart rate and blood pressure increased with exercise. The maximal instantaneous and mean flow rate increased significantly in conjunction with a decrease in the systolic ejection period, so that stroke volume declined slightly with exercise. Despite this fall in stroke volume, cardiac output increased significantly because of the increase in heart rate. Aortic jet maximal and mean velocities (and corresponding pressure gradients) increased significantly with exercise. There was no significant change in the average continuity equation valve area or in the ratio of outflow tract to aortic jet maximal velocities.

The rest-exercise V_{max}/Q_{max} slope ranged from −11.3 to 2.6 (mean 0 ± 2.6). The difference between the predicted and actual slopes ranged from −21.2 to 2.2 (mean −1.2 ± 4.3). The rest-exercise V_{mean}/Q_{mean} slope ranged from −3.6 to 9.1 (mean 1.0 ± 2.1). The difference between predicted and actual slopes ranged from −1.7 to 12.6 (mean 0.3 ± 2.6). Results for subgroups defined by the V_{mean}/Q_{mean} slope were similar to those for groups defined by the V_{max}/Q_{max} slope so that only the latter are presented in the next section.

Comparison between Group I and Group II (Table 3). Subjects with a rest-exercise slope >0 (Group I) were compared with those with a slope ≤0 (Group II). As detailed in Table 3, these groups did *not* differ with respect to rest or exercise blood pressure, heart rate, systolic ejection period, aortic jet velocity or valve area. Cardiac output was higher in Group I with exercise but was not different at rest. Group I subjects tended to be younger with a trend toward a longer exercise duration. Even though rest maximal flow rate did not differ, exercise maximal flow rate was higher in Group I. The percent increase in maximal volume flow rate with exercise was 35 ± 30% in Group I versus −2 ± 12% in Group II ($p < 0.0001$), and the percent increase in aortic jet velocity was also greater in Group I (22 ± 14% vs. 3 ± 9%, $p < 0.0001$). The actual and predicted rest-exercise slopes closely paralleled each other in Group I (Fig. 3), with a difference between the actual and predicted V_{max}/Q_{max} slope of 0.3 ± 0.9. In contrast (Fig. 4), actual and predicted slopes varied more notably in Group II, with a mean difference of −4.7 ± 6.8 ($p = 0.08$).

Continuity equation valve area increased slightly in Group I (7 ± 16%) and decreased slightly in Group II (−5 ± 22%), although this difference did not reach statistical significance ($p = 0.15$).

Rest-exercise response in Group I. In Group I, 12 subjects had an actual rest-exercise slope less than or equal to that predicted (Group IA), whereas 7 subjects had an actual slope greater than that predicted (Group IB). Comparing Groups IA and IB, there was no statistically significant difference for age (53 ± 21 vs. 65 ± 17 years), exercise duration (8.2 ± 5.2 vs. 5.8 ± 4.3 min), rest or exercise heart rate, blood pressure, systolic ejection periods, aortic jet velocity, stroke volume, valve area, left ventricular ejection fraction or mass. Rest maximal volume flow rate and cardiac output were not different. However, Group IA had a higher exercise

Table 2. Rest and Postexercise Data for the 28 Study Subjects

	Rest	Exercise	p Value
Heart rate (beats/min)	71 ± 17	147 ± 28	<0.0001
Systolic blood pressure (mm Hg)	139 ± 15	155 ± 24	<0.0001
Maximal transaortic gradient (mm Hg)	67 ± 31	90 ± 40	<0.0001
Mean transaortic gradient (mm Hg)	39 ± 20	52 ± 26	<0.0001
Systolic ejection period (s)	0.33 ± 0.04	0.24 ± 0.04	<0.0001
Stroke volume (ml)	98 ± 29	89 ± 32	0.01
Cardiac output (liters/min)	6.5 ± 1.7	10.2 ± 4.4	<0.0001
Maximal flow rate (Q_{max}, ml/s)	422 ± 117	523 ± 209	<0.0001
Maximal aortic jet velocity (V_{max}, m/s)	3.99 ± 0.93	4.61 ± 1.12	<0.0001
Mean flow rate (Q_{mean}, ml/s)	300 ± 85	366 ± 159	0.005
Mean jet velocity (V_{mean}, m/s)	2.76 ± 0.75	3.27 ± 0.95	<0.0001
V_{LVOT}/V_{max} ratio	0.27 ± 0.08	0.28 ± 0.10	NS
Aortic valve area (cm^2)	1.17 ± 0.45	1.28 ± 0.65	0.06

V_{LVOT} = maximal left ventricular outflow tract velocity, cm/s.

JACC Vol. 20, No. 5
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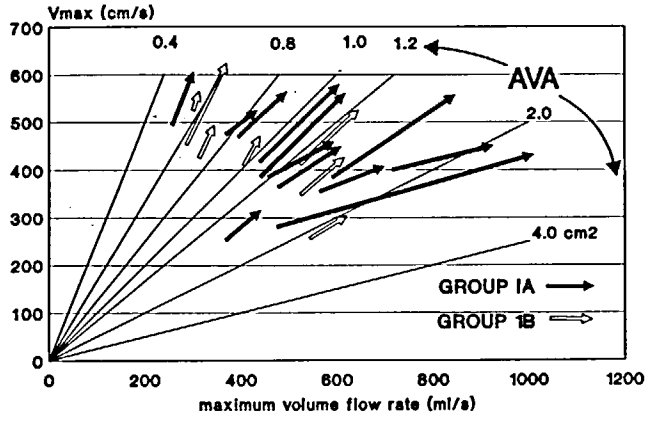


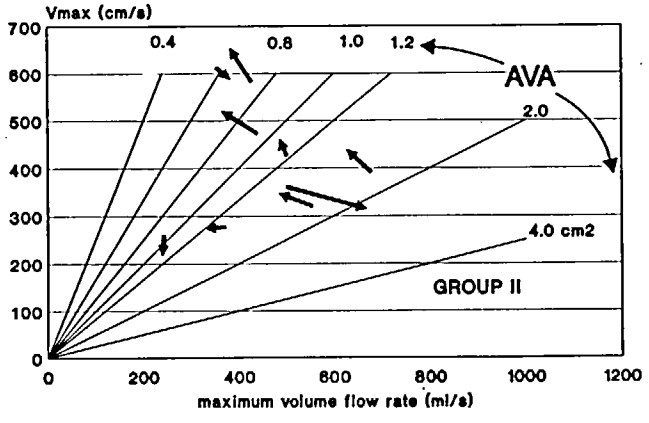
Figure 3. Graph in the same format as Figure 2 comparing the actual rest-exercise responses in Group I subjects (V_{max}/Q_{max} slope >0) with the predicted responses (**solid thin lines**). Data from individual subjects are indicated by an **arrow**, with rest values at the **base** and exercise values at the **tip of the arrow**. Group IA subjects (actual slope less than or equal to that predicted) are indicated by **solid arrows** and Group IB subjects (actual slope greater than that predicted) by **open arrows**. Abbreviations as in Figure 2.

maximal volume flow rate (649 ± 234 vs. 442 ± 127 ml/s, p = 0.02), percent increase in volume flow rate (47 ± 31% vs. 12 ± 7%, p = 0.002) and exercise cardiac output (13.2 ± 4.7 vs. 8.5 ± 2.3, p = 0.01). The difference between the actual and predicted rest-exercise slope was smaller in Group IA (−0.32 ± 0.26 vs. 1.3 ± 0.7, p = 0.001), and there was a nonsignificant difference in the percent increase in valve area with exercise (13 ± 12% vs. −2 ± 18%, p = 0.08).

In Group I, three subjects developed symptoms requiring valve replacement at 6-month follow-up. All three had high rest and exercise aortic jet velocities; two were in Group IB.

Rest-exercise response in Group II. Of the nine subjects with a flat or negative rest-exercise slope, two had a decrease in aortic jet velocity despite a rise in maximal volume flow rate; both of these subjects had the treadmill test stopped because of an exertional decrease in systolic blood pressure ≥10 mm Hg, and one subsequently developed symptoms and underwent aortic valve replacement. In five subjects, aortic jet velocity increased despite a decrease in maximal volume flow rate; one of these subjects had exertional hypotension and one developed symptoms requiring valve replacement by 6-month follow-up. Of the remaining two subjects, one had a slight decrease in volume flow rate with no change in jet velocity, whereas the other had no change in volume flow rate with a slight decrease in jet velocity (in association with atrial fibrillation and a substantial increase in heart rate during exercise).

Figure 4. Graph showing the actual rest-exercise responses in Group II subjects (V_{max}/Q_{max} slope ≤0). Format and abbreviations as in Figures 2 and 3.



Discussion

In this study, we have demonstrated the feasibility of using Doppler echocardiography to assess physiologic changes with exercise in adults with valvular aortic stenosis, described hemodynamic changes in a group of asymptomatic subjects with aortic stenosis and compared the actual rest-exercise change in maximal aortic jet velocity and transaortic volume flow rate with the predicted relation for these variables, assuming a fixed orifice area.

Hemodynamic changes with exercise. In these asymptomatic subjects, cardiac output rose appropriately with exercise. This increase was mediated entirely by an increase in heart rate; group mean stroke volume decreased slightly. A significant increase in aortic jet velocity and transaortic pressure gradient was noted with exercise. Changes in transaortic pressure gradient with changes in volume flow rate have been well documented in previous in vitro, animal and clinical studies with both invasive and noninvasive techniques (15–21). However, the exact relation between the substantial increase in pressure gradient with exercise despite only a minimal change in stroke volume has been poorly defined (15,16). The current study offers a plausible explanation for this observation in that although stroke volume decreases slightly with exercise, the systolic ejection period decreases as well, such that there are increases both in the mean transaortic volume flow rate during the period of flow and in the *maximal* volume flow rate. Thus maximal aortic jet velocity increases as predicted by the continuity equation, and corresponding increases are observed in maximal and mean transaortic pressure gradient (as predicted by the Bernoulli equation).

For the entire study group, there was no significant change in the group mean aortic valve area determined by the continuity equation, suggesting that on average there is no substantial change in physiologic flow area as volume flow rate changes. The apparent discrepancy between this observation and previous measures of valve area with exercise (22,23) may relate to the different assumptions underlying valve area calculations using the Gorlin formula and the continuity equation. However, it is intriguing to note a trend toward an increase in valve area with exercise in some

Table 3. Comparison Between V_{max}/Q_{max} Rest-Exercise Slope Subgroups

	Group I (slope >0) (n = 19)	Group II (slope ≤0) (n = 9)	p Value
Age (yr)	58 ± 20	69 ± 12	0.07
Exercise duration (min)	7.3 ± 4.9	5.3 ± 2.9	0.20
Heart rate (beats/min)			
Rest	70 ± 14	72 ± 22	NS
Exercise	148 ± 32	143 ± 20	NS
Systolic blood pressure (mm Hg)			
Rest	136 ± 17	143 ± 11	NS
Exercise	158 ± 23	149 ± 28	NS
Mean transaortic gradient (mm Hg)			
Rest	37 ± 14	41 ± 29	NS
Exercise	54 ± 20	47 ± 36	NS
Systolic ejection period			
Rest	0.34 ± 0.03	0.32 ± 0.05	NS
Exercise	0.24 ± 0.03	0.25 ± 0.05	NS
Stroke volume (ml)			
Rest	100 ± 27	95 ± 33	NS
Exercise	95 ± 32	74 ± 28	0.11
Cardiac output (liters/min)			
Rest	6.6 ± 1.9	6.3 ± 1.3	NS
Exercise	11.5 ± 4.6	7.4 ± 2.4	0.005
Q_{max} (ml/s)			
Rest	420 ± 119	427 ± 120	NS
Exercise	572 ± 222	419 ± 130	0.03
Change (%)	35 ± 30	−2 ± 12	<0.0001
V_{max} (m/s)			
Rest	3.94 ± 0.75	4.09 ± 1.29	NS
Exercise	4.79 ± 0.92	4.24 ± 1.46	NS
Change (%)	22 ± 14	3 ± 9	<0.0001
Aortic valve area (cm^2)			
Rest	1.2 ± 0.5	1.2 ± 0.5	NS
Exercise	1.4 ± 0.7	1.1 ± 0.5	NS
Change (%)	7 ± 16	−5 ± 22	0.15
Difference between actual and predicted slope (%)	0.3 ± 0.9	−4.7 ± 6.8	0.08
Ejection fraction (%)	67 ± 9	65 ± 8	NS
LV mass index (g/m^2)	82 ± 23	99 ± 23	0.09

All values are expressed as mean value ± 1 SD. LV = left ventricular; Q_{max} = maximal volume flow rate; V_{max} = maximal aortic jet velocity.

subjects with aortic stenosis, whereas others show an apparent decrease in valve area.

Rest-exercise relation. We hypothesized that the rest-exercise change in aortic jet velocity should be predictable for a given change in maximal volume flow rate as shown in Figure 1. In the majority of subjects (Group I, 19 of 28), the actual rest-exercise response did closely parallel this predicted relation, supporting the validity of this hypothesis. Whether the observed differences between subjects with a rest-exercise slope less than or equal to that predicted (Group IA) versus those with a rest-exercise slope greater than that predicted (Group IB) represent actual physiologic differences between these groups is unclear. One could postulate that those with a slope flatter than predicted have an increase in orifice area with exercise due to increased opening of the valve leaflets. Possibly those with a steeper than predicted slope may have stiff valves with a fixed anatomic orifice area, a change in the discharge coefficient and a decrease in functional orifice area with exercise. Conversely, given the technical difficulties in recording outflow tract and aortic jet velocities immediately after exercise and the possibility of a nonparallel intercept angle between flow and the ultrasound beam, these apparent differences may be artifactual.

The more problematic subgroup includes those subjects with a negative rest-exercise slope (Group II). The subjects with a decrease in maximal aortic jet velocity despite an increase in maximal volume flow rate may have increased leaflet opening with exercise resulting in a larger effective orifice area, or aortic jet velocity may have been underestimated immediately after exercise. The five subjects who had an increase in aortic jet velocity despite a decrease in maximal volume flow rate are of interest from two points of view. First, a decrease in maximal flow rate in an asympto-

matic subject is surprising, raising the possibility that these subjects have exercise-induced left ventricular dysfunction and are either denying exercise limitation or will soon develop overt symptoms of aortic stenosis (24,25). Second, an increase in jet velocity despite a decrease in volume flow rate is incompatible with a fixed orifice area, assuming that volume flow rate was measured correctly. Possible explanations for this observation include a decrease in anatomic orifice area due to decreased leaflet opening, or a decrease in the discharge coefficient of the stenotic valve at lower volume flow rates. Technical problems in data recording are the most likely explanation for these findings, especially because the shorter exercise duration in some of these elderly subjects increases the likelihood of error in comparing differences between rest and exercise values. However, the observations that patients with a flat or negative rest-exercise slope are older, have a trend toward a shorter exercise duration and have a higher incidence of exertional hypotension suggest that these may represent actual physiologic differences.

Study limitations. Although Doppler echocardiographic measures of aortic stenosis severity and transaortic volume flow are well validated and reproducible when performed at rest, recording these data immediately after exercise is technically demanding. Some elderly subjects cannot transfer quickly from the treadmill to the echocardiographic stretcher. The nonsteady state nature of the postrecovery period limits the time available for data recording. Outflow tract and aortic jet velocities were recorded within a few seconds of each other in most cases. Respiratory interference limits the number of beats available for measurement. The intrathoracic position of the heart may vary between rest and immediate postexercise recordings, so that care must be taken to obtain a near-parallel intercept angle between the ultrasound beam and direction of blood flow. However, given experience and careful attention to methodology, we think reliable data can be obtained with this technique. Because these patients were asymptomatic, coronary angiography was not performed and a possible confounding influence by coexisting asymptomatic coronary disease cannot be excluded.

Changes in left ventricular ejection fraction were not assessed in this study because of time considerations, although the observed increase in cardiac output (a mean increase of 57%) is similar to that in other studies (26). Possible abnormalities in left ventricular diastolic function also could not be evaluated. Further studies of the rest-exercise changes in left ventricular systolic and diastolic function in asymptomatic aortic stenosis are needed and may provide an explanation for some of the hemodynamic findings observed in the current study.

Risks of exercise testing. Although to date no major complications have been observed, it should be noted that minor complications of treadmill exercise testing (ST depression, ventricular ectopic activity, asymptomatic blood pressure decrease) were common. Further, it must be emphasized that we included only *asymptomatic* adults with valvular aortic stenosis who had normal or only mildly reduced left ventricular systolic function. Larger studies (27–29) on the complication rate of treadmill exercise have shown a similar low incidence of complications in asymptomatic subjects with aortic stenosis, but the complication rate increases dramatically once symptoms occur.

The current study was performed as part of a defined research protocol. At this time, we do *not* advocate clinical exercise testing even in asymptomatic adults with aortic stenosis. The published data indicate that exercise testing should be performed with extreme caution or not at all in patients with symptomatic aortic stenosis.

Clinical implications. In adults with aortic stenosis, prognosis strongly depends on the presence or absence of symptoms (30–32). However, there is marked overlap in hemodynamic severity between symptomatic and asymptomatic patients (31–33). The physiologic explanation for this apparent paradox is unclear.

As in many other cardiac diseases, symptoms in aortic stenosis initially occur with physical exertion. It is possible that symptom onset relates to impairment of cardiac functional reserve rather than to an arbitrary degree of stenosis. If this is true, then the physiologic response to exercise should provide insight into the relation between hemodynamic severity and the onset of clinical symptoms.

Conclusions. We conclude that Doppler echocardiography offers a feasible approach to noninvasive assessment of physiologic changes with exercise in valvular aortic stenosis. There is a predictable relation between aortic jet velocity and maximal volume flow rate for a given orifice area, and the majority of subjects show a rest-exercise response that closely parallels this relation. The potential utility of this approach in elucidating the interaction between the hemodynamic severity of the lesion and the development of clinical symptoms requires further study.

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