Exercise and the Heart

Exercise Testing in Patients with Aortic Stenosis*

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Effort syncope in patients with aortic stenosis (AS) has long been recognized in the medical literature. Recent guidelines regarding exercise testing by the American Heart Association and American College of Cardiology list moderate to severe AS as a contraindication for exercise testing. The following report illustrates the potential danger of exercising adult patients with AS. In addition, we review the mechanisms responsible for effort syncope in aortic stenosis and the value and limits of exercise testing in patients with AS, discuss how to monitor patients with AS during exercise testing, and define clinical situations in which exercise testing may be of value in AS.

CASE REPORT

A 68-year-old retired, physically active high school teacher was evaluated in an emergency room with the complaint of syncope. He had no history of chest pain, symptoms of congestive heart failure, palpitations, or myocardial infarction. A heart murmur had been present since childhood. He quit smoking in 1956, his cholesterol level was 268, and his hypertension had been treated intermittently for five years; there was no diabetes mellitus or family history of heart disease. He was receiving no medication, but had previously been on therapy with hydrochlorothiazide. He had no allergies. His surgical history included only an uncomplicated transurethreal resection of the prostate in 1984.

Despite the history of syncope and a systolic murmur, the patient was exercise tested by his private internist. Standing prior to exercise, the heart rate was 82 and blood pressure 142/90 mm Hg. At one minute (stage IA of the Bruce protocol) the patient's heart rate was 134 and blood pressure 140/88 mm Hg. At three minutes, (1.7 mph/10 percent grade) the patient's heart rate was 138 and blood pressure was 132/84 mm Hg. At the end of four minutes of exercise, the ST segments were depressed and at six minutes the patient became diaphoretic, dyspeptic, and there were frequent PACs. The treadmill test was discontinued, and as the patient was getting off, he lost consciousness. Continuous rhythm strips revealed marked sinus bradycardia as low as 20-30 bpm followed by frequent PVCs and asystole for 12 s with ventricular escape beats. There was 3 mm of downsloping ST depression which flattened at maximal exercise. After chest compressions, adequate ventilation, and epinephrine, there was restoration to a slow junctional rhythm accelerating to sinus tachycardia. Blood pressure was restored and the patient regained consciousness. He was subsequently referred to cardiology where the following physical examination was performed.

Physical Examination

Blood pressure was 150/90 mm Hg, regular pulse rate of 86, and respirations 16. He was a well developed, well nourished elderly white male. HEENT was normal, and the neck was supple without adenopathy. Jugular venous pulse was non-distended with normal a and v waves. Carotids were slightly decreased in amplitude and had a slightly reduced upstroke velocity. No thrills were present, but there was a transmitted murmur from the base of the heart. Lungs were clear to auscultation and percussion. The apical impulse was sustained but not displaced. A normal S1, soft S2, and A2, normal splitting of S2, no S3, no S4, and a grade 2/6 systolic ejection murmur with mid peaking at the right upper sternal border radiating to the neck were heard. A diastolic murmur was not appreciated. The abdomen was normal. Extremities and peripheral pulses were normal. Electrocardiogram revealed normal sinus rhythm, left atrial abnormality, and voltage criteria for left ventricular hypertrophy. Chest x-ray film revealed an enlarged ascending aorta and left ventricular enlargement. Lateral chest x-ray examination revealed calcification of the aortic valve and left ventricular enlargement. Echocardiogram was technically inadequate. Aortic valve calcification was present, but valve leaflet excursion and left ventricular wall thickness could not be assessed. Doppler echocardiography was not performed.

At cardiac catheterization, a 52 mm Hg mean aortic valve gradient and valve area of 0.8 cm were found. His left ventricular end-diastolic pressure was 17 mm Hg, but all other hemodynamic values were normal. His coronary arteries had mild irregularities, but no significant stenoses, and his ejection fraction was normal at 60 percent. He had no aortic valve regurgitation. Following catheterization, the patient underwent aortic valvular replacement and was asymptomatic at follow up.

DISCUSSION

In this patient, inadequate attention had been paid to warning signs. The initial heavy workload of the Bruce protocol (5 METs), infrequent blood pressure monitoring, continuation of the test despite a blunted blood pressure response, and physician inexperience may all have contributed to this catastrophe. Fortunately, the patient survived and underwent successful valve replacement. Recent studies have improved our

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understanding of the patient with AS, and this knowledge will help prevent such events.

Lombard and Selzer have discussed the changing character of aortic stenosis. The previously taught classic findings may be missing in the elderly patient; a soft systolic murmur may be present in 10 percent of this population, and the result of carotid examination may be misleading. Coronary artery disease was observed in 60 percent of patients with AS, and two important categories of symptoms have been profiled: angina/syncope or pre-failure symptoms, and dyspnea/congestive heart failure, indicating various degrees of left ventricular dysfunction.

Since Gallavardin first described syncope in AS, with physical findings during syncope including reduced systolic pressure, an absence of pulses and apical impulse, and disappearance of murmurs with return to baseline upon recovery, several authors have hypothesized various mechanisms for effort syncope in AS. Marvin and Sullivan proposed carotid artery hyperreactivity and inadequate cardiac output leading to "cerebral anemia" and syncope. Flamm et al felt that in 29 patients with near syncope, an inadequate ability to increase cardiac output during exercise because of left ventricular failure was the cause. Schwartz et al reviewed nine cases free of neurologic disease who had syncopal events over a six-year period. Because of the numerous atrial and ventricular arrhythmias observed, they suggested that arrhythmias were the source for syncopal attacks.

Perhaps the most plausible explanation for syncope during exercise in patients with aortic stenosis is left ventricular stretch baroreceptor or mechano-receptor stimulation with concomitant arterial hypotension, reduced venous return, and bradycardia. Ross and colleagues demonstrated that elevation of left atrial and left ventricular pressures in dogs caused a decrease in venous return, and a fall in systemic vascular resistance which was most prominent during extrasystoles. Johnson hypothesized that abrupt elevation of left ventricular systolic pressure without a corresponding rise in aortic pressure could allow left ventricular baroreceptors to produce "a violent depressor reflex." This could lead to bradycardia, peripheral vasodilation, and hypotension, which would reduce coronary arterial flow and result in left ventricular dysfunction and arrhythmias.

Mark et al further elucidated this mechanism in 10 patients with AS, of whom six had a history of exertional syncope. They measured the forearm vascular response to supine leg exercise in the AS patients and five normal subjects. The forearm vascular response in normal subjects was appropriate vasoconstriction. In the patients with aortic stenosis, they noted forearm vasodilation and increased forearm blood flow. This was particularly marked in patients with a history of syncope. Forearm vasodilation reverted to vasoconstriction during exercise in three patients after aortic valve replacement. Activation of left ventricular baroreceptors could have resulted in reflex vasodilation with arterial hypotension and reduced coronary artery perfusion. This reflex plays a role in inhibition of sympathetic drive. Other investigators have demonstrated a reflex withdrawal of alpha adrenergic vasoconstrictor tone in the muscles as well as the skin of dogs in response to elevation of left ventricular pressures. These studies strongly support left ventricular baroreceptors as a major contributor to exertional syncope related to AS.

Four mechanisms leading to decreased cerebral perfusion and syncope—carotid hyperreactivity, left ventricular failure, arrhythmia, and left ventricular baroreceptor stimulation—were addressed by Richards et al. They studied four subjects with aortic stenosis (three with syncope, one with heart failure) using electrocardiographic and pressure monitoring of the pulmonary and brachial arteries. During bicycle exercise, a minimal increase in pressure occurred. However, during abrupt "climbing stairs at a sufficient pace to cause the onset of pre-syncopal symptoms," they noted that even as the heart rate rose, there was an abrupt fall in both pulmonary and systolic arterial pressure associated with signs of tachypnea and pallor. No patients lost consciousness and all recovered within 60 seconds. However, there was only a gradual decrease in heart rate during the recovery period. They emphasized that carotid sinus hyperreactivity was unlikely because of the absence of a sudden bradycardia with the fall in blood pressure. Secondly, they noted no arrhythmias. Thirdly, they ruled out the possibility of left ventricular failure because pulmonary arterial pressures did not rise. They felt that the left ventricular baroreceptor response best explained this phenomenon and attributed a lack of bradycardia, as observed in animals, to species differences. They suggested that the absence of hypotension with bicycle exercise was due to the gradual stepwise incremental exercise versus the sudden onset of strenuous exertion in stair climbing necessary for the receptor response.

In our patient, there was a blunted blood pressure response followed by a 10 mm drop in systolic pressure after the first stage of exercise. After initially developing sinus tachycardia, he developed atrial and ventricular dysrhythmias immediately followed by a profound bradycardia. These are consistent with left ventricular baroreceptor stimulation during exertion. However, other mechanisms cannot be excluded. For example, the patient's marked ST segment depression along with a blunted blood pressure response suggests myocardial ischemia with consequent left ventricular dysfunction and reduced cardiac output. Although the patient had normal coronary arteries by angiography,
it has been demonstrated, using Doppler flow probes, that with ventricular hypertrophy, there is decreased coronary reserve.14 This has been hypothesized to be an important contributor to angina pectoris in patients with normal coronary arteries and aortic stenosis. Subendocardial ischemia has also caused arrhythmias in patients with marked left ventricular hypertrophy and may explain the ventricular arrhythmias, and acute left atrial dilation may be a source for atrial arrhythmias.

**EXERCISE TESTING IN SUBJECTS WITH AORTIC STENOSIS**

Although studies have delineated possible mechanisms for effort syncope in aortic stenosis, a review of the literature (Table 1) demonstrates rare complications from exercise testing when performed with appropriate caution and monitoring. Although used predominantly in pediatric cardiology to assess congenital aortic stenosis and the need for surgical therapy, exercise testing has more recently been performed in adults to resolve disparities between history and clinical findings. With the advent of Doppler echocardiography, asymptomatic aortic stenosis in the elderly has become a challenging therapeutic decision. Glew et al15 reviewed eight cases of sudden death due to congenital aortic stenosis and stressed its rarity and the importance of warning symptoms. In addition, they recommended that invasive evaluation be performed in the presence of symptoms, narrowed peripheral arterial pulses, or evidence on the electrocardiogram of left ventricular strain. They noted that rarely did patients with normal electrocardiograms die suddenly.

Exercise testing has been reported in children with valvular stenosis to distinguish noninvasively those patients who would benefit from surgery. However, these studies were performed before use of Doppler echocardiography was widespread. The approach to the asymptomatic child with aortic stenosis remains perplexing.

Early studies in pediatric patients were concerned with decision-making and predicting the severity of AS. Halloran14 studied 31 children with congenital aortic stenosis using bicycle exercise at a workload sufficient to raise the heart rate to at least 170 beats/min. She noted that all 15 children with gradients of 60 mm Hg or greater had 2 mm or more ST depression in V6. In only one subject of 16 with gradients less than 50 mm Hg was 2 mm ST depression present. Likewise, Chandramouli et al17 noted that among 44 children with AS, 1 mm ST depression predicted a gradient of at least 54 mm Hg, and only one subject without significant ST depression had a gradient of 52 mm Hg. Neither of these studies evaluated blood pressure response or exercise capacity. Kveselis et al18 also noted gradients of greater than 35 mm Hg in children with significant ST depression and suggested that ST depression was more related to the left ventricular oxygen supply-demand ratio. They also observed that two of 12 children with gradients greater than 35 mm Hg had a fall in blood pressure. Barton et al19 demonstrated that in addition to ST depression, a systolic blood pressure increase of less than 30 mm Hg was predictive of at least a 50 mm gradient.

James et al20 developed an exercise profile consisting of ST segment depression of 2 mm or more, a decreased systolic blood pressure response to two standard deviations below normal and a decreased total work capacity of two standard deviations below normal. Two or more of these responses occurred predominantly among those with a resting gradient of greater than 70 mm Hg. Because these authors had previously demonstrated a favorable surgical response occurred in patients with a valve gradient of 70 mm Hg or greater, it was suggested that the exercise test

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**Table 1—Summary of Nine Studies of Exercise Testing in Aortic Stenosis**

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<th>Arnowa16</th>
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<td>31</td>
<td>44</td>
<td>19</td>
<td>23</td>
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<td>11</td>
<td>14</td>
<td>12</td>
<td>20</td>
<td>91</td>
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<tr>
<td>Mean age</td>
<td>(6-17)</td>
<td>(5-19)</td>
<td>(55-58)</td>
<td>11</td>
<td>12 (6-30)</td>
<td>46± 5</td>
<td>13± 3</td>
<td>55± 14</td>
<td>65 (52-78)</td>
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<tr>
<td>Mode</td>
<td>Bike</td>
<td>Treadmill</td>
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<td>Maximal heart rate (beats/min)</td>
<td>15±50</td>
<td>16±20</td>
<td>9±3</td>
<td>18±5</td>
<td>17±4</td>
<td>15±2</td>
<td>11±4</td>
<td>38±1</td>
<td>11±2</td>
<td>16±2</td>
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<td>Exercise capacity</td>
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<tr>
<td>Angina</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
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<tr>
<td>ST depression</td>
<td>&gt;1.0 mm</td>
<td>10-30%</td>
<td>27%</td>
<td>37%</td>
<td>54%</td>
<td>100%</td>
<td></td>
<td>X= 1.33 ± 0.8</td>
<td>55%</td>
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<tr>
<td>Blood pressure response</td>
<td>0-32%</td>
<td>63%</td>
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Parentheses denote range, dependent upon subgrouping.

bNot available.

cSelected subgroup with >1.0 mm ST depression.

dSelected subgroup without CAD.
offered a safe, noninvasive method for predicting patients with a high gradient.

Whitmer and co-workers observed a drop in systolic pressure among patients with the highest pressure gradients (greater than 100 mm Hg) and that in five of these seven patients, ST mm of ST segment depression greater or greater was observed. Chest pain was common in those with a high gradient, and only in those with gradients greater than 70 mm Hg did symptoms of dizziness develop. After surgery, work capacity markedly improved except in those with the most severe gradients. Heart rate remained the same before and after surgery. Exercise-induced ST segment depression returned to normal postoperatively, but took longer to do so among patients with severe aortic stenosis. In patients lacking a normal ST segment response postoperatively, the authors suggested the possibility of residual obstruction or cardiac dysfunction.

In adults with AS, Scandinavian cardiologists have reported no complication in over 600 tests. Areskog reviewed 50,000 exercise tests performed in Sweden and reported only two deaths—one of these was a patient with AS. It was concluded that exercise testing is a low-risk procedure which can evaluate exercise capacity, symptoms, evoke signs of hemodynamic compromise, and is a valuable tool for following the course of valvular disease. Linderholm et al. have tested over 500 patients with aortic stenosis without any complications. However, no mention was made of the blood pressure response during exercise. A 92 percent predictive accuracy for coronary artery disease was demonstrated in patients with aortic stenosis. The greatest accuracy was obtained using a “coronary insufficiency index score,” expressed in degree of ST depression relative to predicted exercise capacity. This score was surprisingly effective even in patients who had left ventricular hypertrophy and were receiving digitalis. They also looked at an effort-angina score based on its duration, and found no correlation with pressure gradient and a low diagnostic accuracy for coronary artery disease. In contrast, Aronow and Harris safely tested 19 patients with significant aortic stenosis (gradients ranging from 53 to 80 mm Hg) to 90 percent of their maximal predicted heart rate and found significant ST depression in seven patients despite no evidence of hypertrophy. Because of the absence of coronary artery disease they concluded that ST depression was “a functional sign and not an anatomic sign” of limited myocardial perfusion. Almendral et al. and Nylander et al. noted ST segment abnormalities, but did not comment on its relation to coronary artery disease.

The most complete description of exercise testing in adults is by Nylander et al. who paid particular attention to exercise capacity, symptoms and blood pressure response. They tested 76 adults ranging from 52 to 78 years of age; 77 percent had a history of chest pain, 74 percent had congestive heart failure, and 46 percent had symptoms of dizziness, vertigo or syncope on effort. No patient without angina had evidence of coronary artery disease, and 24 percent of those with angina had evidence of coronary artery disease (>75 percent stenosis of a major vessel). They noted a 10 mm Hg or more drop in systolic blood pressure in 29 patients, and 33 patients had a subnormal increase in blood pressure defined as less than a 10 mm Hg increase in SBP per 30 watt workload. Thirteen of these patients had no symptom of effort vertigo or syncope. This study demonstrated the frequency of an abnormal blood pressure response, the disparity between the history and actual work capacity, the lack of coronary artery disease in patients without angina, and the safety of exercise testing in this population.

Although this case presentation demonstrates the potentially dangerous consequences of exercise testing in patients with AS, much of the literature suggests it is a relatively safe procedure in both the pediatric and adult patient, when appropriately performed. Attention should be focused on the minute-by-minute response of blood pressure, the patient’s symptoms, and the heart rate for slowing and premature ventricular and atrial arrhythmias. In the presence of an abnormal blood pressure response, a patient with AS should undergo at least a two-minute cool-down walk at a lower stage of exertion to avoid the acute left ventricular volume overload which may occur when placed supine. As in the elderly, detrained, or CAD patient, when testing patients with AS, protocols with high (>2 METs) and unequal work increments should be avoided.

Prospective studies of exercise testing in adult patients with aortic stenosis are needed to further evaluate its role in therapeutic decision-making. Exercise plays an important role in the objective assessment of symptoms, hemodynamic response, and functional capacity. Whether ST segment depression indicates significant CAD or not remains unclear. By performing exercise testing pre- and postoperatively, the benefits of surgery and baseline impairment can be quantified. Exercise testing offers the opportunity to evaluate disparities between history and clinical findings; for example, in the elderly “asymptomatic subject” with physical and/or Doppler findings of severe aortic stenosis. Often echocardiographic studies are inadequate in such patients, particularly when they are smokers. When Doppler echocardiography reveals a significant gradient in the asymptomatic patient with normal exercise capacity, he could be followed closely until symptoms develop. In patients with an inadequate systolic blood pressure response, ie, less than 10 mm Hg increase per stage or a fall in
systolic BP from the resting value when symptoms occur, surgery appears to be indicated.

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