Abnormal Vascular Responses to Exercise in Patients with Aortic Stenosis

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ABSTRACT We tested the hypothesis that the normal forearm vasoconstrictor response to leg exercise is inhibited or reversed in patients with aortic stenosis, possibly because of activation of left ventricular baroreceptors. Forearm vascular responses to supine leg exercise were measured in 10 patients with aortic stenosis and in 2 control groups of 6 patients with mitral stenosis and 5 patients without valvular heart disease.

Forearm vasoconstriction occurred during exercise in the control groups. In contrast, forearm blood flow increased and forearm vascular resistance did not change in patients with aortic stenosis. In six patients with aortic stenosis and a history of exertional syncope, forearm vasodilatation occurred during the second minute of leg exercise. Inhibition or reversal of forearm vasoconstrictor responses in aortic stenosis was asscociated with significant increases in left ventricular pressure.

In three patients with aortic stenosis and exertional syncope, forearm vasodilator responses to exercise changed to vasoconstrictor responses after aortic valve replacement.

The results indicate that forearm vasoconstrictor responses to leg exercise are inhibited or reversed in patients with aortic stenosis, possibly because of activation of left ventricular baroreceptors. The observations suggest that reflex vasodilatation resulting from activation of left ventricular baroreceptors may contribute to exertional syncope in patients with aortic stenosis.

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INTRODUCTION

The mechanism of exertional syncope in patients with aortic stenosis has been debated since 1935 when Marvin and Sullivan (1) proposed that it resulted from a sensitive carotid sinus baroreceptor reflex. Several years later, Contratto and Levine (2) demonstrated that carotid sinus massage failed to produce syncope in patients with aortic stenosis and suggested that the carotid sinus reflex was not involved. Since then exertional syncope in aortic stenosis usually has been attributed to an inability to increase cardiac output (3–4), a sudden arrhythmia (4–5) or abrupt left ventricular failure (3–6).

We considered the possibility that reflexes arising from activation of baroreceptors in the left ventricle contribute to exertional syncope in patients with aortic stenosis. Several investigators demonstrated that activation of left ventricular baroreceptors produced by increases in left ventricular pressure or stretch causes reflex vasodilatation and hypotension in dogs (7–9). This study evaluated the possibility that exercise in patients with aortic stenosis increases left ventricular pressure, activates ventricular baroreceptors, and promotes reflex vasodilatation. During leg exercise, reflex vasoconstriction normally occurs in the resting forearm and contributes to maintenance of arterial pressure (10). In these experiments we tested the hypothesis that this normal forearm vasoconstrictor response to leg exercise is inhibited or reversed in patients with aortic stenosis, possibly because of activation of left ventricular baroreceptors.

We compared forearm vascular responses to leg exercise in patients with aortic stenosis with responses in two control groups: patients without valvular heart disease and patients with mitral stenosis. Responses in aortic stenosis were compared with responses in mitral

stenosis for two reasons. First, we wanted to determine if the stimulus for abnormal vascular responses in aortic stenosis arose in the left ventricle or in left atrium and pulmonary vessels. Stretch receptors in atria and pulmonary vessels influence vascular tone, and left atrial and pulmonary venous pressures as well as left ventricular pressures increase with exercise in aortic stenosis. By studying patients with mitral stenosis, in whom left atrial pressures also increase during exercise, we attempted to evaluate the contribution of low pressure receptors in atria and pulmonary vessels in aortic stenosis. Second, we wanted to compare responses in patients with aortic stenosis with responses in a group of patients with approximately comparable functional capacity. In addition to comparing patients with aortic stenosis with patients in the two control groups, we also tested the hypothesis by restudying three patients with aortic stenosis after aortic valve replacement.

METHODS

Responses to supine leg exercise performed on a bicycle ergometer were studied in 10 patients with aortic stenosis, 6 patients with mitral stenosis, and 5 patients without valvular heart disease during diagnostic cardiac catheterization. Meperidine, 100 mg, and diazepam, 10 mg, were given intramuscularly 1–2 h before the study. Forearm blood flow was measured with a mercury-in-silastic strain gauge plethysmograph (11). The forearm was elevated and supported so that the proximal part of the forearm was approximately 10 cm above the anterior chest wall. The strain gauge was applied 4–8 cm distal to the elbow to measure changes in forearm volume. A pneumatic cuff was placed around the arm proximal to the elbow and inflated intermittently above venous pressure for 8–10 s to produce venous occlusion. A second cuff was applied to the wrist and inflated to suprasystolic pressure during measurements to exclude the hand circulation from the measurements. Since venous occlusion interrupts venous outflow but does not interfere with arterial inflow until the veins become distended, the rate of increase of forearm volume during the first few seconds of venous occlusion reflects forearm blood flow. Forearm blood flow was determined from the rate of increase in forearm volume using the formula and measuring device described by Greenfield, Whitney, and Mowbray (12). The rationale and validity of this method has been discussed in detail by Greenfield et al. (12). Forearm vascular resistance, expressed in arbitrary units, was calculated by dividing mean arterial pressure by forearm blood flow. Systemic arterial and left ventricular pressures were measured with conventional fluid-filled cardiac catheters and pressure transducers. Systemic arterial pressure was obtained with a polyethylene cannula introduced percutaneously into the right femoral artery. Left ventricular pressure was measured with a no. 7 or no. 8 French National Institutes of Health catheter introduced into the right brachial artery via cutdown and advanced into the left ventricle. In patients in whom the left ventricle could not be catheterized with this method, a transeptal puncture was performed and a Brockenbrough catheter was advanced into the left ventricle. The left ventricular catheter was positioned in the left ventricular outflow tract. Right heart catheterization was performed using a Swan-Ganz balloon catheter introduced into the right antecubital vein. The catheters were positioned and left ventricular, systemic arterial and pulmonary arterial wedge pressures were obtained simultaneously during the first 4 min of exercise. The Swan-Ganz catheter was then withdrawn to the main pulmonary artery to obtain a sample of mixed venous blood which was used in measurement of cardiac output by the Fick method. The pressures were recorded with Statham P23Db pressure transducer (Statham Instruments, Inc., Oxnard, Calif.) and an Electronics for Medicine DR 16 recorder (Electronics for Medicine, Inc., White Plains, N. Y.). Left ventricular volumes and ejection fraction were measured after the exercise study using the methods described by Dodge, Hay, and Sandler (13). The area of aortic and mitral valve orifices was calculated by the Gorlin formula (14). Aortic and mitral valve flow were calculated from left ventricular cineangiograms in patients with coexisting aortic and mitral insufficiency, respectively. The estimated severity of aortic stenosis was based on the report by Braunwald et al. (15) and of mitral stenosis on the study of Lewis, Gorlin, Houssay, Haynes, and Dexter (16).

After measurements were obtained at rest, observations were made while the patients performed leg exercise at 50–400 kg/min in the supine position for 5 min. The workloads were selected on the basis of an estimate of the functional capacity of each patient as judged by increase in heart rate and oxygen consumption. The functional capacity and, therefore, the workloads for the patients with aortic and mitral stenosis were approximately similar. The functional capacity and, therefore, the workloads required to cause the same increase in heart rate and oxygen consumption tended to be greater in patients with no valvular heart disease. Forearm blood flow and vascular resistance were calculated from the average of flows throughout the second minute of exercise and again throughout the fourth minute of exercise. Values for forearm blood flow during the first minute of exercise were not taken for analysis because movement of the forearm often introduced artifacts in the recording at the start of exercise and because Bevegard and Shepherd (17) demonstrated that the vasoconstrictor response to exercise usually does not occur during the first minute of exercise. Cardiac output, determined by the Fick method, was measured at rest and during the fourth minute of exercise. The mixed venous sample was obtained from the main pulmonary artery and the arterial sample from the femoral artery. Hemoglobin and oxygen saturation were determined in duplicate with an Instrumentation Laboratories Co-oximeter Model IL 182 (Instrumentation Laboratory, Inc., Lexington, Mass.). Air for oxygen consumption was collected with a Tissot spirometer (Warren E. Collins Co., Boston, Mass.) and analyzed with a Beckman Model E2 oxygen analyzer (Beckman Instruments, Inc., Spinco Div., Palo Alto, Calif.). In patients with aortic stenosis, we also measured forearm vascular resistance during application of ice to the forehead for 1 min to determine if inhibition of reflex vasoconstrictor responses to exercise was the result of nonspecific depression of reflex pathways and vascular smooth muscle or was specific for exercise.

Three of the patients with aortic stenosis were restudied several months after recovery from replacement of the aortic valve with a prosthesis. We measured forearm blood flow, arterial pressure (indirect measurement), heart rate, and oxygen consumption before and during supine leg exercise.

The t test for paired data was used to compare values before and during exercise in the same group (18). The t test for unpaired data was used for comparisons between groups (18).

TABLE I

Responses to Exercise in Aortic Stenosis

Patient (workload)	Forearm blood flow			Forearm vascular resistance			Mean arterial pressure			Left ventricular systolic pressure			Left ventricular end diastolic pressure		
	R*	E_2	E_4	R	E_2	E_4	R	E_2	E_4	R	E_2	E_4	R	E_2	E_4
kg/min	*ml/min × 100 ml*			*U*			*mm Hg*			*mm Hg*			*mm Hg*		
Aortic stenosis with a history of exertional syncope															
J. A. (100)	3.6	6.3	4.5	24.4	14.0	19.6	88	88	88	215	226	230	22	40	32
W. H. (100)	2.4	3.4	2.1	40.0	32.1	53.8	96	109	113	217	243	245	13	2	7
F. W. (100)	5.7	7.3	1.9	17.5	13.2	57.9	100	96	110	255	248	241	9	16	16
O. D. (100)	3.9	4.1	5.0	26.9	25.1	24.2	105	103	121	176	187	215	11	14	17
G. P. (50)	4.4	5.8	6.0	18.6	15.1	14.1	82	87	84	235	247	245	19	23	20
L. P. (250)	5.6	7.5	8.9	17.9	13.2	11.7	100	99	104	236	258	262	27	37	32
Mean	4.3	5.7‡	4.7	24.2	18.8‡	30.2	95	97	103‡	222	235‡	240§	17	22	21
SE	0.5	0.7	1.1	3.5	3.2	8.3	4	3	6	11	11	7	3	6	4
Aortic stenosis without a history of exertional syncope															
D. B. (150)	2.1	4.3	4.7	52.4	29.1	27.9	110	125	131	172	196	215	20	20	21
H. D. (100)	6.7	6.9	7.3	13.4	16.2	12.6	90	112	92	196	210	210	12	13	26
R. H. (150)	2.6	2.7	1.8	35.8	40.7	68.9	93	110	124	174	188	205	16	16	20
G. S. (100)	2.4	0.9	1.4	30.7	77.8	52.9	75	70	72	187	182	181	23	31	—
Mean	3.5	3.7	3.8	33.1	41.0	40.6	92	104	105	182	194	203	18	20	22
SE	1.1	1.3	1.4	8.0	13.3	12.6	7	12	14	6	6	8	2	4	2
Both groups															
Mean	3.9	4.9‡	4.4	27.8	27.7	34.4	94	100§	104‡	206	219‡	225‡	17	21	21‡
SE	0.5	0.7	0.8	3.9	6.3	6.9	3	5	6	9	9	8	2	4	3

* R, resting values; E_2, average of values obtained throughout second minute of exercise; and E_4, average of values throughout fourth minute of exercise.

‡ Values significantly different from resting observations ($P < 0.05$).

§ Values which tended to be different from resting observations ($P < 0.10$).

RESULTS

Clinical data. The average age of patients with aortic stenosis, mitral stenosis, and no valvular heart disease averaged 44±3.8 (SE), 46±1.2, and 31±7.3 yr, respectively. Body surface areas of the three groups averaged 1.8±0.1, 1.8±0.1, and 2.0±0.1 m^2, respectively. 8 of 10 patients with aortic stenosis and 6 of 11 patients in the control groups were male. Aortic valve orifice averaged 0.5±0.1 cm^2/m^2 body surface area (BSA) in aortic stenosis, and mitral valve orifice averaged 0.9±0.3 cm^2/m^2 BSA in mitral stenosis.

Resting left ventricular pressure was higher in patients with aortic stenosis (Table I) than in the control groups (Table II). Cardiac output was higher and arteriovenous oxygen difference was lower in aortic stenosis than in mitral stenosis (Table III).

There were no other significant differences in resting values between patients with aortic stenosis and the control groups (Tables I–III). Left ventricular end diastolic and end systolic volumes were not significantly different in the groups and averaged 93±15 (SE) and 31±5 ml/m^2 BSA, respectively, in aortic stenosis, and 78±8 and 28±4 ml/m^2, respectively, in the control groups. Left ventricular ejection fraction averaged 60±5% in aortic stenosis and 68±4% in the control groups ($P > 0.05$).

Responses to leg exercise in control groups. Forearm vasoconstriction occurred during exercise in both control groups (Table II and Figs. 1–2). During the second minute, left ventricular and mean arterial pressures did not change. By the fourth minute left ventricular systolic pressure increased and end diastolic pressure tended to decrease in patients without valvular heart disease. Left atrial or pulmonary arterial wedge pressure rose from 20.3±5.3 mm Hg before exercise to 32.2±5.7 mm Hg during the fourth minute of exercise in mitral stenosis. Arterial pressure tended to increase by the fourth minute in patients with mitral stenosis. Arterial pulse pressures in the control groups averaged 50.0±7.7 mm Hg at rest and 51.7±6.9 mm Hg during exercise ($P > 0.05$).

TABLE II

Responses to Exercise in Mitral Stenosis and in Patients without Valvular Heart Disease

Patient (workload)	Forearm blood flow			Forearm vascular resistance			Mean arterial pressure			Left ventricular systolic pressure			Left ventricular end diastolic pressure		
	R*	E_2	E_4	R	E_2	E_4	R	E_2	E_4	R	E_2	E_4	R	E_2	E_4
	kg/min	*ml/min × 100 ml*			*U*			*mm Hg*			*mm Hg*			*mm Hg*	
Mitral stenosis															
L. H. (50)	2.1	1.2	0.7	60.5	110.8	190.0	127	133	133	185	185	185	15	9	9
E. S. (150)	4.0	2.5	2.3	24.0	36.0	40.9	96	90	94	113	120	111	—	—	—
R. H. (150)	2.4	2.0	1.3	46.3	53.5	90.8	111	107	118	128	122	131	14	12	10
N. B. (100)	3.6	4.1	3.4	26.4	24.6	29.7	95	101	101	133	147	137	12	12	12
I. C. (100)	5.1	4.3	0.8	22.0	27.0	180.0	112	116	144	186	180	200	17	16	17
E. M. (50)	3.4	1.8	—	24.4	45.0	—	83	81	—	108	113	—	9	16	—
Mean	3.4	2.7§	1.7§	33.9	49.5§	106.3§	104	105	118	142	145	153	13	13	12
SE	0.4	0.5	0.5	6.4	13.0	33.8	6	8	9	14	13	17	4	1	2
No valvular heart disease															
G. K. (150)	9.0	7.0	6.7	10.5	14.9	14.3	94	104	96	124	—	134	7	—	4
C. J. (150)	5.9	4.3	3.7	15.3	20.3	25.0	90	88	93	112	110	123	10	7	8
L. M. (300)	1.6	1.4	1.5	67.5	74.8	67.7	110	107	105	133	131	129	10	12	8
P. C. (300)	3.0	1.9	1.6	23.3	40.0	51.3	70	76	82	92	98	100	9	9	9
M. P. (400)	8.6	6.5	5.8	9.9	13.4	15.7	85	87	91	103	104	109	9	6	6
Mean	5.6	4.2‡	3.9‡	25.3	32.7‡	34.8	90	92	93	113	111	119§	9	9	7
SE	1.5	1.2	1.1	10.8	11.6	10.6	7	6	4	7	7	6	1	1	1

See legend for Table I.

Cardiac output, heart rate, oxygen consumption, and arteriovenous oxygen difference increased significantly with exercise in both groups (Table III). Increases in cardiac output, expressed as milliliter per minute per 100 ml increase in oxygen consumption, averaged 438±156 in mitral stenosis and 983±174 in patients without valvular heart disease.

Responses to leg exercise and ice on the forehead in patients with aortic stenosis. During the second minute of exercise, forearm blood flow and mean arterial pressure increased in patients with aortic stenosis (Table I and Fig. 2). Forearm vascular resistance did not change (Table I and Fig. 2). In the patients with aortic stenosis and a history of syncope, forearm vascular resistance decreased significantly during the second minute of exercise (Table I and Figs. 2 and 3).

Left ventricular systolic pressure increased and end diastolic pressure tended to rise during the second minute in patients with aortic stenosis (Table I). Arterial pressure increased during the second minute in the entire group, but not in the patients with aortic stenosis and a history of syncope (Table I). Arterial pulse pressure averaged 55.0±5.0 mm Hg before and 57.5±6.2 mm Hg during exercise ($P > 0.05$).

TABLE III

Cardiac Responses to Exercise

	Cardiac output		Heart rate		O_2 consumption		A-V O_2 difference	
	R*	E_4	R	E_4	R	E_4	R	E_4
Aortic stenosis	5.3	8.5‡	82	117‡	249	774‡	4.8	9.0‡
(n = 10)	0.4	0.6	3	6	13	73	0.3	0.6
Mitral stenosis	3.3	4.3‡	79	121‡	232	482‡	7.2	12.3‡
(n = 6)	0.3	2.0	6	9	14	38	1.1	2.0
No valvular heart disease	5.6	10.8§	84	109‡	233	725‡	4.5	7.5‡
(n = 5)	0.6	1.5	6	5	16	74	0.2	0.5

See legend for Table I.

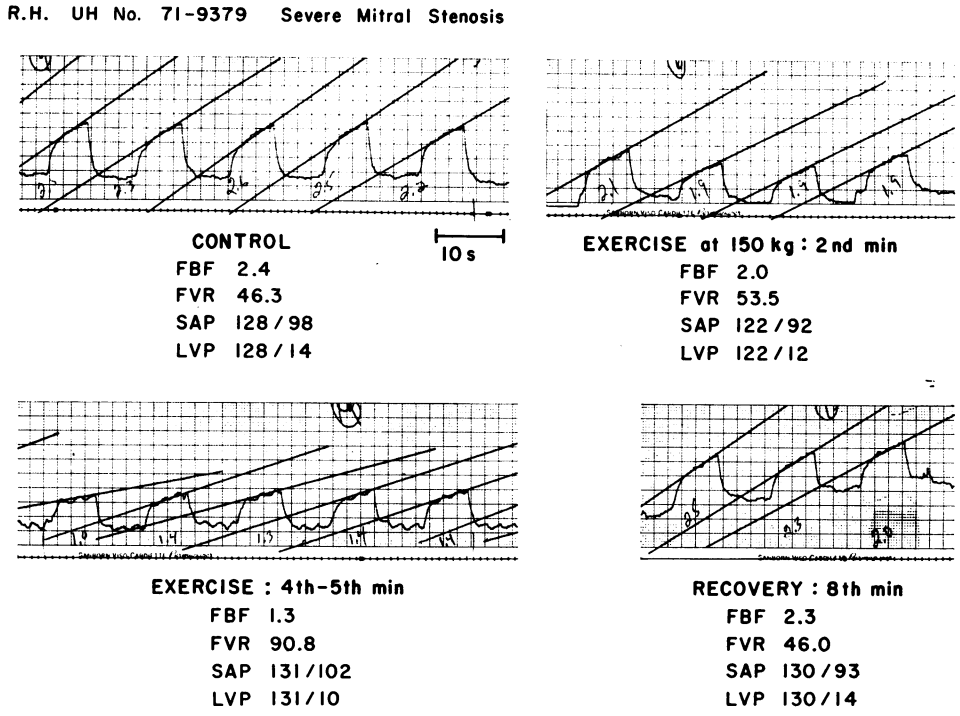

FIGURE 1 Forearm vascular responses to exercise in a patient with mitral stenosis. The segments of record show plethysmographic measurements of forearm blood flow (FBF). Flow is calculated from the slope of the increase in forearm volume during venous occlusion and is expressed in milliliter per minute per 100 forearm volume. The initial upward displacement during venous occlusion represents artifact from inflation of the congesting cuff. FVR, forearm vascular resistance in arbitrary units. SAP, systemic arterial pressure in mm Hg. LVP, left ventricular pressure in mm Hg.

During the fourth minute blood flow returned toward control and forearm vascular resistance tended to increase in patients with aortic stenosis. Left ventricular and mean arterial pressures remained elevated (Table I).

Cardiac output, heart rate, oxygen consumption, and arteriovenous oxygen difference increased significantly with exercise in aortic stenosis (Table III). Increases in cardiac output, expressed as milliliter per minute per 100 ml increase in oxygen consumption, averaged 666±91 in patients with aortic stenosis and 624±138 in patients with aortic stenosis and syncope.

Forearm vascular resistance increased 11.70±3.52 U ($P < 0.05$) during application of ice to the forehead in patients with aortic stenosis.

Comparison of responses in patients with aortic stenosis and in control groups. Increases in forearm blood flow in aortic stenosis were significantly different ($P < 0.05$) from decreases in each control group. In addition, decreases in forearm vascular resistance in patients with aortic stenosis and a history of syncope were significantly different ($P < 0.05$) from increases in each control group during the second minute of leg exercise.

Increases in left ventricular pressure tended to be greater ($P < 0.10$) in aortic stenosis than in the control groups. Cardiac output and oxygen consumption increased less ($P < 0.05$) in mitral stenosis than in aortic stenosis.

Responses after aortic valve replacement. Three patients with aortic stenosis, a history of syncope and a forearm vasodilator response to leg exercise were restudied several months after recovery from aortic valve replacement (Table IV). After operation, vasoconstriction occurred in the forearm during exercise in all three (Table IV and Fig. 3).

DISCUSSION

This study indicates that forearm vasoconstrictor responses to leg exercise are inhibited or reversed in patients with severe aortic stenosis and suggests that this may result from reflexes arising in left ventricular baroreceptors. The abnormality of the forearm vascular response in aortic stenosis was greatest during the second minute and then, probably as a result of circulating constrictor stimuli, returned toward control.

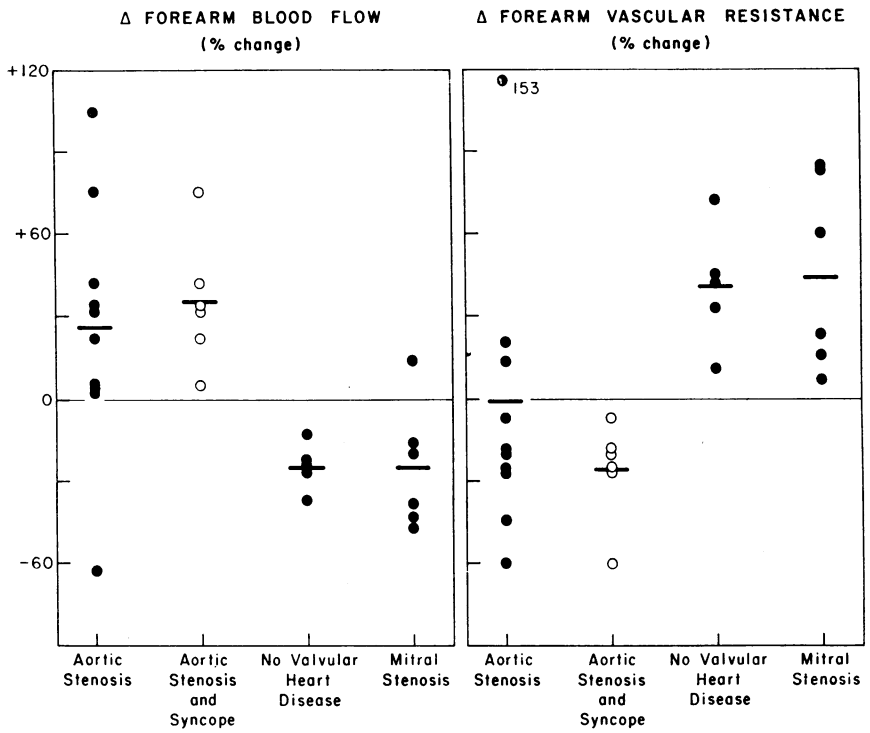

FIGURE 2 Per cent change in forearm blood flow (left) and forearm vascular resistance (right) during the second minute of exercise. Dots represent responses in individual patients. The horizontal lines indicate means of responses in each group.

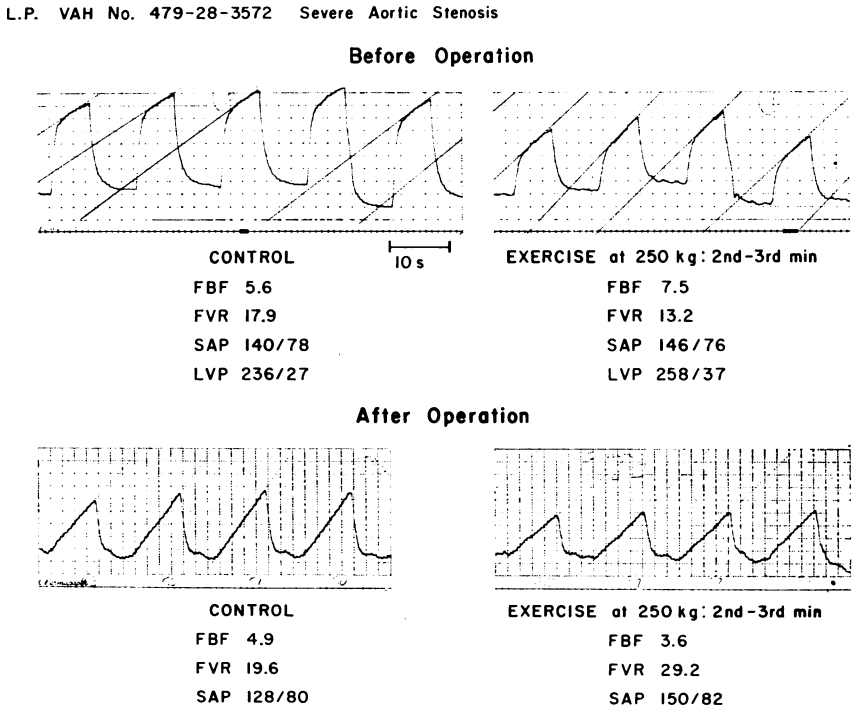

FIGURE 3 Responses to supine leg exercise in a patient with aortic stenosis before and after aortic valve replacement. Left ventricular pressure was not measured in the postoperative study.

TABLE IV

*Responses to Exercise before and after aortic Valve Replacement in Three Patients with Aortic Stenosis**

Patient and workload	Δ Forearm blood flow		Δ Forearm vascular resistance		Δ Mean arterial pressure		Δ Oxygen consumption		Δ Heart rate	
	Before	After	Before	After	Before	After	Before	After	Before	After
	ml/min × 100 ml		*U*		*mm Hg*		*ml/min*		*b/min*	
J. A.										
100 kg/min	+2.7	−1.1	−10.4	+8.0	0	+1	+653	+232	+45	+9
200 kg/min		−0.6		+4.6		+3				+24
G. P.										
50 kg/min	+1.4	−1.5	−3.5	+4.0	+5	+8	+79	+94	0	+4
150 kg/min		−3.1		+9.6		+12		+347		+16
L. P.										
250 kg/min	+1.9	−1.4	−4.7	+10.2	−1	+9	+689	+234	+36	+20
400 kg/min		−1.3		+10.1		+13		+345		+24

* Responses were taken during the second minute at each level of exercise.

Because this study was directed at the neurogenic control of forearm vessels, we placed greater emphasis on responses during the second minute of exercise when the contribution of humoral influences was probably minimal.

Since ice on the forehead produced reflex vasoconstriction in patients with aortic stenosis, inhibition or reversal of vasoconstriction during exercise apparently did not result from nonspecific depression of cardiovascular reflexes or vascular smooth muscle. The presence of vasoconstriction during ice on the forehead and the observation that vasoconstriction occurred during exercise in patients in the control groups who also received meperidine and diazepam 1–2 h before study indicates that these drugs did not cause the inhibition or reversal of vasoconstrictor responses in aortic stenosis.

We considered the possibility that activation of arterial baroreceptors inhibited the vasoconstriction, although vasoconstriction normally occurs during exercise despite increases in arterial pressure (10). Arterial pressure increased slightly in the patients with aortic stenosis, but did not increase significantly during the vasodilator response in the patients with aortic stenosis and a history of syncope. In addition, in the three patients who were restudied after aortic valve replacement, vasodilatation reverted to vasoconstriction during exercise despite increases in arterial pressure. Rhyneer, Kloster, Pickering, Sleight, and Bristow (19) recently demonstrated that the sensitivity of arterial baroreceptors is not enhanced in aortic stenosis, and pulse pressure did not increase with exercise in patients with aortic stenosis. These observations make it unlikely that inhibition or reversal of vasoconstriction resulted from activation of arterial baroreceptors.

Reflexes arising in low pressure stretch receptors in left atrium and pulmonary vessels (20–21) probably did not contribute to inhibition or reversal of the vasoconstriction, since vasoconstrictor responses were not inhibited in patients with mitral stenosis in whom left atrial or pulmonary arterial wedge pressures increased by 9.4±1.5 mm Hg during exercise.

We believe the results suggest that activation of left ventricular baroreceptors promoted reflex vasodilatation during exercise in aortic stenosis. Several investigators (7–9, 22) have demonstrated that increases in left ventricular pressure and distension produce reflex vasodilatation and inhibit sympathetic discharge in dogs, but the precise determinants of activity of ventricular baroreceptors are not known. Ross, Frahm, and Braunwald (9) reported that left ventricular baroreceptors are sensitive to changes in systolic pressure, but noted that more striking alterations occur when end diastolic pressure and left atrial pressure also increase. These investigators suggested that the intracardiac receptors of greatest importance in the control of systemic vascular resistance are those sensitive to elevation of left ventricular diastolic and/or left atrial pressure. We cannot from our data define precisely the stimulus which might activate ventricular baroreceptors and produced abnormal vascular responses in severe aortic stenosis. It does not appear to be increases in left atrial pressure since reflex vasodilatation did not occur with exercise in mitral stenosis. We speculate that a combination of several factors in patients with aortic stenosis may contribute to activation of ventricular baroreceptors: (*a*) elevated resting ventricular pressure and wall tension, (*b*) increases in left ventricular systolic pressure during exercise, (*c*) increases in end diastolic volume

during exercise reflected by increases in left ventricular diastolic pressure, and (*d*) early or rapid increases in left ventricular pressure during exercise. In this regard, 5 of the 10 patients with aortic stenosis had early and persistent vasodilatation during exercise (J. A., O. B., G. P., L. P., and D. B.), and 4 of these 5 were the only patients who manifested a combination of all these factors. The fifth patient with persistent vasodilation (D. B.) and three patients with transient vasodilatation either early or late (W. H., F. W., and H. D.) exhibited most of these changes. In the control groups, left ventricular systolic pressure increased significantly during the fourth minute of exercise, but the increase was less than that in aortic stenosis and end diastolic pressure usually did not increase. The combination of changes which we speculate might influence the activity of ventricular baroreceptors and which was associated with abnormal responses in some of the patients with aortic stenosis did not occur in the control groups.

We did not attempt to precipitate syncope in these patients by using higher workloads, but Flamm, Braniff, Kimball, and Hancock (6) have described hemodynamic events during exercise and "near-syncope" in a patient with aortic stenosis. In their patient cardiac output and arterial pressure increased and systemic vascular resistance decreased initially during exercise. With the sudden onset of near-syncope, cardiac output dropped to normal and arterial pressure fell from 165/84 mm Hg to 44/32 mm Hg without an increase in vascular resistance. Since vascular resistance should increase passively during a striking fall in arterial or distending pressure (23), the absence of an increase in resistance during the fall in pressure indicates active withdrawal of vasomotor tone. These investigators suggested that exertional syncope in aortic stenosis occurred in association with acute left ventricular failure (a fall in cardiac output and a rise in filling pressure) at critical levels of exercise, but vascular resistance and vasomotor tone should increase both actively and passively during hypotension initiated by ventricular failure. We raise the possibility that the initiating events were activation of ventricular baroreceptors and reflex vasodilatation and that these precipitated ventricular failure either by decreasing arterial pressure and coronary perfusion or by inhibiting sympathetic drive to the heart (24).

In conclusion, the results of this study suggest that forearm vascular responses to exercise are abnormal in patients with severe aortic stenosis. These responses revert to normal after recovery from aortic valve replacement. The results are consistent with the hypothesis that activation of ventricular baroreceptors may promote reflex vasodilatation during exercise in aortic stenosis.

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