A Prospective Study of Mitral Valvular Prolapse in Young Men

James A. Sbarbaro, M.D.; David J. Mehlman, M.D.; Louis Wu, MD; and Harold L. Brooks, M.D.

A cardiac history, a physical examination, an electrocardiogram, phonocardiograms in the supine and standing positions, and an M-mode echocardiogram were obtained in 100 randomly selected, presumably healthy, male medical students (mean age, 26 years). Four percent met standard echocardiographic criteria for mitral valvular prolapse. No midystolic clicks or late systolic murmurs were appreciated in this group, and none complained of chest pain or palpitations. To elucidate further the clinical implications of the echocardiographic pattern of mitral valvular prolapse, 24-hour ambulatory ECGs, multistage exercise tests, and scintiscans of myocardial perfusion at rest and after exercise (using radioactive 13-nitrogen-labelled ammonium) were obtained, with normal results. The absence of life-threatening arrhythmias and exercise-induced abnormalities in these four asymptomatic subjects without abnormal physical findings suggests that the echocardiographic pattern of mitral valvular prolapse in such individuals may represent a variant of normal which does not require extensive evaluation.

Despite considerable investigation into the nature of the syndrome of mitral valvular prolapse, many of its basic features remain obscure. Although significant clinical complications have been associated with the syndrome, including mitral insufficiency,1,4 infective endocarditis,5,6 atypical chest pain,7,9 myocardial infarction,10 transient ischemic attacks,11 life-threatening arrhythmias,12-15 and sudden death,16-18 the high incidence of asymptomatic cases has recently been pointed out.19-21 Because M-mode echocardiograms can demonstrate a characteristic abnormal pattern of mitral valvular motion, they have been widely utilized for the diagnosis and investigation of this clinical disorder.

Previous studies of the frequency of the pattern of mitral valvular prolapse on the M-mode echocardiogram in asymptomatic populations over a broad range of ages suggest that the pattern is more common in women than in men (Table 1); however, since none of these groups was randomly chosen, it is possible that they represent biased samples.

Our study was designed to determine echocardiographically the frequency of the pattern of mitral valvular prolapse in a randomly selected, young male

Table 1—Incidence of Mitral Valvular Prolapse as Diagnosed by Various Criteria

<table>
<thead>
<tr>
<th>Criteria and Series</th>
<th>No. of Patients</th>
<th>Sex</th>
<th>Incidence of Age, Prolapse, yr percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echocardiographic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brown et al19</td>
<td>520</td>
<td>F</td>
<td>17-40</td>
</tr>
<tr>
<td>Markiewicz et al22</td>
<td>180</td>
<td>M</td>
<td>17-39</td>
</tr>
<tr>
<td>Gardin et al23</td>
<td>100</td>
<td>F</td>
<td>17-35</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>M</td>
<td>17-55</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>F</td>
<td>40-93</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>M</td>
<td>40-93</td>
</tr>
<tr>
<td>Auscultatory-Phono-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cardiographic (A-P)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brown et al19 (A-P)</td>
<td>520</td>
<td>F</td>
<td>17-40</td>
</tr>
<tr>
<td>Markiewicz et al22 (P)</td>
<td>180</td>
<td>M</td>
<td>17-39</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>F</td>
<td>17-35</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>F</td>
<td>17-35</td>
</tr>
<tr>
<td>Rizzon et al24 (A-P)</td>
<td>1,009</td>
<td>F</td>
<td>14-18</td>
</tr>
<tr>
<td></td>
<td>1,169</td>
<td>F</td>
<td>17-54</td>
</tr>
<tr>
<td>Angiographic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aranda et al16</td>
<td>95</td>
<td>M</td>
<td>38-66</td>
</tr>
<tr>
<td>Smith et al17</td>
<td>330</td>
<td>M+F</td>
<td>13-71</td>
</tr>
<tr>
<td>Autopsy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pomerance28</td>
<td>3,083</td>
<td>M+F</td>
<td>51-98</td>
</tr>
<tr>
<td>Hill et al29</td>
<td>204</td>
<td>M+F</td>
<td>&lt;40-50</td>
</tr>
</tbody>
</table>

*From the Department of Medicine/Cardiology, the University of Chicago. Supported in part by Public Health Service training grant HL-05073, Specialized Center of Research on Ischemic Heart Disease grant HL-17648, and the Research Career Award Program of the National Institutes of Health. Presented in part at the annual scientific session of the American College of Cardiology, Anaheim, Calif, March 9, 1978.

**Presently at the Cardiopulmonary Unit, Medical Center Hospital of Vermont, Burlington.

†Presently at the Department of Medicine, Barnes Hospital, St. Louis.

‡Presently at the Division of Cardiology, Medical College of Wisconsin, Milwaukee.

Manuscript received September 11; revision accepted November 14.

Reprint requests: Dr. Sbarbaro, Mary Fletcher Unit, Burlington, Vermont 05405

CHEST, 75: 5, MAY, 1979

MitrAL VAlVULAR ProlAPSE IN YOUNG Men 555
population. Furthermore, we attempted to determine the clinical significance of the echocardiographic pattern in terms of symptoms, arrhythmias, exercise tests, and scintiscans of myocardial perfusion.

MATERIALS AND METHODS

Using lists from medical school enrollment, we randomly invited 118 presumably healthy, male medical students to serve as unpaid subjects in this study; 100 agreed to participate. Their ages ranged from 23 to 32 years, with a mean of 26 years. After cardiac and family histories were obtained, each participant was examined in the standing and supine positions by two observers, with special attention to clicks or murmurs. Each subject then had an electrocardiogram, phonocardiograms recorded in both the standing and supine positions, and an echocardiogram using an ultrasonic scope (Unirad or Hoffrel) equipped with a 2.25-MHz ultrasonic transducer having a pulse frequency of 1,538/sec. With the subject supine or in the left lateral decubitus position, the echocardiogram was obtained, with special attention to simultaneously examining both leaflets of the mitral valve in front of the left atrium with the transducer perpendicular to the chest wall at the third, fourth, or fifth intercostal space to the left of the sternum. No special interventions, such as the Valsalva maneuver or the administration of amyl nitrite, were performed to evoke prolapse.

If the echocardiogram showed evidence of mitral valvular prolapse, the subject was requested to enter a second phase of special testing, including 24-hour ambulatory electrocardiographic monitoring, multistage exercise testing to 85 percent of age-adjusted maximal heart rates using the protocol of Bruce et al.30 and scintiscans of myocardial perfusion at rest and after exercise using 13nitrogen-labelled ammonium and standard techniques and equipment.31 Each subject with an echocardiographic pattern of mitral valvular prolapse had a repeat cardiac history, physical examination, and echocardiogram one year later.

The criteria used to determine the presence of mitral valvular prolapse are those described by Popp.32 An echocardiogram was considered to show prolapse if there was a smooth pansystolic echo deviating more than 2 mm posteriorly from the CD line or if there was a late systolic posterior echo deviating at least 2 mm from the CD line. For the purposes of this study, equivocal records were considered normal.

RESULTS

Four of the 100 subjects examined had echocardiographic patterns of mitral valvular prolapse. A representative example demonstrating pansystolic hammocking with late systolic accentuation is shown in Figure 1. One of the three additional subjects with the pattern of mitral valvular prolapse had pansystolic hammocking; late systolic prolapse was noted in the remaining two.

The data are summarized in Figure 2. There were 100 participants. None of the four subjects with echocardiographic patterns of mitral valvular prolapse had a midsystolic click or late systolic murmur in the supine or standing positions on auscultation or phonocardiograms or complained of chest pain or palpitations either initially or one year later. Resting ECGs were normal, and 24-hour electrocardiographic monitoring showed no atrial or ventricular arrhythmias. Multistage exercise tests were also normal in this group. Three of the four agreed to undergo scintigraphic studies of myocardial perfusion using 13nitrogen-labelled ammonium, and these scintiscans were normal both at rest and after exercise.

None of the 100 individuals studied had abnormal values for the right ventricular diameter, the left

Figure 1. Representative echocardiogram showing mitral valvular prolapse, with pansystolic hammocking and late systolic accentuation (arrows). First complex was recorded at slightly different angle of transducer, and pattern of prolapse is not apparent.

556 SBARBARO ET AL.

CHEST, 75: 5, MAY, 1979
ventricular septal and posterior wall thicknesses, the left ventricular systolic and diastolic dimensions, the shortening of the minor axis, the aortic root or left atrial diameter, the mitral valvular excursion, or the E/F slope. In addition, no evidence suggestive of an atrial septal defect or pericardial effusion was noted in any subject.

Of the 96 individuals who did not have mitral valvular prolapse on the echocardiogram, two had midsystolic clicks but no late systolic murmurs. A history of atypical chest pain was elicited in one of these subjects. Complaints of chest pain (five subjects), palpitations (14 subjects), or both (one subject) were frequently noted in those 94 subjects who had a normal mitral valve on the echocardiogram and no evidence for nonejection clicks or systolic murmurs (or both) on auscultatory and phonocardiographic evaluations. No subject had any of the clinical features of Marfan's syndrome.

**Discussion**

We have studied a group of 100 presumably healthy young men and have identified four subjects with an unequivocal pattern of mitral valvular prolapse on the M-mode echocardiogram but with no other abnormalities by history, auscultation, ECGs, ambulatory monitoring of cardiac rhythm, multistage exercise test, and scintiscans of myocardial perfusion. These results suggest that the pattern of mitral valvular prolapse on the M-mode echocardiogram is not rare in presumably healthy young men, the incidence being 4 percent in this study; however, this is appreciably less than the incidence of 21 percent reported in a similar population of young female subjects.23

The absence of an absolute standard for making the diagnosis of mitral valvular prolapse has retarded efforts to fully elucidate clinical, prognostic, and therapeutic aspects of this syndrome. Table 1 shows the incidence of mitral valvular prolapse as measured by several diagnostic techniques in diverse patient populations. Although the range of incidences within each method is large, the variation in ranges of incidences among the various methods is even more striking. It seems reasonable that some of the discrepancy may be related to differences in sex, age, and degree of coexisting cardiac pathologic abnormalities in the various samples; however, more importantly, each diagnostic method employs differing criteria to gauge possibly different phenomena which may or may not be necessary and sufficient for diagnosis of the syndrome of mitral valvular prolapse. One pertinent example is the recent cross-sectional echocardiographic study by Sahn et al23 showing that M-mode echocardiograms can yield both false-positive and false-negative patterns of mitral valvular prolapse if the body of the mitral valvular leaflet, rather than the edge of the leaflet, is examined. Despite these uncertainties, it seems clear that a clinical spectrum exists in patients with mitral valvular prolapse, however defined. On the one hand are individuals with life-threatening ventricular arrhythmias,34 while our study and others recently reported19,22,25 demonstrate the high incidence of asymptomatic patients with echocardiographic mitral valvular prolapse.

Palpitations and nonspecific chest pain were reported in 7 percent and 16 percent, respectively, of these 100 presumably healthy young men; an incidence of 2 percent for midsystolic or late systolic clicks was noted upon auscultation. The higher incidences of palpitations (30 percent), chest pain (29 percent), and auscultatory clicks (4 percent) in a population of healthy young female subjects22 may be explained by the differing methods of selecting patients (randomly selected unpaid volunteers in this study vs paid volunteers obtained through advertisement). Although 7 percent of the young female population22 had midsystolic to late systolic murmurs recorded by phonocardiograms, it is of interest that no such murmurs were heard during auscultation in any subject in either of these two series. Furthermore, in neither study was the

**Figure 2.** Results in 100 subjects. E+, Echocardiographic pattern of mitral valvular prolapse present; E−, normal echocardiographic pattern of mitral valve; MSC, midsystolic click; LSM, late systolic murmur; CP, chest pain; PALPS, palpitations; HOLTER, 24-hour ambulatory electrocardiographic monitoring; and MSET, graded multistage exercise test.
incidence of palpitations and chest pain related to the presence of the pattern of mitral valvular prolapse on the echocardiogram.

This study may have been strengthened by the use of maneuvers (eg, administration of amyl nitrite) designed to evoke mitral valvular prolapse; however, our review of the literature suggests that there is no consensus regarding the clinical significance of provable echocardiographic mitral valvular prolapse. We are currently using left ventricular angiograms and echocardiograms before and after administration of amyl nitrite to investigate this question in a group of patients without clinical evidence of mitral valvular prolapse.

We believe that there are several plausible explanations for the absence of echocardiographic mitral valvular prolapse in the two subjects with midsystolic clicks. First, mitral valvular prolapse may have been intermittent in nature in these individuals. Alternatively, it is conceivable that the sounds may not have originated from the mitral valve or that the echocardiograms in these two cases gave false-negative results. Finally, the results of several series emphasize the fact that there is a small cohort of patients with midsystolic clicks in whom echocardiographic mitral valvular prolapse cannot be demonstrated.

It seems likely that physicians will continue to encounter increasing numbers of asymptomatic patients with echocardiographic mitral valvular prolapse, both because of the widespread use of echocardiography as a tool for screening for the presence of cardiovascular disease and because of the significant incidence of the pattern of mitral valvular prolapse in presumably healthy individuals. The results of this study suggest that young men (aged 21 to 35 years) with the echocardiographic pattern of mitral valvular prolapse who do not complain of chest pain or palpitations, who have no evidence of mitral valvular insufficiency, and who are free of resting electrocardiographic abnormalities do not appear to warrant additional diagnostic evaluation or therapy. Indeed, it is possible that the echocardiographic findings described herein may represent, in such individuals, a variant of normal. Whether these results can be extrapolated to other groups of asymptomatic patients with echocardiographic mitral valvular prolapse awaits further study.

ACKNOWLEDGMENTS: We thank John S. Hanson, M.D., and Thomas C. Gibson, M.D., for their critical review of this manuscript and Ms. Heidi Keefe and Ms. Phyllis Sousa for their secretarial assistance.

REFERENCES
23 Cardin JM, Henry WL, Savage DD, et al: Echocardiographic evaluation of an older population without clinical-

American Medical Research Expedition to Everest

In the fall of 1981, a group of scientists and climbers will mount the first primarily scientific expedition to attempt to climb Mt. Everest. The principal objective will be to obtain information on cardiopulmonary function at extreme altitudes including the summit itself (8,848 m; 29,028 feet). Much of the data will be recorded on miniature tape recorders carried by the climbers. Additional physiologic measurements will be made in a laboratory camp situated at an altitude of approximately 6,100 m (20,000 feet) where sophisticated equipment will be available. It is hoped that the expedition will result in a better understanding of cardiopulmonary function during extreme hypoxia. Further information about the expedition can be obtained from John B. West, M.D., Ph.D., Department of Medicine, M-023, University of California San Diego, La Jolla, California 92093. Contributions for support of the expedition (tax deductible) are being sought. Checks should be made payable to the American Medical Research Expedition to Everest, and sent to F. Duane Blume, Ph.D., P.O. Box 9038, Bakersfield, California 93389.