Abnormal Responses of the Systolic Time Intervals to Exercise in Patients with Angina Pectoris

By Jean M. Pouget, M.D., Willard S. Harris, M.D., Bart R. Mayron, M.D., and John P. Naughton, M.D.

SUMMARY
The effects of a 4-min exercise on the duration of the systolic time intervals were determined in 20 patients with angina and 20 age-matched normal controls. The pre-ejection period was shortened 26 msec in normal subjects and 35 msec in angina patients. In normal subjects, total electromechanical systole corrected for heart rate (Q2e) decreased 24 msec, while the left ventricular ejection time corrected for heart rate (LVETc) remained unchanged. In the angina group, by contrast, Q2e failed to change, while LVETc lengthened 23 msec. The angina patients developed similar abnormalities, without pain, after 2 min of exercise. Changes in arterial pressure, cardiac output, and stroke volume failed to explain these systolic temporal abnormalities. Similar abnormalities occurred in 12 patients with primary myocardial disease and heart failure, but not in seven noncardiac patients with nonanginal chest pain. Owing to impaired left ventricular performance and increased afterload, mild exercise prolongs left ventricular ejection in patients with angina. This abnormal prolongation contributes to the development of angina and has value in its diagnosis.

Additional Indexing Words:
Pre-ejection period QS2 interval Left ventricular ejection time Angina
Mean rate of left ventricular ejection Ischemic heart disease Chest pain
Heart failure

In the medical care of patients suspected of having ischemic heart disease, an atraumatic and objective method for assessment of their left ventricular performance would be valuable. Although useful diagnostically, electrocardiography at rest or with exercise gives only meager hemodynamic information, while cardiac catheterization and angiography are time-consuming and expensive procedures, which incur risk and discomfort for the patient. Determination of the phases of left ventricular systole from external recordings provides a convenient, sensitive, and noninvasive method for assessment of changes in cardiac performance.1-5 To evolve and test the use of this method, conjoined with exercise, for studying patients with ischemic heart disease, we investigated the effects of moderate exercise on the phases of left ventricular systole in normal subjects and in patients with angina pectoris.

Methods
Twenty patients with angina pectoris and 20 normal, age-matched controls were studied (table

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From the Section of Cardiology, Department of Medicine, University of Illinois College of Medicine, and West Side Veterans Administration Hospital, Chicago, Illinois.

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Table 1

Sex, Age, and Oxygen Consumption of Normal Controls and Patients with Angina

<table>
<thead>
<tr>
<th></th>
<th>Sex</th>
<th>Age (years)</th>
<th>Oxygen consumption (ml/min/kg)</th>
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<tr>
<td></td>
<td>Mean ± SE</td>
<td>Range</td>
<td>Mean ± SE</td>
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<td></td>
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<tr>
<td>Normal subjects (n = 20)</td>
<td>Men 16</td>
<td>53 ± 2.4</td>
<td>35-63</td>
<td>4.4 ± 0.2</td>
<td>17.1 ± 0.7</td>
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<td></td>
<td>Women 4</td>
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<tr>
<td>Angina patients (n = 20)</td>
<td>Men 18</td>
<td>54 ± 2.1</td>
<td>35-63</td>
<td>4.1 ± 0.2</td>
<td>17.1 ± 0.8</td>
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<td>Women 2</td>
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</table>

1. All patients had recurrent substernal pain that was precipitated by exertion, cold, meals, or emotion, and relieved promptly by rest and nitroglycerin. Four had a myocardial infarction a year or more before study. Five had mild systemic hypertension controlled with thiazides alone. None had clinical evidence of congestive heart failure, but three had minimal cardiomegaly on chest X-ray. Fifteen patients accepted cardiac catheterization. Selective coronary cineangiography showed greater than 50% narrowing of the left circumflex coronary artery in one patient, of two major coronary arteries in 13 patients, and of all three coronary arteries in one patient. Of the 14 patients studied with regional sampling of coronary sinus blood, 13 had myocardial production of lactate at rest or during isoproterenol infusion. The normal controls were hospital and laboratory workers of sedentary habit, without a history of heart disease, and with a normal cardiac physical examination, chest X-ray, and electrocardiogram. All subjects gave informed consent and were studied without sedation and in the postabsorptive state.

A bipolar electrocardiographic lead across the anterior thorax was obtained, with the negative electrode in the second intercostal space at the right midclavicular line and the positive electrode in the fifth intercostal space at the left midaxillary line. A contact microphone, placed over the third intercostal space at the left sternal border, was strapped firmly to the chest. The indirect carotid pulse tracing was obtained with a pulse pickup (Electronics for Medicine pulse-sound microphone PS-1b) held manually over the common carotid artery in the neck.

With the subject resting supine, his arterial pressure was measured with a cuff sphygmomanometer on the arm and his electrocardiogram, phonocardiogram, and carotid pulse tracing were recorded simultaneously at 100 mm/sec paper speed with 20-msec time lines on an Electronics for Medicine multichannel photographic recorder. With the electrocardiographic lead and chest microphone kept in place, the subject then stood erect and stepped up and down a 6-inch platform for 4 min at 24 steps/min, keeping pace with a metronome. While he was standing, a 1-min sample of his expired air was collected in Douglas bags once before exercise and again during the last minute of exercise. The oxygen and carbon dioxide concentrations of the expired air were determined with a Beckman oxygen analyzer (model E2) and medical gas analyzer (model LB-1). Immediately after exercise, the subjects lay down, the carotid pulse pickup was reapplied, and 30 sec after the end of exercise and again at 2.5, 5, and 10 min of the recovery period, arterial pressure was measured and recordings were obtained for the phases of systole. Several weeks after performing this 4-min exercise test, six patients with angina and six normal controls repeated it, but exercised only 2 min instead of the usual 4 min.

The pre-ejection period (PEP) was calculated by subtraction of the LVET from the QS2 interval. All intervals were determined as the average of measurements on 10 consecutive beats, each read to the nearest 5 msec. Heart rate was derived by dividing the average R-R interval into 60. The LVET and the QS2 intervals were corrected for the effects of heart rate by use of the regression equations of Weissler. When corrected in this way for heart rate, these intervals will be referred to as the LVETc and the QS2c.

In six patients with angina and six normal subjects, the studies of the phases of systole were combined with hemodynamic measurements. A radiopaque catheter,* 24 inches long, was inserted percutaneously through a 14 gauge needle into an antecubital vein and advanced under fluoroscopic control into the right atrium. A 6 inch catheter needle assembly† was used for cannulation of the brachial artery. Brachial arterial and right atrial pressures were measured with Statham P23Gb strain gauge transducers.

*Mardic Deseret
†Longdwell
Table 2
Systolic Time Intervals Before and After Exercise in 20 Normal Subjects and 20 Patients with Angina

<table>
<thead>
<tr>
<th></th>
<th>Heart rate (beats/min)</th>
<th>Arterial pressure</th>
<th>Qr (msec)</th>
<th>LVETc (msec)</th>
<th>PEP (msec)</th>
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<tr>
<td></td>
<td></td>
<td>Systolic</td>
<td>Diastolic</td>
<td></td>
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<tr>
<td>Normal subjects</td>
<td>70 ± 2.7</td>
<td>121 ± 4.3</td>
<td>70 ± 2.0</td>
<td>551 ± 5.1</td>
<td>414 ± 4.5</td>
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<td>Angina patients</td>
<td>74 ± 2.0</td>
<td>139 ± 8.7</td>
<td>81 ± 2.2</td>
<td>547 ± 5.1</td>
<td>400 ± 4.8</td>
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<td>&lt;0.001</td>
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<td>118 ± 3.7</td>
<td>108 ± 3.4</td>
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<td>&lt;0.05</td>
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<td>30 sec after exercise</td>
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<tr>
<td>Normal subjects</td>
<td>87 ± 4.5</td>
<td>154 ± 7.6</td>
<td>71 ± 2.1</td>
<td>527 ± 6.0</td>
<td>410 ± 5.7</td>
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<tr>
<td>Angina patients</td>
<td>106 ± 5.1</td>
<td>193 ± 6.9</td>
<td>94 ± 3.6</td>
<td>543 ± 6.3</td>
<td>423 ± 5.7</td>
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<td>&lt;0.001</td>
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<td>84 ± 4.3</td>
<td>87 ± 3.5</td>
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<td>&lt;0.001</td>
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<td>Changes from resting control 30 sec after exercise</td>
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<tr>
<td>Normal subjects</td>
<td>17 ± 2.6</td>
<td>33 ± 5.2</td>
<td>1 ± 1.5</td>
<td>-24 ± 4.1</td>
<td>-4 ± 2.6</td>
</tr>
<tr>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>NS</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
<tr>
<td>Angina patients</td>
<td>32 ± 4.2</td>
<td>54 ± 6.4</td>
<td>13 ± 2.6</td>
<td>-4 ± 4.5</td>
<td>23 ± 2.5</td>
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<td>&lt;0.001</td>
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<td>NS</td>
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<tr>
<td>P for difference between post-exercise responses of normal and angina groups</td>
<td>&lt;0.01</td>
<td>&lt;0.02</td>
<td>&lt;0.001</td>
<td>&lt;0.005</td>
<td>&lt;0.001</td>
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*Mean ± se.

Abbreviations: NS = not significant at 0.05 level.

Placed in a plane 10 cm anterior to the subject’s back and connected to pressure amplifier channels of the Electronics for Medicine photographic recorder. Mean pressures were obtained by electronic integration. For the purpose of determination of cardiac output, indocyanine green (6.25 mg) was injected into the right atrium while brachial arterial blood, withdrawn at a constant rate by a Harvard pump, was sampled continuously through a Gilford cuvette densitometer. Before beginning the upright exercise and 30 sec after its end, the subjects lay supine while dye-dilution curves for cardiac output, recorded at 5 mm/sec paper speed, and tracings for the systolic time intervals, recorded at 100 mm/sec paper speed, were inscribed simultaneously on separate Electronics for Medicine recorders. Total peripheral resistance (TPR, in dyne-sec-cm⁻⁵) was calculated from the formula

\[ TPR = \frac{BAM - RAM}{CO} \times 1332 \]

where BAM is mean brachial arterial pressure (mm Hg), RAM is mean right atrial pressure (mm Hg), CO is cardiac output (ml/sec), and 1332 is the factor for converting pressure from mm Hg to dyne/cm². The mean rate of left ventricular ejection (ml/sec) was determined by division of the stroke volume (ml) by the ejection time (sec).

In addition, the systolic time intervals before and after exercise were determined by the same method in seven patients who had nonanginal chest pain and normal hearts and in 12 patients who had mild symptoms of congestive heart failure caused by primary myocardial disease. Of the patients with primary myocardial disease, three were recovering from myocarditis, presumed viral, and the other nine had nonobstructive idiopathic myocardial infarction. The mean age ± se of these 12 patients was 37 ± 3.2 years (range 21–52 years). None had systemic hypertension or electrocardiographic evidence of myocardial infarction. All had cardiomegaly on chest X-ray and both S₄ and S₃ gallop sounds. In the eight patients with primary myocardial disease who underwent cardiac catheterization, the left ventricular end-diastolic pressures averaged 14 ± 1.6 mm Hg at rest and 22 ± 2.3 mm Hg during supine exercise on a bicycle ergometer. Their ejection fractions, determined from single-plane cineangiograms in the right anterior oblique projection, averaged 25 ± 4.2% (range 15–40%), and their resting cardiac outputs averaged 2.2 liters/min/m² (range 1.7–3.2 liters/min/m²). Selective coronary cinearteriography, done in six patients, was normal. Statistical analyses were performed by Student’s t-test.

**Results**

Before exercise, the angina and normal groups did not differ significantly in heart rate, systolic arterial pressure, or Qₑ, but the
anginal group had a significantly higher diastolic arterial pressure \( (P < 0.001) \), longer preejection period \( (P < 0.05) \), and shorter LVET\(_c\) \( (P < 0.05) \) (table 2). Both groups had similar oxygen consumptions at rest, and four-times greater oxygen consumptions during exercise (table 1). During and after exercise, the heart rate and the systolic and diastolic arterial pressures rose more in the angina patients than in the normal subjects. Thus, 30 sec after the exercise ended, the diastolic arterial pressure remained at preexercise levels in the normal subjects, but increased an average \( \pm \text{SE} \) of 13 \( \pm 2.6 \) mm Hg \( (P < 0.001) \) in the angina patients. The duration of the QRS complex was similar in both groups, averaging 78 \( \pm 8.1 \) msec at rest and 81 \( \pm 7.6 \) msec 30 sec after exercise in the normal patients and 75 \( \pm 8.2 \) msec at rest and 80 \( \pm 9.0 \) msec 30 sec after exercise in the angina patients. Thirty seconds after exercise, the preejection period had fallen below its preexercise level by 28 \( \pm 3.1 \) msec in the normal subjects and 35 \( \pm 2.5 \) msec in the angina patients \( (P \) for the 9-msec difference between the mean responses of the two groups \( <0.02 \) \) (fig. 1). The two groups differed significantly from one another in the responses of the Q\(_2c\) and LVET\(_c\) \( (P < 0.001) \) 30 sec after exercise (fig. 2). At this time the Q\(_2c\) was shortened 24 \( \pm 4.1 \) msec in the normal subjects but only a small and insignificant amount, 4 \( \pm 4.5 \) msec, in the angina patients, while the LVET\(_c\) was shortened 4 \( \pm 2.6 \) msec, an insignificant change, in the normal subjects but was lengthened 23 \( \pm 2.5 \) msec \( (P < 0.001) \) in the angina patients.

A relation between LVET\(_c\) and arterial pressure was looked for but not found. In neither the anginal nor the normal subjects was there a significant correlation at rest or 30 sec after exercise between the LVET\(_c\) or the changes in the LVET, and the systolic or diastolic levels of arterial pressure. Likewise, the prolongation of the LVET\(_c\) in the anginal patients failed to be correlated significantly with the rises in either their systolic \( (r = 0.31, P < 0.2) \) or diastolic \( (r = 0.38, P < 0.2) \) arterial pressures. A comparison between those

**Figure 1**

Mean \( (\pm \text{SE}) \) changes from resting levels in the pre-ejection period \( (\Delta \text{PEP}) \) 0.5, 2.5, 5, and 10 min after the end of exercise in 20 normal controls and 20 anginal patients. One-half minute after exercise the average shortening of the preejection period in the anginal group exceeded that of the normal group by 9 msec \( (p \) for difference between group means \( <0.02 \)).

**Figure 2**

Changes from resting levels in total electromechanical systole and LVET corrected for heart rate \( (Q2c, \text{LVET}) \) 30 sec after exercise. \( P \) values refer to differences between the means of the two groups.
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angina patients and normal subjects who had similar rises of arterial pressure revealed that the LVET_c lengthened markedly only in the former.

All 20 angina patients had chest pain, which began during the fourth minute of exercise or at its end. Several weeks later, when six of these anginal patients and six of the normal controls repeated the test but exercised only 2 min instead of 4 min, chest pain failed to occur. Nevertheless, 30 sec after exercise, the angina patients again had prolongation of their LVET_c by 22 msec (P<0.001) while the normal subjects again did not (fig. 3).

Figure 4 compares the six normal controls and the six angina patients with respect to their hemodynamic and LVET_c responses 30 sec after the end of exercise. The two groups differed significantly in their responses of LVET_c (P<0.01), stroke volume (P<0.05), and mean rate of left ventricular ejection (P<0.05), but not of cardiac output or total peripheral resistance. Whereas the stroke volume rose 8±2.1 ml/m² in the normal subjects, it fell 4±3.4 ml/m² in the angina group; although by itself neither change of stroke volume was significant, the difference between them was. The LVET_c shortened insignificantly in the normal subjects but lengthened significantly (P<0.001) in the angina patients.

Thirty seconds after the exercise ended, the seven patients with nonanginal chest pain had an insignificant mean prolongation in the LVET_c of 4.7±1.7 msec, a response differing significantly (P<0.001) from that of the 20 angina patients but not from that of the 20 normal subjects.

In the group of 12 patients with heart failure due to primary myocardial disease, the resting preexercise measurements were: heart rate, 88±4.1 beats/min; arterial pressure, 119±4.1/78±2.4 mm Hg; Q_{2c}, 551±4.5 msec; LVET_c, 381±5.2 msec; and preejection period, 134±7.0 msec. Thirty seconds after the exercise ended, they had increases in heart rate of 33±4.2 beats/min (P<0.001) and in arterial pressure of 31±3.8/10±3.3 mm Hg (P<0.001/P<0.02). At the same time, the preejection period decreased 39±5.5 msec (P<0.001), the Q_{2c} was prolonged 8.0±7.3 msec, which was not significant, and the LVET_c lengthened 32±3.5 msec (P<0.001). These responses of the preejection period, Q_{2c}, and LVET_c differed significantly (P<0.05, P<0.001, and P<0.001, respectively) from those of the normal group. In contrast to their responses of the preejection period and Q_{2c}, which failed to differ significantly from those of the angina group, the lengthening of the LVET, in the patients with myocardial disease was even greater (P<0.05) than that of the angina group.

**Discussion**

At rest, the angina group had a preejection period 10 msec longer and an LVET_c 14 msec shorter than did the control group. Their longer preejection period may have resulted, in part, from a higher arterial diastolic pressure. On the other hand, the combination of a long preejection period and short LVET_c suggests that ventricular function may have
been mildly impaired at rest in some of the anginal patients. Because the two groups overlapped considerably in their measurements, the systolic time intervals at rest failed to discriminate well between individuals with and without angina. In contrast, the responses of these intervals, particularly the LVETc and Q2c, to exercise differentiated clearly between patients with angina and their normal controls. In the normal subjects, exercise shortened the prejection period and Q2 but either failed to change the LVETc or shortened it slightly. In the anginal group, by contrast, although the same exercise shortened the prejection period an average of 9 msec more than in normals, it left the Q2c unchanged and greatly prolonged the LVETc. Thus, not only does rhythmic exercise markedly alter the left ventricular systolic time intervals, but it does so abnormally in patients with ischemic heart disease.

These results are understandable in terms of the hemodynamic effects of exercise and the determinants of the systolic time intervals. For example, the prejection period is shortened by two effects of exercise. By increasing venous return, which increases end-diastolic wall stress and myofiber length, exercise evokes the Starling mechanism. By causing a discharge of catecholamines, which activates the adrenergic β-receptors, exercise augments myocardial contractility. Both myocardial responses accelerate the isovolumic development of left ventricular pressure, thereby abbreviating the time required for the left ventricular pressure to rise.

*Figure 4* Changes from resting levels in the LVETc and in hemodynamic measurements 30 sec after the end of exercise in six normal subjects and six patients with angina. The LVETc lengthened only in the angina group, although the rise in their cardiac output was no greater than normal and their stroke volume actually fell. The mean rate of left ventricular ejection (MRLVE) rose in the normal subjects, but not in the patients with angina.
from its end-diastolic to aortic diastolic levels and shortening the preejection period.³

Why do patients with angina respond to exercise with an excessive shortening of the preejection period? It cannot be attributed to their abnormal elevations of arterial diastolic pressure. These would tend to prolong the preejection period.³ Nor can it be caused by their greater than normal rises of heart rate. As studies with atrial pacing and atropine have shown,³ cardioacceleration by itself fails to shorten the preejection period. Left ventricular dysfunction during exercise is the most likely cause for the excessive shortening of this interval in angina patients. In normal subjects, exercise elevates left ventricular end-diastolic pressure little, if at all.¹⁴ By contrast, when the patient with angina exercises, his end-diastolic pressure rises markedly, for example, by 10 to 20 mm Hg.¹⁵,¹⁶ narrowing the gap between itself and aortic diastolic pressure and, thereby, tending to shorten the isovolumic period of ventricular pressure development. Moreover, despite a depressed function, if the end-diastolic volume and adrenergic stimulation of the ischemic ventricle were greater than those of its normal counterpart, it might be able to raise its pressure isovolumically at a rate that is normal (or even high) for the given exercise. Previous reports lend support to these possibilities. Phillips and associates¹⁷ found that in normal subjects the systolic transverse diameter of the heart invariably decreases immediately after upright exercise, while that of patients with ischemic heart disease, in contrast, either remains unchanged or increases. Raab and Gigeel⁸ and Gazes and coworkers¹⁹ found higher plasma levels of catecholamines during exercise in patients with coronary artery disease than in normal subjects. Wiener and associates²⁰ showed that in anginal patients maximum dp/dt of the left ventricular pressure curve is increased markedly during exercise and remains elevated for several minutes after its end. Thus, the excessive shortening of the preejection period by exercise in patients with angina may be attributed to abnormally great increments in left ventricular end-diastolic pressure and volume, in adrenergic stimulation of the myocardium, or in both. Confirmation and a precise definition of the role of these factors must await direct measurements of left ventricular pressures and volumes.

As previous studies in animals²¹,²² and man²³–²⁵ have shown, if heart rate is kept constant or if its effects are corrected for by a regression formula, the left ventricular ejection time varies directly with venous return, stroke volume, or cardiac output and with afterload, and inversely with myocardial inotropy. The duration of the LVETₚ is determined by the admixture of these factors. Although the augmentation of venous return and cardiac output by exercise tends to prolong the LVETₚ, the positive inotropic effects of exercise, which increase the velocity of myocardial fiber shortening⁶,²⁶ tend to abbreviate it. Because these two opposite effects of exercise are nearly balanced, the LVETₚ of normal subjects remains unchanged after exercise or even shortens slightly.

In contrast, a striking and distinctive abnormality found in the patients with angina is the marked prolongation of their LVETₚ immediately after exercise. This lengthening of the LVETₚ occurred even though their cardiac output increased less than that of the normal controls, and their stroke volume, which rose in the normal subjects, fell. Neither arterial pressure nor its exercise-induced elevation was correlated significantly with the lengthening of the LVETₚ in the angina patients. Despite this failure to demonstrate that arterial pressure, by itself, is causally related to the prolongation of the LVETₚ in the angina patients, we believe that an abnormally great afterload does contribute, in part, to this prolongation. Identical increases of systolic arterial pressure may affect the duration of left ventricular ejection differently among various individuals. For example, owing to the Laplace relation, a given systolic pressure would impose a bigger afterload,²⁷,²⁸ and hence a greater lengthening of the ejection period relative to stroke output,²⁸ in the ventricle that has a larger volume. Moreover, for expressing the contribution of

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pressure to the average or total afterload of the left ventricle, peak systolic arterial pressure, the measurement that we obtained, would be less accurate than mean systolic aortic pressure.

In the present study, the same exercise test prolonged the LVET, markedly in all 12 patients with congestive heart failure due to primary myocardial disease. This finding supports the concept that the primary cause for the marked prolongation of the LVET, after mild or moderate exercise in patients with ischemic heart disease is an impairment in left ventricular performance. This impairment could reflect the appearance in the ischemic left ventricle, under the stress of exercise, of a generalized reduction in myocardial contractility, of localized asynergy,29,30 or of both.

The lengthening of the LVET, by exercise is not caused by, but rather precedes the onset of, angina pain. Nearly the same lengthening occurred after the 2-min exercise test, without pain, as after the 4-min test, with pain (fig. 3). By increasing myocardial oxygen requirements, this prolongation of left ventricular ejection relative to heart rate, stroke volume, and aortic pressure may contribute to the development of angina.31

Exercise markedly shortens the QS2, or total electromechanical systole corrected for heart rate, in normal subjects but not in patients either with angina or with heart failure due to primary myocardial disease. Positive inotropic interventions, such as the administration of isoproterenol, epinephrine, tyramine, calcium, and the cardiac glycosides increase the maximal shortening velocity of the isolated cat papillary muscle36,32 and shorten total electromechanical systole in man.2,5,33,34 Likewise, it is probably through its positive inotropic effects9 that rhythmic exercise abbreviates total electromechanical systole in normal subjects. The failure of the QS2 to shorten after exercise in patients with either angina or primary myocardial disease may reflect the ischemic or failing heart's inability to translate the inotropic stimuli of exercise into a normal heightening of overall left ventricular performance. As shown previously20,35 and reconfirmed here (fig. 4), the enhancement of the mean rate of left ventricular ejection by rhythmic exercise is markedly depressed or absent in patients with ischemic heart disease. Because the ejection rate in these patients responds poorly, their need for an increased cardiac output during exercise must be met, in part, by a prolongation of left ventricular ejection. In patients with angina, as in those with heart failure due to myocardial disease, this abnormal lengthening of the ejection phase appears to offset and conceal the shortening effects of rhythmic exercise on total electromechanical systole.

Interpretation of changes in the LVET and QS2 intervals requires a correction for the effects of heart rate. Using data from supine normal adults at rest, Weissler and associates6 derived linear regression equations that relate heart rate on the abscissa to duration of the systolic time intervals on the ordinate. The difference between the observed LVET or QS2 interval and that predicted for the observed heart rate from the normal regression equation equals the difference between the LVET, or QS2, and the intercept of the mean regression line with the ordinate (0 heart rate). A change in LVET or QS2, therefore, equals a change in the observed time interval relative to the mean regression line for heart rate. Relative to the normal regression lines for heart rate at rest, exercise lengthens the LVET markedly in patients with angina or myocardial disease but not in normal subjects and, conversely, shortens the QS2 markedly in normal subjects but not in those with angina or myocardial disease. Viewed another way, in the present range of heart rates, exercise raises the LVET regression line for heart rate in patients with angina and myocardial disease but not in normal subjects, and lowers the QS2 interval regression line for heart rate in normal subjects but not in patients with angina or myocardial disease. These changes in the LVET and QS2 interval relative to the normal regression lines for heart rate, reflect the effects of exercise on ventricular filling.
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afterload, contractility, or synchrony of contraction, singly or in combination. One must distinguish clearly between the systolic time intervals at rest and their responses to exercise. In patients with myocardial dysfunction, whether associated with angina or with heart failure due to primary myocardial disease, both kinds of measurements deviate from the normal, but in opposite directions. Although, at first glance, this divergence in direction might seem paradoxical, it is not. It simply reflects the differences of ventricular loading imposed by rest and exercise. When patients with myocardial dysfunction rest in the supine position, their abnormally long preejection periods and short LVETc correlate well with their low cardiac outputs and stroke volumes. Exercise increases venous return above its resting levels. Through the Starling mechanism, this increase of venous return causes healthy and diseased ventricles alike to raise their cardiac output, which tends to prolong the duration of ejection.

By increasing the velocity of left ventricular ejection, however, the positive inotropic effects of exercise normally keep the ejection time from lengthening. This is not true for the failing or ischemic left ventricle. Presumably because its inotropic response is inadequate and its afterload is high, it raises its cardiac output in response to the increased venous return of exercise only at the expense of a longer ejection time. On the other hand, the larger end-diastolic volume of the malfunctioning ventricle and its exposure to higher levels of circulating catecholamines, both of which help to accelerate the isovolumic rise of pressure, and its greater end-diastolic pressure may, in combination, account for the normal or greater than normal shortening of the preejection period. Thus, the responses to exercise that characterize the failing or ischemic left ventricle include a slightly excessive shortening of the preejection period and a markedly abnormal lengthening of the LVETc. These responses reflect the inability of such a ventricle to handle normally the enhanced venous return of exercise.

Normal subjects and patients with ventricular failure or ischemia overlap considerably in the resting levels of their systolic time intervals. The sensitivity and precision of the systolic time intervals in differentiating between patients with normal and abnormal left ventricular function may be increased by determination of the responses of these intervals to a standard exercise test.

The present exercise test is a valuable adjunct in the diagnosis of angina pectoris. Because the marked prolongation of the LVETc after exercise reflects left ventricular dysfunction, it has not been found either in normal subjects or in persons with normal hearts and nonanginal chest pain. The present results suggest that shortening the exercise to 2 min or less may prevent the appearance of anginal pain, without diminishing the diagnostic sensitivity of the systolic temporal responses. The diagnostic and investigative uses of this simple, sensitive, and noninvasive test of left ventricular performance during exercise warrant further study.

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Abnormal Responses of the Systolic Time Intervals to Exercise in Patients with Angina Pectoris

JEAN M. POUGET, WILLARD S. HARRIS, BART R. MAYRON and JOHN P. NAUGHTON

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