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Postural Exercise Abnormalities in Symptomatic Patients With Mitral Valve Prolapse

THOMAS M. BASHORE, MD, FACC, CINDY L. GRINES, MD, DAVID UTLAK, MD, HARISIOS BOUDOULAS, MD, FACC, CHARLES F. WOOLEY, MD, FACC
Columbus, Ohio and Durham, North Carolina

The hemodynamics of the supine and upright exercise response in 16 symptomatic women with mitral valve prolapse (Group I) was compared with that in 8 asymptomatic normal control women (Group II). All subjects had supine and upright echocardiography and phonocardiography at rest and none demonstrated mitral regurgitation. All participants then underwent same day graded bicycle exercise, with simultaneous radionuclide angiography in both the upright and the supine posture. Catecholamines were measured, and a variety of volumetric and hemodynamic data were obtained.

Group I (patients with mitral valve prolapse) demonstrated a reduced exercise tolerance, especially during upright exercise, as measured by both total exercise duration and maximal work load achieved. Mean total catecholamine measurements were similar between the two study groups at comparable mean heart rate, mean blood pressure and mean rate-pressure (double) product. No difference was observed in the ratio of right to left ventricular stroke counts at rest or during exercise regardless of posture, suggesting that exercise-induced mitral regurgitation did not occur.

A difference was noted, however, in left ventricular end-diastolic volume index. At rest, Group I patients exhibited a 42% decrease in this index when sitting upright, and this difference from supine values persisted at submaximal (300 kpm/min) and peak work loads (34 and 29% difference, respectively). This contrasted with the control subjects whose upright end-diastolic volumes at rest, at 300 kpm/min and at peak exercise were reduced 21, 10 and 3%, respectively, compared with supine values. Cardiac index measurements reflected the reduced left ventricular end-diastolic volume observed. Other measurements, including ejection fraction, left ventricular end-systolic volume index and peak systolic pressure/end-systolic volume ratio, were similar between the two groups at each posture and level of exercise. The percent stroke volume ejected during each third of systolic ejection was also not remarkably different between the groups.

In summary, as compared with control subjects, patients with mitral valve prolapse exhibit an exaggerated reduction in left ventricular end-diastolic volume throughout upright exercise. The associated reduction in cardiac output at each level of exercise may contribute to the reduction in exercise tolerance observed in this symptomatic patient subset.

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Patients with the mitral valve prolapse syndrome frequently present with postural tachycardia, orthostatic hypotension, dizziness, syncope and exertional dyspnea and fatigue (1). A number of studies have suggested that at least some of these symptoms may be related to orthostasis (2) or some form of autonomic dysfunction (3,4). Contraction of total blood volume may also be present in symptomatic patients (5), possibly reflecting catecholamine excess (5–7). Because this symptom complex appears to be accentuated in the upright posture and exacerbated by exercise, this study sought to define further the hemodynamics of upright and supine exercise in symptomatic patients with mitral valve prolapse and compare the results with a sex- and age-matched control group.

From the Division of Cardiology, Department of Medicine, The Ohio State University, Columbus, Ohio. This study was supported in part by the Central Ohio Heart Association and the Overstreet Teaching and Research Laboratory, The Ohio State University, Columbus.

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Address for reprints: Thomas M. Bashore, MD, Box 3012, Duke Medical Center, Durham, North Carolina 27710.

Methods

Study patients (Table 1). Sixteen carefully chosen women with symptomatic mitral valve prolapse formed the study group. With reference to the symptoms reported, dizziness

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Table 1. Baseline Characteristics of 16 Patients With Mitral Valve Prolapse (MVP) and 8 Normal Subjects

	MVP (n = 16)	Control (n = 8)
Age (yr)	27 ± 8	25 ± 5
Female gender	100	100
Symptoms		
Dizziness (%)	88	0
Exertional dyspnea (%)	82	0
Syncope (%)	75	0
Chest pain (%)	67	0
Palpitation (%)	13	0
Medications	None	None
Auscultatory mitral regurgitation	None	None

was the most common complaint (thus making this a select group of patients), followed by exertional dyspnea, syncope, chest pain and palpitation. All medications except for birth control pills were discontinued 10 to 14 days before the study. All patients underwent a complete history and physical examination to exclude any associated systemic disease. Mitral valve prolapse without mitral regurgitation was documented in all study patients by both auscultation and M-mode or two-dimensional echocardiography. The patients were compared with an age-matched group of eight normal women volunteers, none of whom had either mitral valve prolapse or any of the symptom complex noted. In all volunteers mitral valve prolapse was excluded by echocardiographic and phonocardiographic evaluation. All subjects gave informed consent in accordance with local Biomedical Subject Review Committee guidelines.

Protocol. After the history and physical examination, all subjects underwent supine and sitting two-dimensional and M-mode echocardiography and phonocardiography in the Overstreet Teaching/Research Laboratory at The Ohio State University. Echocardiographic criteria for mitral valve prolapse required either posterior motion of the mitral valve past the mitral anulus in the long-axis view on the two-dimensional echocardiogram or at least 2 mm posterior systolic motion of the mitral valve inferior to the line from mitral closure to mitral opening on the M-mode study (8).

After an overnight stay in the clinical research unit, the subjects were brought to the cardiovascular nuclear medicine exercise laboratory after eating a light breakfast. Patients were then randomly assigned to either upright or supine stress initially. A second study in the opposing posture was performed 1 hour after the first study was completed. Supine exercise was performed initially in 9 of 16 patients in Group I and 4 of 8 subjects in Group II. Each group had plasma catecholamines (epinephrine and norepinephrine) drawn from an antecubital vein at baseline and at peak exercise in both postures.

Radionuclide angiographic methods. Twenty minutes after the intravenous injection of 1.7 mg of stannous pyrophosphate, 25 to 30 mCi of technetium-99m pertechnetate was given intravenously for in vivo labeling of the blood pool. Three view (right anterior oblique, modified left anterior oblique and left lateral) gated radionuclide angiography was performed at rest. The modified left anterior oblique view was repeated at the common work load of 300 kpm/min and again at fatigue-limiting maximal exertion on a bicycle ergometer. Data were acquired on either a Picker Dyna-Mo or GE Med III small head Anger camera using a slant-hole collimator. Gating was achieved by use of a Physio-Control Lifepak 6. Acquisition was in a 64 × 64 matrix at 20 frames per RR interval, and data analysis was performed on an MDS A^2 40,000 system. After elimination of the final two, frequently low count, frames, the 18 frame study was both temporally and spatially filtered. In standard fashion, semiautomated background-subtracted time-activity curves were generated from the left anterior oblique data and a three point smoothing process was applied.

The counts per frame were determined with the maximal counts assumed to represent end-diastole. Left ventricular ejection fraction was then determined and stroke counts were noted. To convert ventricular count data to volume measurements, exactly 1 ml of blood was counted on the scintillation camera after each exercise session, and the counts per milliliter of blood were determined. After correction of the left ventricular counts for the cycles acquired, time per frame and radionuclide decay, ventricular counts were converted to volume data in the manner suggested by others (9) and validated in our own laboratory, where uniform attenuation was assumed. The validation data were based on findings in 17 patients studied acutely during catheterization and compared with the results from cineangiography.

The sequence of equation used was:

$$1)\ LVC_c = \frac{LVC}{Cycles \times time/frame} \times e^{-(0.0019)(t)} \times \frac{1}{Sample\ counts/per\ ml}.$$

$$2)\ LV\ Volume = 6.5\ LVC_c - 20\ ml.$$

where LVC = left ventricular counts, LVC_c = corrected left ventricular counts and t = time in minutes between the actual study and counting of the 1 ml blood sample.

Using the functional stroke volume image, the ratio of left ventricular stroke counts to right ventricular stroke counts was determined and a regurgitant index obtained (10). The peak systolic blood pressure/end-systolic volume relation was calculated using peak systolic blood pressure measured by cuff and minimal volume derived from the volume curve data (11). To determine the ejection fraction during each third of the ejection time, ejection time was first determined from end-diastole to end-systole as defined by the radionu-

clide angiographic time-activity curve. This duration was divided into three equal time intervals. The percent of the stroke volume ejected during each third of this ejection time was then determined.

Exercise protocol. Each subject began exercise at 150 kpm/min, and the exercise work load was increased by 150 kpm/min every 2 minutes. All subjects underwent radionuclide angiography at rest, at a common work load of 300 kpm/min and at peak stress. When radionuclide acquisition was being performed, the stage was increased to 3 minutes, allowing 1 minute of equilibrium before the initiation of the 2 minute study. No arrhythmias were present at rest in any subject. Exercise was discontinued because of fatigue in all subjects. Two of the patients with mitral valve prolapse had short runs of atrial tachyarrhythmias during exercise (one patient during supine and one during upright stress). One patient with mitral valve prolapse had occasional premature ventricular complexes during upright exercise. No arrhythmias occurred in the control subjects during exercise.

Norepinephrine and epinephrine were measured from blood drawn at baseline and peak exercise by a radiometric enzymatic assay method similar to that described by Cryer et al. (12). For the sake of simplicity, only the total (norepinephrine plus epinephrine) levels are reported here.

Statistical methods. The supine and upright data and the rest, mid-exercise and peak exercise data within each group and between groups were analyzed by analysis of variance. A p value <0.05 was considered significant between data sets. Data are displayed as mean values ± SD.

Results

Exercise tolerance. The 16 patients with mitral valve prolapse exercised 11.5 ± 2.1 min in the supine position and 10.9 ± 1.7 min in the upright position (p = NS). The eight control subjects exercised 12.7 ± 1.3 min in the supine position and 13.1 ± 1.7 min in the upright position (p = NS). When the patients with mitral valve prolapse were compared with the control subjects, the latter exercised longer in both the supine (12.7 ± 1.3 versus 11.5 ± 2.7 min, $p < 0.05$) and upright (13.1 ± 1.7 versus 10.9 ± 1.7 min, $p < 0.001$) posture.

The maximal work load achieved differed coincident with the total exercise duration. The patients with mitral valve prolapse exercised to a maximum of 660 ± 136 kpm/min in the supine position and 618 ± 144 kpm/min in the upright position (p = NS). The control subjects achieved 800 ± 106 kpm/min while supine and 816 ± 132 kpm/min while upright (p = NS). Compared with patients with mitral valve prolapse, the control subjects achieved a greater maximal work load both supine (800 ± 106 versus 660 ± 136 kpm/min, respectively, $p < 0.01$) and upright (618 ± 144 versus 816 ± 132 kpm/min, respectively, $p < 0.005$).

Heart rate and blood pressure response. In Figure 1, heart rate and peak systolic blood pressure in each posture at rest, at the common work load of 300 kpm/min and at peak exercise are presented. The heart rate was greater with the patient upright than supine, both at rest and at each level of stress in both study groups. A significant decrease in systolic blood pressure was evident in the upright posture only at rest in the patients with mitral valve prolapse. With that exception, in each group and at each level of stress, the upright systolic blood pressure was insignificantly lower than the supine values.

Catecholamine response. Figure 2 outlines the measured mean total plasma catecholamine levels in each posture at rest and during peak exercise. To assess whether the catecholamine response appeared to be inappropriate for any measured variable, the mean data are plotted versus simultaneous heart rate, blood pressure and rate-pressure (double) product. On assumption of the upright posture, the total plasma catecholamine level in the patients with mitral prolapse increased from 422 ± 166 to 649 ± 273 μmol ($p < 0.05$). The increase was slightly smaller in the control subjects from 415 ± 172 to 551 ± 190 μmol; p = NS). At peak exercise, a postural difference was evident. At peak exercise, total plasma catecholamine level was 802 ± 274 supine versus 1,323 ± 745 μmol upright ($p < 0.05$) in the patients with mitral valve prolapse compared with 1,035 ± 399 and 1,649 ± 729 μmol, respectively, ($p < 0.05$), in the control subjects.

Although upright blood pressure was lower in the patients with mitral valve prolapse than in the control subjects, Figure 2 suggests that, in general, for any level of blood pressure, heart rate or rate-pressure product, the accompanying measured total plasma catecholamine level seemed grossly appropriate.

Radionuclide angiographic results. Table 2 summarizes the data obtained in all subjects at rest, at the common work load of 300 kpm/min and at peak exercise. Supine and upright data were compared, and patients with mitral valve prolapse were compared with control subjects. Few significant differences were observed. Postural changes did not result in a significant difference in the ejection fraction, ratio of left ventricular to right ventricular stroke counts (left ventricular/right ventricular regurgitant index) or peak systolic pressure/end-systolic volume ratio at rest or any level of exercise.

As noted, at rest, none of the patients had audible or phonocardiographic evidence for mitral regurgitation when either supine or upright. The lack of increase in the left ventricular/right ventricular regurgitant index suggests that exercise-induced mitral regurgitation did not occur in any of the subjects studied. All patients were exercised to fatigue, and exertional symptoms did not provide a differentiating point between the two groups.

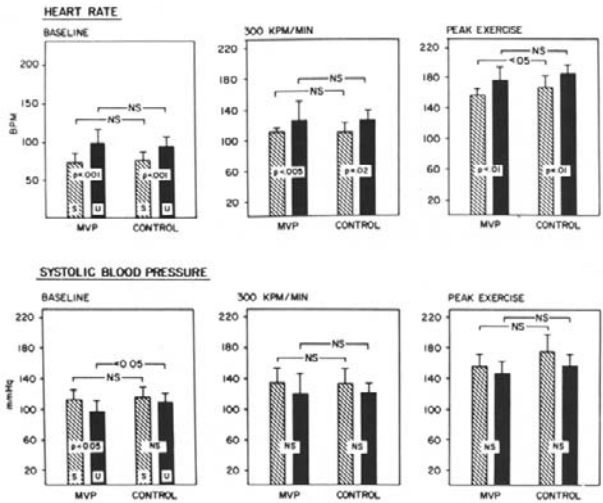

Figure 1. Heart rate and systolic blood pressure response during supine (S) and upright (U) exercise. No significant differences were noted between the patients with mitral valve prolapse (MVP) and the control subjects in heart rate response except at peak exercise (upper panel). At every level of exercise in both groups, the upright heart rate was greater than the supine value. Only the patients with mitral valve prolapse had a lower blood pressure when upright. During exercise, differences in systolic blood pressure were no longer apparent (lower panel). BPM = beats per minute; KPM/MIN = kilopond-meters per minute.

To determine whether patients with mitral valve prolapse might have a temporal abnormality in ejection volumes as a result of the presence of the ballooning mitral leaflets, the percent stroke volume ejected during each third of systole was determined (Table 3). In the supine position, approximately 30% of the stroke volume was reduced during the first third of ejection, approximately 50% during the middle third, with the remaining 20% during the final third. This pattern was unaltered during supine exercise in either of the study groups. When the patients with mitral valve prolapse became erect, there was some reversal of this ejection pattern at rest, with less ejection occurring early (24 ± 8%) and more volume loss occurring in the latter third of systole (33 ± 6%). This postural difference in the first third ejection fraction (31 ± 10 supine versus 24 ± 8% upright) in the patients with mitral valve prolapse was significant ($p < 0.05$), as was the postural difference during the last third of systole (19 ± 7 supine versus 33 ± 6% upright, $p < 0.05$). No other significant postural differences were noted in either the patients with mitral valve prolapse or control subjects.

Left ventricular volumetric data (Fig. 3). In the supine position, the patients with mitral valve prolapse did not differ from control subjects in any of the volumetric measurements. During supine exercise, the left ventricular end-diastolic and end-systolic volume indexes and the cardiac index were similar in the two groups. In the upright posture, however, patients with mitral valve prolapse consistently exhibited smaller end-diastolic volume and cardiac indexes compared with those in the supine posture, and this difference continued throughout stress. In fact, after a modest initial increase in the end-diastolic volume index during stress, the volume did not increase further during exercise. In contrast, although the control subjects exhibited a decrease in left ventricular end-diastolic volume in the upright posture, by the time peak exercise was achieved, the upright volume values were similar to the supine values. The upright left ventricular end-diastolic volume index was similar between control subjects and patients with mitral valve prolapse at rest and at 300 kpm/min.

Figure 4 graphically depicts the percent differences due

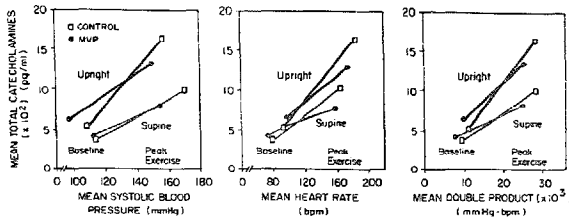

Figure 2. Total plasma catecholamine responses. The mean total plasma catecholamine levels for the control subjects and patients with mitral valve prolapse (MVP) were compared with simultaneously obtained average systolic blood pressure, heart rate and rate-pressure (double) product in both the supine and the upright posture. Catecholamine response to postural and exercise stress appeared similar between the patients with mitral valve prolapse and control subjects. bpm = beats per minute.

to posture. At rest, assumption of the upright posture resulted in a dramatic 42% ($p < 0.01$) fall in the left ventricular end-diastolic volume index in patients with mitral valve prolapse, while in the control group, this decline was only 10% (p = NS). At 300 kpm/min and peak exercise the end-diastolic volume index in the upright position becomes similar to the supine value in the control subjects, but not in the patients with mitral valve prolapse. Cardiac index paralleled the left ventricular volume differences.

Discussion

Characteristics of the study group. Patients with mitral valve prolapse frequently present with symptoms that are difficult to explain. Within this symptom complex, often referred to as the mitral valve prolapse syndrome (1,13), are certain patient groups whose symptoms are particularly disabling. This study is an analysis of the exercise hemodynamics in this particular subset of patients. It demonstrates that exercise capacity is poor in these patients and that cardiac filling during upright exercise appears to be reduced.

Cardiac symptoms were universal in the patient group studied (Table 1), and all patients were young and female. These patients were compared with similar young female control subjects in whom mitral valve prolapse was not present by any postural echocardiographic or auscultatory criteria. In addition, no patient had auscultatory mitral regurgitation. The study cohort is, therefore, highly selective and is meant to represent a relatively "pure" subset of symptomatic patients with mitral valve prolapse. Thus, even though the data derived may not be applicable to other patient groups with mitral valve prolapse, they represent the exercise hemodynamics of a troublesome subset of patients seen by physicians in general. By comparing the results from these patients with those from an age- and sex-matched control group, the potential difficulties encountered when using varied ages and different genders are more readily avoided (14).

Mechanisms of poor exercise tolerance. Poor exercise tolerance was present in both groups, especially when compared with that in normal men (15). Patients with mitral valve prolapse, as compared with control subjects, achieved an even lower level of maximal work load, exercised for a shorter time and had a lower calculated exercise cardiac index. The maximal cardiac index in the mitral valve prolapse group was particularly reduced during upright exercise.

New mitral regurgitation. One possible explanation for the reduced exercise tolerance was that the patients with mitral valve prolapse developed new mitral valve regurgitation in the upright posture that was not present while supine. This appears unlikely for several reasons. First, in no patient was mitral regurgitation present at rest, and repeat echocardiography, auscultation and phonocardiography in the upright posture failed to reveal new mitral insufficiency related to posture. Second, the radionuclide regurgitant index during exercise revealed no evidence for an increase in left ventricular stroke counts out of proportion to right ventricular stroke counts. Although it is possible that simultaneous mitral and tricuspid regurgitation of equal amounts may have occurred during stress, this seems unlikely. Most importantly, left ventricular end-diastolic volume did not increase excessively during exercise, as might be expected if new mitral regurgitation had developed.

Disordered ejection pattern. The left ventricular ejection pattern was also evaluated by noting the stroke volume ejected during each third of systole in an effort to determine whether some of the reduction in forward output related to retention of blood under ballooning mitral leaflets (Table 3). Although some postural differences are evident, the exact role that the ejection pattern changes might play in the

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Table 2. Postural Volumetric Results From Radionuclide Angiography at Baseline at the Common Work Load of 300 kpm/min and at Peak Exercise

	Rest			300 kpm/min			Peak Exercise		
	MVP (n = 16)	Control (n = 8)	p	MVP	Control	p	MVP	Control	p
EF (%)									
Supine	72 ± 10	71 ± 6	NS	79 ± 9	75 ± 8	NS	83 ± 8	78 ± 7	NS
Upright	69 ± 11	68 ± 8	NS	77 ± 8	73 ± 8	NS	80 ± 8	79 ± 8	NS
LV/RV index									
Supine	1.4 ± 0.3	1.3 ± 0.3	NS	1.5 ± 0.3	1.4 ± 0.2	NS	1.5 ± 0.5	1.4 ± 0.4	NS
Upright	1.4 ± 0.5	1.3 ± 0.3	NS	1.7 ± 0.7	1.5 ± 0.3	NS	1.8 ± 0.7	1.6 ± 0.7	NS
PSP/ESV									
Supine	5 ± 4	5 ± 3	NS	10 ± 10	6 ± 4	NS	15 ± 14	9 ± 5	NS
Upright	8 ± 8	6 ± 4	NS	8 ± 7	7 ± 4	NS	14 ± 14	9 ± 6	NS

No significant differences were shown to be related to either posture or the presence of mitral valve prolapse syndrome.

EF = ejection fraction; LV/RV index = left ventricular/right ventricular regurgitant index; MVP = mitral valve prolapse; PSP/ESV = peak systolic pressure/end-systolic volume index.

hemodynamic derangements observed was not well defined by our study and this seemed an unlikely explanation for the results observed.

Blunted response to catecholamines. Another possible explanation for poor exercise tolerance might be a blunted response to catecholamine support during upright exercise. Abnormal postural hemodynamics have previously been noted in patients with symptomatic mitral valve prolapse. These postural changes have prompted the proposal that autonomic insufficiency exists (15). Increased catecholamine levels have also been shown to be present in the plasma of patients with mitral valve prolapse on rising acutely from the supine position (2,5) and in the urine over the course of 24 hours (6). In the present study, total plasma catecholamine levels did not significantly differ from those of control subjects when either the blood pressure, heart rate or rate-pressure product was taken into account (Fig. 2). Although only rest and peak exercise catecholamine levels in each posture were obtained, we are unaware of any data relating the catecholamine response to exercise in patients with mitral valve prolapse in any more detail. The interpretation of plasma catecholamine responses during exercise may not always accurately reflect sympathoadrenal activity (16), however, thus, although subtle changes in catecholamine response to postural change and exercise may have been missed by the methods employed, these data suggest that a grossly inappropriate catecholamine response was not a contributing factor to the results noted.

Lack of increase in end-diastolic volume in upright posture. The observation that left ventricular end-diastolic volume in the patients with mitral valve prolapse did not appear to increase during stress in the upright posture when compared with supine values is the most relevant observation of this study. In the control group during upright exercise, left ventricular end-diastolic volume gradually increased until peak supine values were approached. In the patients with mitral valve prolapse, the initial increase in end-diastolic volume did not appear to augment further as upright exercise continued (Fig. 4). Although the data in our control women may appear divergent from those observed

Table 3. Percent of Stroke Volume Ejected During Each Third of Systolic Ejection Time

	Patients With MVP			Control Subjects		
	1/3	2/3	3/3	1/3	2/3	3/3
Supine						
Rest	31 ± 10	50 ± 3	19 ± 7	32 ± 4	48 ± 3	19 ± 5
300 kpm/min	33 ± 9	48 ± 6	19 ± 7	33 ± 3	48 ± 2	19 ± 3
Peak	32 ± 7	49 ± 4	19 ± 4	32 ± 6	48 ± 2	19 ± 6
Upright						
Rest	24 ± 8	53 ± 3	33 ± 6	31 ± 7	50 ± 5	19 ± 3
300 kpm/min	*34 ± 13	44 ± 13	*21 ± 12	32 ± 4	48 ± 4	20 ± 6
Peak	*34 ± 8	47 ± 5	*19 ± 5	27 ± 8	50 ± 5	23 ± 6

*$p < 0.05$ compared with rest value.

The data in each posture and at each level of stress are shown for the first third (1/3), second third (2/3) and final third (3/3) of ejection. The pattern of 30, 50 and 20% ejection was consistent, except for the patients with mitral valve prolapse (MVP) during the upright rest study.

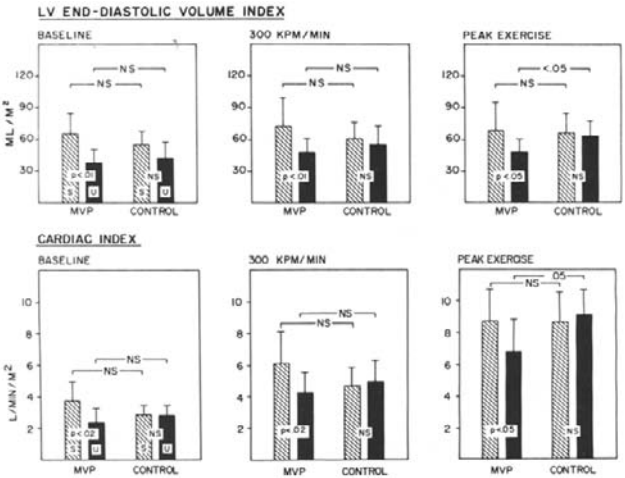


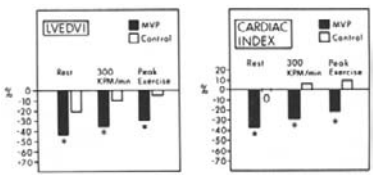
Figure 3. Left ventricular end-diastolic volume index (ml/m^2) and cardiac index (liters/min per m^2) at rest, at submaximal exercise and at peak exercise. For both variables, upright values in the patients with mitral valve prolapse (MVP) are less than supine. This difference was seen at baseline, at the common work load of 300 kpm/min and at peak exercise. Abbreviations as in Figure 1.

by Higgenbotham et al. (15) in control men, it is noteworthy that when normal men exercise upright, the left ventricular end-diastolic volume index increases progressively, then declines as peak exercise is approached. The limited exercise exhibited by the normal women in this study may have obscured the late decrease in left ventricular end-diastolic volume seen in a normal group of men. Thus, the data from the control women in this study are actually quite similar to those observed in normal men at the same level of effort.

The increase in heart rate in the mitral valve prolapse group may have affected left ventricular end-diastolic volume measurements. This group exhibited a slightly higher heart rate in the upright position at each level of stress. However, although some of the reduced left ventricular diastolic volume was likely a function of reduced diastolic time at a higher heart rate, the reduced total forward cardiac output compared with control suggests that the left ventricular end-diastolic volumetric changes were inappropriately low at these heart rates.

Comparisons with previous studies. The finding that upright left ventricular volume changes less in patients with mitral valve prolapse during upright exercise is similar to that reported by Gaffney et al. (17) in abstract form. How-

Figure 4. Percent differences between the upright and supine values for the left ventricular end-diastolic volume index (LVEDVI) and cardiac index in patients with mitral valve prolapse (MVP) and control subjects. Data are presented relative to the supine rest value and expressed as a percent difference for clarity. Note that in control subjects, with exercise the left ventricular volumes upright values gradually become similar to supine values but a postural discrepancy persists in the patients with mitral valve prolapse. The cardiac index in the control subjects is remarkably similar regardless of posture at rest and at each level of exercise. The cardiac index achieved by patients with mitral valve prolapse is consistently less upright than in the supine posture at each level of stress. *$p < 0.05$ upright versus supine values. KPM = kilopond-meters per minute.



ever, using first pass radionuclide angiography, Newman et al. (18) reported that left ventricular end-diastolic volume increased during upright stress. The reasons for these discrepancies might relate to methodologic differences, such as the use of a count-based volumetric measurement in this and other (17) gated blood pool studies, while an area-length volumetric approach was used by Newman et al. (18).

Our finding of a lower upright exercise end-diastolic volume in patients with mitral valve prolapse was also dissimilar to results of studies (18,19) involving women with chest pain and normal coronary arteries whose left ventricular volume manifested an increase with exercise similar to that in the control group in our study. Contemporary studies (15,20) in normal subjects using both sexes have revealed that upright left ventricular diastolic volume increases to a greater extent early in exercise rather than later. The progressive increase in cardiac output during normal upright exercise, therefore, appears to be primarily due to increased heart rate and the Frank-Starling mechanism in early exercise and to an increased heart rate response and lower end-systolic volume in later exercise. The reduced upright left ventricular end-diastolic volume in the patients with mitral valve prolapse thus suggests inappropriate ventricular filling during upright posture. This may be a function of reduced venous return as a result of either reduced total blood volume or an inappropriate response of the venous capacitance system.

Although there are data supporting reduced total blood volume (5), data using lower body negative pressure have failed to reveal any evidence for such an abnormal increase in venous pooling in these patients. In fact, a reduced response to lower body negative pressure and an increase in forearm conductance have led others (5) to postulate that there is abnormal basal alpha-adrenergic tone and an associated reduction in the venous reservoir of these patients.

Limitations. Certain limitations of this study should be pointed out. First, the method we used for measuring ventricular volumes assumes uniform radionuclide attenuation. The method corrects for radionuclide decay and, by drawing the sample blood to be counted as a calibration factor in close temporal proximity to each study, the known hemoconcentration that occurs during exercise (21) is reduced. In our laboratory, the use of uniform attenuation has produced results similar to those described by Dehmer et al. (9). Nevertheless, some volumetric errors might be expected. In addition, because the two studies were performed in sequence with approximately 1 hour rest in between, some dehydration may have occurred between exercise sessions. This latter bias was minimized by randomly assigning the initial posture for exercise.

Importantly, this study was limited to women with symptomatic mitral valve prolapse, and the application of results to other patients groups is uncertain. Sexual differences in exercise hemodynamics have been well described and, in fact, up to 30% of normal women may experience no increase or a decrease in the ejection fraction response to upright stress (19). The reason women may have a different response to exercise than men is unclear. Indeed, the control group of women in this study exhibited relatively poor exercise performance compared with that in studies of normal men (15). Women with symptomatic mitral valve prolapse appear to exercise even less. Unfortunately, symptoms observed during exercise in this study did not correlate well with symptoms that had led the patients to seek medical advice.

Conclusions. This study in symptomatic women with mitral valve prolapse demonstrated a difference in the upright exercise hemodynamics compared with findings in an age- and sex-matched control group. There were no demonstrable differences in catecholamine levels at rest or peak stress. The patients with symptomatic mitral valve prolapse did not appropriately increase left ventricular end-diastolic volume during exercise in the upright posture, but did so when supine. The resultant upright cardiac indexes and diastolic volumes at rest, submaximal exercise and maximal exercise were less than in the control subjects. These data suggest that reduced left ventricular filling may be responsible for at least some of the exercise-induced symptoms seen in patients with symptomatic mitral valve prolapse.

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References

1. Wooley CF. The mitral valve prolapse syndrome. Hosp Pract 1983;18:163–74.
2. Santos AD, Mathew PK, Hilal A, Wallace WA. Orthostatic hypotension: a commonly unrecognized cause of symptoms in mitral valve prolapse. Am J Med 1981;71:746–50.
3. Gaffney FA, Karlsson ES, Campbell W, et al. Autonomic dysfunction in women with mitral valve prolapse syndrome. Circulation 1979; 59:894–901.
4. Coghlan HC, Phares P, Cowley M, Copley D, James TN. Dysautonomia in mitral valve prolapse. Am J Med 1979;67:236–44.
5. Gaffney FA, Bastian BC, Lane LB, et al. Abnormal cardiovascular regulation in the mitral valve prolapse syndrome. Am J Cardiol 1983;52:316–20.
6. Pasternac A, Tubau JF, Puddu PE, Krol RB, DeChamplain J. Increased plasma catecholamine levels in patients with symptomatic mitral valve prolapse. Am J Med 1982;73:783–90.
7. Boudoulas H, Reynolds JC, Mazzaferri E, Wooley CF. Metabolic studies in mitral valve prolapse syndrome. A neuroendocrine-cardiovascular process. Circulation 1980;61:1200–5.
8. Markiewicz W, Stoner J, London E, Hunt SA, Popp RL. Mitral valve prolapse in one hundred presumably healthy young females. Circulation 1976;53:464–73.
9. Dehmer GJ, Lewis SL, Hillis LD, et al. Determination of left ventricular volumes from the time-activity data derived from equilibrium gated blood pool scans. Am J Cardiol 1980;45:293–300.

10. Alderson PO. Radionuclide quantification of valvular regurgitation. J Nucl Med 1982;23:851–5.

11. Nivatpumin T, Katz S, Scheuer J. Peak left ventricular systolic pressure/end-systolic volume ratio: a sensitive detector of left ventricular disease. Am J Cardiol 1979;43:969–74.

12. Cryer PE, Santiago JV, Shah S. Measurement of norepinephrine and epinephrine in small volumes of human plasma by a single isotope derivative method: response to the upright posture. J Clin Endocrinol Metab 1974;39:1025–9.

13. Wooley CF, Boudoulas H. Mitral valve prolapse: a basis for diagnostic classification. In: Warren JV, Lewis RP (eds). Diagnostic Procedures in Cardiology. Chicago: Year Book Medical Publishers, 1985:137–44.

14. Hancock EW. Is there a mitral valve prolapse syndrome? Int J Cardiol 1982;1:443–4.

15. Higgenbotham MB, Morris KC, Williams RS, McHale PA, Coleman RE, Cobb FR. Regulation of stroke volume during submaximal and maximal upright exercise in normal man. Circ Res 1986;58:281–91.

16. Galbo H. Catecholamines and muscular exercise: assessment of sympathoadrenal activity. In: Poortmans J, Niset G (eds). Biochemistry of Exercise IV-B. Baltimore: University Park Press, 1981:3–19.

17. Gelfrey FA, Huxley RL, Nicol P, et al. Abnormal cardiovascular regulation in mitral valve prolapse syndrome (MVPS) during exercise (abst). Circulation 1981;64(suppl IV):IV-240.

18. Newman GE, Gibbons KJ, Jones RH. Cardiac function during rest and exercise in patients with mitral valve prolapse: role of radionuclide angiography. Am J Cardiol 1981;47:14–9.

19. Higgenbotham MB, Morris KG, Coleman RE, Cobb FR. Sex related differences in normal cardiac response to upright exercise. Circulation 1984;26:557–66.

20. Steingart RM, Wexler JL, Slugle S, Scheuer J. Radionuclide ventriculographic response to graded supine and upright exercise: critical role of the Frank-Starling mechanism at submaximal exercise. Am J Cardiol 1984;53:1671–7.

21. Konttam MA, Tu'Meh S, Wynne J, Beck JB, Kozlowski J, Holman BL. Effect of exercise on erythrocyte count and blood activity concentration after technetium-99m in vivo red cell labelling. Circulation 1982;66:638–42.