Left Ventricular Dysfunction in Symptomatic Mitral Valve Prolapse

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Idiopathic MVP is characterized by a late systolic click or murmur from myxomatous mitral valvar dysfunction. It may be complicated by atypical chest pain, ventricular arrhythmias, and ECG changes that can mimic the symptoms of coronary artery disease. We prospectively performed radionuclide cineangiograms before and after stress tests in MVP patients with chest pain compared with asymptomatic MVP patients and symptomatic normal control patients. In ten patients with MVP, chest pain, and normal coronary anatomy, the LVEF remained essentially unchanged (increase of $-0.5 \pm 4$ percent) after exercise. In ten patients with MVP and no chest pain and in nine with normal cardiovascular system and chest pain, the exercise LVEF increased by 11.5 $\pm 2$ percent ($p<0.05$) and 17.4 $\pm 3$ percent ($p<0.005$), respectively. The resting LVEF was significantly lower ($p<0.02$) in the symptomatic MVP patients (59 $\pm 3$ percent) than in the asymptomatic MVP (76 $\pm 5$ percent) or symptomatic normal patient control subjects (70 $\pm 3$ percent). Patients with MVP and chest pain had a lower resting LVEF and an abnormal left ventricular functional response to exercise compared with asymptomatic MVP patients or symptomatic normal subjects. Therefore, exercise radionuclide ventriculography may not adequately differentiate between chest pain due to MVP or coronary artery disease.

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MPI is a common hereditary disorder of the mitral valve that may present with angina-type or atypical chest pain, ventricular arrhythmias, or ECG abnormalities that may simulate the symptoms of coronary artery disease. Previous reports suggested that, like patients with coronary artery disease, patients with MVP have abnormal left ventricular functional reserve as assessed by radionuclide cineangiography, but those articles did not stratify patients according to symptoms of chest pain.

In this study we used radionuclide cineangiography to assess left ventricular performance at rest and after exercise in MVP patients without coronary disease. The patients were grouped into symptomatic patients with typical anginal or atypical chest pain, and asymptomatic patients. Results of stress radionuclide angiography were compared between these groups and with a group of control patients without MVP or coronary artery disease who had a history of chest pain.

MATERIAL AND METHODS

Twenty-nine patients were studied. Group 1s (symptoms) consisted of ten patients with MVP; chest pain, and normal coronary anatomy. Group 1a (asymptomatic) consisted of ten patients with MVP and no chest pain or history consistent with coronary artery disease. Group 2 consisted of nine patients without MVP, with histories of chest pain, and with angiographically proved normal coronary anatomy. A patient was judged to have MVP if echocardiographic (group 1a) or echocardiographic and angiographic (group 1s) criteria were present. All patients had a complete history, physical examination, and resting ECG. Informed consent was obtained. Subjects were excluded from the study if there was clinical or angiographic evidence of myocardial, coronary, or valvular disease other than MVP.

Echocardiograms

Echocardiograms were performed using the ATL Mark 600 and IREX System 3B, M-mode and two-dimensional echocardiographic units. Patients were studied in the supine or left lateral decubitus position. The mitral valve was imaged from the left 4th or 5th interspace. The echocardiograms were reviewed by two blinded observers, and mid-systolic buckling or pansystolic ham-mocking determined MVP.

Left Ventricular Angiography

Left ventricular angiography was performed before coronary arteriography in the 30° right anterior oblique view in all patients in groups 1s and 2. A sinus beat was chosen for analysis. The criteria for determining the presence of MVP are based on the guidelines of Engel et al. Briefly, the mitral fulcrum was identified and a perpendicular drawn from that point connecting the long axis of the ventricle. Systolic protrusion of the mitral valve greater than 11 mm beyond this line determined the presence of MVP.

Selective Coronary Arteriography

Selective coronary arteriography in multiple views was performed using the technique of Judkins. Patients with greater than 40 percent stenosis of a coronary artery were considered to have significant coronary artery disease and were excluded from the study. The patients in group 1a had no indications for, and did not undergo, coronary arteriography. All of these patients had echocardiographic diagnosis of MVP and no symptoms of, or risk factors for, coronary artery disease.

Radionuclide Cineangiography

Radionuclide cineangiography was performed in the supine position at rest and during maximal symptom-limited supine bicycle
exercise. Twenty-five to 30 millcuries of technetium-99m (99mTc) was injected 15 min after bolus injection of stannous pyrophosphate to label RBCs in vivo. After equilibration, the gamma camera was oriented in the left anterior oblique position to optimize septal separation of the right and left ventricles, and imaging was performed with the use of a computer-based procedure gated to the ECG. After rest image acquisition, a symptom-limited supine bicycle exercise test was performed commencing at 200 kpm/min. The exercise load was increased by 200 kpm at 2-min intervals and was continued until the patient achieved 85 percent of the predicted maximum heart rate or exercise was limited by severe dyspnea, fatigue, or chest pain. Gated images were recorded when the patient indicated moderate fatigue or symptoms and continued for 2 1/2 to 3 min until the termination of exercise. The LVEF was determined by automated computerized analysis of left ventricle time-activity curves. Each subject had continuous ECG monitoring during and up to 10 min after exercise. Heart rate and blood pressure were recorded at 2-min intervals during and after exercise. Regional wall motion was determined visually by at least two observers unaware of the patient's diagnosis and symptomatic status. Data were analyzed using Student's t test for paired data and an analysis of variance for intergroup comparison. Data are expressed as the average value ± SEM. A p value of <0.05 was sufficient to reject the null hypothesis.

RESULTS

The patients were classified into three groups on the basis of physical and echocardiographic evidence of MVP, symptoms of chest pain, and angiography. Group 1s consisted of ten patients with symptoms of chest pain and angiographically and echocardiographically demonstrated MVP with normal coronary anatomy. Group 1a consisted of ten asymptomatic patients with physical and echocardiographic evidence of MVP. Group 2 consisted of nine control patients with symptoms of chest pain and angiographically and echocardiographically normal mitral valves and coronary anatomy.

The resting ECG was abnormal in four patients in group 1s and two patients in group 2. Four group 1s patients developed chest pain during exercise. The patients of group 1a all had normal exercise ECGs, and none developed exercise-induced chest pain. Three patients in group 2 developed chest pain during exercise.

The echocardiographic criteria for MVP were met in all group 1s and group 1a patients. Four patients with angiographic but not echocardiographic determinants for MVP were excluded from the study.

All patients in groups 1s and 2 had normal coronary anatomy. The angiographic ejection fraction was 61.4 ± 3.2 percent in group 1s and 75 ± 2.7 percent in group 2. Two patients in group 1s had mild mitral regurgitation, while none of the group 2 patients demonstrated mitral insufficiency.

All study patients underwent rest/stress radionuclide cineangiography. The heart rate at rest in the symptomatic MVP group 1s patients was 71 ± 3 beats per minute (bpm), which increased to 120 ± 6 bpm at peak stress and did not differ significantly from the resting rate of 73 ± 6 and peak stress heart rate of 128 ± 7 bpm in the symptomatic control patients in group 2. The younger asymptomatic MVP patients in group 1a achieved higher rates of 79 ± 4 at rest and 158 ± 5 at peak stress.

In the symptomatic MVP patients of group 1s, the resting LVEF was 59 ± 3 percent and remained un-
changed at 59±3 percent (differences = NS) after exercise (Fig 1). The mean change in ejection fraction with stress was −0.5 ± 4 percent. Eight patients (80 percent) in group 1s exhibited a decrease or a subnormal increase in ejection fraction with stress. Two of the eight patients with an abnormal response had significant angiographic mitral regurgitation (Fig 1). In the asymptomatic MVP patients of group 1a, the mean resting ejection fraction of 76±2 percent increased to 85±2 percent (p<0.01) at peak stress (Fig 1), with a mean change in ejection fraction of 11.5±2 percent. Seven group 1a patients (70 percent) had normal responses to exercise, while three patients had more modest increases in ejection fraction. In the normal (but symptomatic) group 2 patients, the resting LVEF of 70±3 percent increased with stress to 82±3 percent (p<0.01) (Fig 1). The mean increase in ejection fraction was 17.4±3 percent. This value is well within our normal parameters (increase in ejection fraction greater than 7 percent) for this test. Eight of the group 2 patients (89 percent) showed a normal response to stress. In no group 1a or group 2 patients did the ejection fraction decrease after exercise.

**DISCUSSION**

Primary MVP is a disorder in which myxomatous degeneration of the mitral valve leaflets results in valvular distortion and insufficiency.1 However, other abnormalities in the syndrome such as typical and atypical chest pain,1,9 arrhythmias,10,13 ischemic ECG changes,14 and unexplained sudden death11,14 suggest more widespread myocardial involvement. Evidence of abnormal left ventricular wall motion and decreased left ventricular functional exercise response,7,8,15 as well as pathologic studies that have shown myocardial fibrosis and mitochondrial degeneration,16 further the notion of a myocardial abnormality in at least some patients with MVP.

In the present study, patients with MVP were stratified according to symptoms and compared with symptomatic control patients. The symptomatic MVP patients showed a significantly decreased angiographic and radionuclide angiographic ejection fraction at rest compared with the other groups. However, although the group 1s resting ejection fraction was lower at 59 percent than 76 percent and 70 percent for the other groups, it is not below the accepted normal range, and therefore would not be a particularly useful clinical test for differentiating chest pain due to MVP from ischemic chest pain. The exercise ejection fraction response in the group 1s patients remained unchanged compared with the normal stress response in groups 1a and 2. Furthermore, eight of the ten patients (80 percent) had a clearly abnormal stress response compared with 11 percent of group 2 and 30 percent of group 1a patients. These abnormalities are more striking when it is noted that the resting and exercise heart rate and blood pressure responses for groups 1s and 2 were very similar. Therefore, the differences in exercise left ventricular response are not secondary to varying amounts of stress. The group 1a patients did achieve a significantly higher peak stress heart rate. This is most likely because these patients were younger than those of the other groups in a purposeful attempt to lessen the likelihood of coronary artery disease since they did not undergo coronary arteriography.

The reasons for abnormal left ventricular function in symptomatic MVP patients are unclear. Direct involvement of the myocardium in MVP is supported by results of endomyocardial biopsy in patients with MVP and chest pain,16,17 which showed diffuse myocardial abnormalities including myocardial fibrosis and mitochondrial degeneration. Epicardial coronary artery disease or spasm could result in abnormal stress left ventricular function, but the former was excluded by coronary arteriography in the present study, and the latter is unlikely in view of the negative results with exercise thallium-201 scintigraphy observed in MVP patients.18 Our results do not shed any light on this quandary, but do suggest that patients exhibiting symptoms of chest pain with MVP have more extensive involvement, resulting in left ventricular dysfunction at stress.

We conclude that patients with MVP and symptoms of chest pain demonstrate a decreased resting LVEF and an abnormal response to stress compared with asymptomatic MVP patients and normal, but symptomatic, control subjects. Furthermore, asymptomatic MVP patients have normal resting and stress left ventricular function as assessed by radionuclide cineangiography. Therefore, stress radionuclide cineangiography is unsuitable for distinguishing symptomatic MVP from coronary artery disease.

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