Electrocardiographic Response to Exercise in Patients with Mitral Stenosis

By LLOYD H. RAMSEY, M.D., and JOHN BEEBLE, M.D.

On the assumption that a positive Master 2 step exercise test is good evidence for the existence of myocardial ischemia, the coronary circulation of 40 patients with rheumatic heart disease and isolated mitral stenosis has been tested by this means. The findings in patients of classes I to III are discussed regarding factors that might be responsible and the relationship of the findings to symptomatology in patients with mitral stenosis.

DURING THE PAST several years, clinicians and physiologists alike have devoted considerable attention to the anatomic and physiologic defects proximal to a stenosed mitral valve. The circulatory abnormalities that occur downstream from the obstructed valve and their effects on the over-all functional cardiac reserve of the patient with mitral stenosis have received comparatively little attention.

Hickam and Carghill have demonstrated the inability of the patient with mitral stenosis to increase cardiac output significantly with exercise, in spite of the elevation of pulmonary artery pressure that occurs. Master, Pordy, and Chesky infer that coronary circulation may be impaired by mitral stenosis in their statement that the 2 step exercise test may be useful in determining cardiac function or the status of the coronary circulation in patients with rheumatic heart disease. Yu, Bruce, Lovejoy, and McDowell have reported the effects of exercise on the electrocardiograms of 48 patients with various types of heart disease, which included an undisclosed number of patients with mitral stenosis. Stuckey has demonstrated abnormalities in the postexercise electrocardiograms of patients with mitral stenosis and angina pectoris, but the exercise was severe, being stopped only after the subject developed pain, fatigue, or severe dyspnea. To our knowledge, however, there are no reports of a systematic study of the effects of standardized exercise on the electrocardiogram of patients with rheumatic heart disease and isolated mitral valvular abnormalities.

Based upon the assumption that the changes in the postexercise electrocardiogram that define a positive 2 step exercise test are related to myocardial hypoxia, this study was designed to obtain information concerning the efficiency of the coronary circulation in patients with mitral stenosis who had no associated valvular abnormalities, irrespective of symptoms of chest pain. Patients included in the study had varying degrees of functional cardiac impairment as determined by conventional methods.

METHODS

Changes in the electrocardiogram following exercise have been widely employed as a method for detecting coronary insufficiency in man. The most popular and well standardized exercise test used for this purpose is the Master 2 step exercise test. Master has performed a large number of 2 step exercise tests on normal individuals, making it unnecessary to run large groups of control tests on normal individuals if one adheres to his methods. The results of these control studies allow one to determine, with reasonable certainty, the electrocardiographic changes following exercise that constitute a positive Master test. The test is easily performed, comparatively safe, requires minimal equipment, and the type of exercise is not strange to most patients. For these reasons, the Master single 2 step exercise test was used in this study.
ELECTROCARDIOGRAPHIC RESPONSE TO EXERCISE

Patients were selected at random as they were seen in the hospital and outpatient clinics of the Peter Bent Brigham Hospital and the Vanderbilt University Hospital. A complete history and physical examination was performed on each patient, following which a routine electrocardiogram, cardiac fluoroscopy, and films of the heart were obtained. With this information, the patients were classified as to the severity of their heart disease according to the criteria established by the New York Heart Association.

The presence of a typical murmur of mitral stenosis was considered sufficient evidence for the diagnosis of rheumatic heart disease with mitral stenosis unless other findings raised doubt as to the diagnosis. Patients with multiple valvular lesions were excluded from the study. No attempt was made to determine the degree of mitral insufficiency present or its part in the production of symptoms. Several patients were included in this study who had soft decrescendo diastolic murmurs along the left sternal border in the second to the fourth interspaces. However, these patients had no systolic murmur at the base, a normal pulse pressure, and no evidence of left ventricular enlargement by fluoroscopy or electrocardiogram, and were thought to have relative pulmonary insufficiency and Graham Steell murmurs rather than aortic insufficiency. All patients included in this study had normal sinus rhythm.

Subjects thus selected then performed a single 2 step exercise test at least 2 hours after their last meal. The test was performed as prescribed by Master, and the number of steps climbed during a period of 90 seconds was determined from his published tables. A 12 lead electrocardiogram was taken immediately before exercise. The extremity electrodes were left in place during the exercise by disconnecting the cables at the direct-writing electrocardiograph recorder, and leads V4, 1, 2, 3 were obtained in that order immediately following the exercise. Five minutes later, a 12 lead electrocardiogram was repeated. Interpretation of the electrocardiograms was made without identification of the patient. Master’s criteria were used for determining which tests were positive.

Results

Studies have been completed on 40 patients who met the criteria. The subjects’ ages ranged from 18 years to 56 years, with a mean age of 33+ years. There were no serious reactions to the exercise although some patients in class III became quite dyspneic following the exercise. Four subjects, all with positive exercise tests, experienced substernal pain with the exercise, which disappeared in less than 5 minutes in each case. Eight patients gave histories of chest pain, anginal in character.

While Master’s criteria were used to evaluate the postexercise electrocardiographic changes, isolated directional T wave changes, or atrioventricular and intraventricular conduction defects were not seen in any of the patients tested. With 1 exception the electrocardiographic changes that made the test positive was S-T segment depression of more than 0.5 mm. The exception was a patient who temporarily developed frequent premature ventricular contractions and runs of bigeminal rhythm immediately following exercise.

The results in terms of positive and negative tests are presented for the whole group and each class in table 1.

Table 1.—Results of Master Test in Patients with Mitral Stenosis

<table>
<thead>
<tr>
<th>Class</th>
<th>No. of patients</th>
<th>Positive</th>
<th>Negative</th>
<th>Positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>40</td>
</tr>
<tr>
<td>II</td>
<td>21</td>
<td>16</td>
<td>5</td>
<td>76</td>
</tr>
<tr>
<td>III</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>32</td>
<td>8</td>
<td>80</td>
</tr>
</tbody>
</table>

Fig. 1. Positive exercise test. The S-T segment depression is more than 0.5 mm, in lead V4 immediately after and 1 minute after standard exercise.
Figure 1 shows portions of the electrocardiograms, before and after exercise, of a 26 year old woman who had acute rheumatic fever at age 7 years. She had been known to have a mitral diastolic murmur for 9 years, but was without symptoms and led a normal life.

Figures 2 and 3 show the tracings of 2 other class II patients. While the pulse rate was almost doubled in patient C.A., the postexercise electrocardiogram showed no other changes and the test was interpreted as negative. A similar rate increase in patient P.H. was associated with significant S-T depression.

The tracings in figure 4 are those of a 28 year old woman, class II, who later died during a surgical attempt to relieve mitral stenosis. At autopsy the coronary vessels were completely normal.

**Discussion**

Apparently a large percentage of patients with mitral stenosis have positive single 2 step exercise tests. This electrocardiographic evidence of myocardial ischemia is present in some patients who are asymptomatic and appear by conventional clinical methods to have little or no impairment of cardiac reserve. This is a particularly striking finding because of the exclusion from the study of patients who revealed any clinical or laboratory evidence of aortic valvular disease.

The possibility must be considered that factors other than coronary insufficiency produced the S-T depression noted following exercise. It is possible that the large number of positive tests resulted in part from the fact that patients were selected from a hospital and outpatient population, and frequently were first seen because of some complaint relating to their heart disease. This selection obviously accounts for the regrettably small number of class I patients. This factor is unimportant, however, when one considers the patients in their clinical class grouping based on history and physical findings. However, the mean age of the group (33 years) would indicate that the patients were, in general, people who had had valvular lesions for some years. This fact is in part counterbalanced by the fact that none of the subjects studied had developed atrial fibrillation, a common later manifestation of mitral stenosis.

It is possible, but unlikely, that hyperventilation per se could be an important factor in the production of electrocardiographic changes in these patients. While the 2 step test does not cause significant hyperpnea in normal subjects, the presence of mitral stenosis makes dyspnea following the test a more prominent feature. However, the changes in the electrocardiogram following voluntary hyperventilation reported by Barker, Shrader, and Rouzoni were minor T wave changes and no major S-T depressions were observed. In addition, the vast majority of the subjects in the present study, particularly those in class I and class II, had little or no dyspnea or hyperpnea during or following the exercise.
Fourteen of the 40 patients were taking digitalis at the time the exercise test was performed. Yu and his co-workers have reported S-T and T wave changes in the post-exercise electrocardiograms of normal subjects following acute digitalization that were not seen under similar conditions in the same subjects before digitalization. Unfortunately the exercise employed in their study was not comparable to that employed in the 2 step test. Nevertheless, it is quite possible that those subjects taking digitalis have S-T depression at least in part as a result of digitalization. Table 2 shows the results of the Master test in the patients who were not taking digitalis. There is little difference in the percentage of positive tests in the patients not taking digitalis when compared to the whole group.

Recently Myers and Talners have raised an important question regarding the change in pulse rate that follows exercise and its effect on the T wave of the P wave. These workers consider that frequently the S-T depression seen after exercise can be explained by the change in the amplitude of the P wave and its following T wave. This is believed to result in an elevation of the P-Q segment rather than a depression of the S-T segment. They point out that the contour of the S-T segment is of much more importance than the depression of the S-T segment at its origin. The change in rate following exercise in our patients with mitral stenosis had no constant relationship to significant S-T depressions. However, no attempt was made to define P-Q elevation as a cause of apparent S-T depression, since Master's criteria were used in defining positive tests.

While all the factors discussed above may play at least a minor role in the production of significant changes in the electrocardiogram, from the data available in Master's large experience with the 2 step exercise test, it seems likely that the cause of S-T depression following exercise in the patient with mitral stenosis is coronary insufficiency.

Several events that arise from the mechanical block to blood flow occurring in mitral stenosis may cause this relative coronary insufficiency. Hickam and Carghill have demonstrated the inability of the patient with mitral stenosis to increase cardiac output with exercise in spite of a concurrent rise in pulmonary artery pressure and increase in heart rate. When the right ventricle works against the increase in pulmonary artery pressure, pressure work increases. This increase in work load results in increased myocardial oxygen consumption, which must primarily be supplied by an increase in coronary blood flow. If this demand for increase in coronary artery perfusion is not met, the result is relative coronary insufficiency.

In the patient with mitral stenosis this demand is made at a time when aortic flow is not increased. Therefore coronary perfusion can be increased only by an increase in arterial perfusion pressure (systemic arterial pressure) or by a decrease in the venous capillary resistance. If the limit of coronary dilatation is reached before or early in exercise and the systemic tissue demands for an increase in blood flow with the exercise prevent an elevation of systemic pressure, the result would be a relative decrease, in relation to need, of coronary perfusion.

Salisbury has been able to demonstrate that failure of the dog's right ventricle in the presence of acute pulmonary hypertension is directly related to the systemic arterial...
TABLE 4

<table>
<thead>
<tr>
<th>Class</th>
<th>No. of patients</th>
<th>Positive</th>
<th>Negative</th>
<th>Positive (%)</th>
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<td>Total</td>
<td>26</td>
<td>18</td>
<td>8</td>
<td>70</td>
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</table>

pressure. That is, the dog's right ventricle is capable of withstanding many times the pressure load that usually results in failure when systemic arterial pressure is proportionally elevated. Apparently the increase in coronary artery perfusion pressure accompanying the systemic hypertension results in an augmentation of coronary flow and allows the right ventricle to withstand markedly abnormal strains of pressure work.

In addition to the pressure work factors that may influence the relative coronary perfusion in the patient with mitral stenosis, the increase in heart rate with exercise results in a decrease in the diastolic time component of the cardiac cycle. This also shortens the time available for diastolic perfusion of coronary vessels and could be a further factor in preventing the needed increase in coronary blood flow.

The association of chest pain with mitral stenosis has long been recognized but poorly understood. As Burgess and Ellis\textsuperscript{11} pointed out in 1942, there are several types of chest pain in the patient with rheumatic heart disease and mitral stenosis. The psychosomatic type and the pain associated with active rheumatic fever and pancarditis need little discussion. The present studies and those of Stuckey\textsuperscript{4} and Salisbury\textsuperscript{10} add further evidence that the other 2 categories of pain, angina pectoris and hypercyanotic angina, are caused by a relative coronary insufficiency occurring in an age group not likely to have significant disease of the coronary arteries. It seems probable from the present studies and those of Stuekey that myocardial ischemia does exist in a large percentage of patients with mitral stenosis. The explanation for the variability in occurrence of the symptoms of chest pain and the lack of response of such pain to nitroglycerin and apparent relief with oxygen\textsuperscript{12} may well lie in the findings of Salisbury.\textsuperscript{10} If systemic arterial pressure bears such a close relationship to cardiac reserve in patients with pulmonary hypertension, it is not difficult to see that the peripheral vasodilatation accompanying the use of nitroglycerin in these patients might well offset the minor coronary artery dilatation expected to occur in normal coronary vessels. Likewise, the lowering of pulmonary artery pressure that may accompany inhalation of 100 per cent oxygen, plus the increase in dissolved oxygen that also accompanies high alveolar oxygen tensions, may actually relieve the myocardial hypoxia by supplying more oxygen per unit blood flow and by decreasing the demand for oxygen by lowering the pressure work load.

**SUMMARY**

Two step exercise tests performed by 40 patients with rheumatic heart disease and isolated mitral valvular deformities reveal 40 per cent of class I, 76 per cent of class II, and 100 per cent of class III patients to have positive Master tests. It seems unlikely that digitalis, hyperventilation, or rate change with exercise can explain the S-T segment depressions seen on the postexercise electrocardiograms.

It is suggested that myocardial ischemia during exercise in these patients is the cause of the electrocardiographic changes and is a result of the rise in pulmonary artery pressure and the increase in heart rate, which occur in the absence of a significant increase in cardiac output and systemic blood pressure. These factors may well result in a decrease in diastolic perfusion time and effective perfusion pressure of the coronary circulation when the cardiac work load is greatest.

These factors may be important in the production of chest pain in many patients with mitral stenosis and may account for the poor response of the pain to nitroglycerin, since the latter may cause a fall in systemic blood pressure. A resultant decrease in coronary perfusion pressure might well occur if coronary vessels are already maximally dilated.
Summario in Interlingua

Tests de exercitio a due scalones, executate per 40 patientes con rheumatic morbo cardiac e isolate deformitates del valvula mitral, revelava resultatos positive secundo Master in 40 pro cento del patientes de classe I, 76 pro cento de classe II, e 100 pro cento de classe III. Il es pauc probabile ue digitalis, hyperventilation, o alteration del frequentia como effecto del exercitio pote explicar le depressiones del segmento S-T vidite in le electrocardiogrammas post le exercitio.

Es suggerite que ischemia myocardial durante le exercitio in iste patientes es le causa del alterationes electrocardiographie e que iste ischemia mesme resulta de un augmento del pression pulmono-arterial e del augmento del frequentia cardiac le quales occurre in le absentia de un augmento significative del rendimento cardiac e del pression de sanguine systemie. Iste factores pote ben resultar in un reduction del tempore de perfusion diastolic e del efficace pression de perfusion in le circulation coronari quando le carga del labor cardiac es le plus grande.

Il es possibile que iste factores es importante in le production de dolores thoracie in multe patientes con stenosis mitral. Illos explica possibilemente le non-satisfacente responsa del dolores al efecto de nitroglycerina, viste que iste agente pote causar un reduction del pression de sanguine in le circulation major. Il es ben possibile que un reduction del pression de perfusion coronari occurre alora si le vasos coronari es jam dilatate maximalmente.

REFERENCES


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