Hemodynamic Determinants of Exercise ST-Segment Depression in Coronary Patients

By Jean-Marie R. Detry, M.D., Franz Piette, M.D., and Lucien A. Brasseur, M.D.

SUMMARY

Eight patients with coronary heart disease were studied during two periods of exercise separated by 30 min of rest; workload was increased in a stepwise fashion every minute of exercise up to a level that produced limiting symptoms of angina, fatigue, or dyspnea. The magnitude of ST-segment depression and the central aortic pressure were measured during exercise and recovery periods, and myocardial oxygen requirements were estimated by the pressure-time index (systolic aortic pressure \times heart rate \times ejection time).

Seven of the eight patients exhibited a close relationship (r ranged from 0.74 to 0.98) between magnitude of exercise ST-segment depression and indices expressing myocardial oxygen requirements; heart rate, blood pressure, and ejection time were also related to magnitude of exercise ST-segment depression. These relationships were reproducible during two consecutive exercises. Like onset of angina, magnitude of exercise ST-segment depression is usually related to hemodynamic factors influencing myocardial oxygen needs. Consequently, comparisons of exercise-induced ST depression before and after therapy (drugs, physical training, and surgery) are valid only if ECG findings are compared at the same level of myocardial oxygen requirements.

In contrast, absence of such a relationship during recovery suggests an important difference in mechanisms of the post-exercise electrocardiogram.

Additional Indexing Words:
Exercise electrocardiogram Post-exercise electrocardiogram Pressure-time index

Angina Pectoris with exertion is a syndrome reflecting an acute imbalance between myocardial oxygen requirements and oxygen supply restricted by diseased coronary arteries.

Myocardial oxygen needs vary with tension developed in the ventricular wall and are closely related to indices derived from systolic and mean blood pressure, systolic ejection time, and heart rate.\(1^-3\) Changes in ventricular volume or in contractile state of myocardium are also determinants of myocardial oxygen consumption.\(^4\)

In a given patient, angina occurs at a critical level of myocardial oxygen requirement, whether it is increased by exercise\(^5\) or by atrial pacing.\(^6\) It is unclear whether the same relationship applies to both procedures\(^7^-8\) or to electrocardiographic changes which usually precede the pain.

This study was undertaken to determine whether the appearance and the magnitude of exercise-induced ST-segment depression were related to hemodynamic factors influencing myocardial oxygen requirements.
Methods

Eight male patients (table 1) with coronary heart disease (CHD), documented by previous acute myocardial infarction or by a typical history of angina pectoris, were selected on the basis of a normal ST-T segment at rest and significantly abnormal ST responses after a Master double twostep test. Ages ranged from 46 to 64 years. Patients with cardiomegaly, clinically manifest heart failure, hypertension (resting BP ≥ 160/95 mm Hg), or receiving digitalis, quinidine, diuretics, or beta-blocking agents were excluded. Informed consent was obtained verbally before initiating the study.

Patients were studied either fasting or more than 2 hours after a light meal. Under local anesthesia, a polyethylene radiopaque catheter was introduced percutaneously into the brachial artery by Seldinger technique and advanced into the ascending aorta. Aortic pressure was recorded with a strain gauge (Statham P23Db) on a Cardiopan S recorder (Liechtli, Bern) and monitored by oscilloscope; mean pressures were electrically integrated. Zero level was the fourth intercostal space in sitting position. The ECG was recorded from electrodes attached proximally to limbs and to precordial V4, V5, and V6 positions.

Each subject sat on a bicycle ergometer\(^9\) for a 10-min rest before performing exercise at an initial workload of 10 watts, which was increased by 10 watts every minute. Exercise continued until either angina pectoris or exhaustion occurred; ST-segment depression was never a reason for stopping. No subject exhibited multiple premature ventricular beats or ventricular tachycardia. After exercise was terminated, each subject rested for 30 min, while sitting in an armchair, before repeating the same exercise. In one subject (T.E.) hypotension developed after exercise, and the second test was delayed for 2 mo; no other complications occurred.

The ECG (I, II, III, aV\(_R\), aV\(_L\), aV\(_F\), V\(_4\), V\(_5\), and V\(_6\)) and aortic pressure were recorded at the end of each rest period, at each minute of exercise, and during the first 10 min of recovery. Only horizontal or downslope depressions of ST segment were considered and their magnitude was measured at the J point, with the junction of the R-P segment and the Q wave as reference level in the lead in which the depression was most marked (either V\(_4\) or V\(_5\)). Ejection time was measured from onset of the pressure wave to the incisura. Systolic aortic pressure, ejection time, and magnitude of ST-segment depression were averaged over two respiratory cycles.

Three indices reflecting myocardial oxygen requirements were calculated: (1) product of heart rate, peak systolic aortic pressure, and ejection time (pressure-time index)\(^3, 5, 10\); (2) product of heart rate and peak systolic aortic pressure\(^6\); and (3) product of heart rate and mean aortic pressure.\(^2\)

Results

A close relationship (r ranged from 0.74 to 0.98) between magnitude of exercise ST-segment depression and indices expressing myocardial oxygen requirements was observed during both exercises in seven of eight patients (table 2). All the factors (heart rate, blood pressure, ejection time) on which these indices are based were also related to the magnitude of ST-segment depression, the closest relationship being for heart rate. Relationships between magnitude of exercise ST-segment depression and pressure-time index in each subject are illustrated in figure 1.

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Table 1

**Clinical Data on Patients**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Resting BP (mm Hg)</th>
<th>Comments*</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.A.</td>
<td>54</td>
<td>150/90</td>
<td>Angina pectoris since 1965</td>
</tr>
<tr>
<td>C.G.</td>
<td>46</td>
<td>130/80</td>
<td>Angina pectoris (emotional) since 1966</td>
</tr>
<tr>
<td>H.J.</td>
<td>51</td>
<td>150/90</td>
<td>Posterior myocardial infarction 3/67; no angina</td>
</tr>
<tr>
<td>L.M.</td>
<td>50</td>
<td>120/80</td>
<td>Angina pectoris since 1968</td>
</tr>
<tr>
<td>M.C.</td>
<td>55</td>
<td>140/80</td>
<td>Angina pectoris with very heavy exercises since 1968</td>
</tr>
<tr>
<td>T.A.</td>
<td>55</td>
<td>130/80</td>
<td>Status anginosus 9/66; no residual angina</td>
</tr>
<tr>
<td>T.E.</td>
<td>64</td>
<td>110/80</td>
<td>Anterolateral infarction 12/67; no angina</td>
</tr>
<tr>
<td>W.T.</td>
<td>63</td>
<td>150/90</td>
<td>Status anginosus 2/69; no residual angina</td>
</tr>
</tbody>
</table>

*All the studies were performed between April and November, 1969.
Table 2

<table>
<thead>
<tr>
<th>Subject</th>
<th>HR</th>
<th>BP, S</th>
<th>BP, M</th>
<th>ET</th>
<th>HR × BP, S × ET</th>
<th>HR × BP, S</th>
<th>HR × BP, M</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.A.</td>
<td>0.94</td>
<td>0.90</td>
<td>0.95</td>
<td>0.86</td>
<td>0.93</td>
<td>0.94</td>
<td>0.95</td>
</tr>
<tr>
<td>C.G.</td>
<td>0.85</td>
<td>0.62</td>
<td>0.68</td>
<td>0.51</td>
<td>0.92</td>
<td>0.93</td>
<td>0.88</td>
</tr>
<tr>
<td>H.J.</td>
<td>0.91</td>
<td>0.74</td>
<td>0.80</td>
<td>0.72</td>
<td>0.84</td>
<td>0.91</td>
<td>0.92</td>
</tr>
<tr>
<td>L.M.</td>
<td>0.97</td>
<td>0.91</td>
<td>0.93</td>
<td>0.95</td>
<td>0.95</td>
<td>0.98</td>
<td>0.98</td>
</tr>
<tr>
<td>M.C.</td>
<td>0.91</td>
<td>0.59</td>
<td>0.63</td>
<td>0.85</td>
<td>0.74</td>
<td>0.90</td>
<td>0.90</td>
</tr>
<tr>
<td>T.A.</td>
<td>0.84</td>
<td>0.83</td>
<td>0.90</td>
<td>0.91</td>
<td>0.92</td>
<td>0.95</td>
<td>0.97</td>
</tr>
<tr>
<td>T.E.</td>
<td>0.96</td>
<td>0.68</td>
<td>0.85</td>
<td>0.97</td>
<td>0.82</td>
<td>0.94</td>
<td>0.95</td>
</tr>
<tr>
<td>W.T.</td>
<td>0.27</td>
<td>0.01</td>
<td>0.10</td>
<td>0.19</td>
<td>0.18</td>
<td>0.20</td>
<td>0.28</td>
</tr>
</tbody>
</table>

Table 3

<table>
<thead>
<tr>
<th>Name</th>
<th>Tension-time index at ST depression of 2 mm</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.A.</td>
<td>5.233</td>
<td>-0.9</td>
</tr>
<tr>
<td>H.J.</td>
<td>6.692</td>
<td>-1.4</td>
</tr>
<tr>
<td>L.M.</td>
<td>4.332</td>
<td>-2.1</td>
</tr>
<tr>
<td>M.C.</td>
<td>5.437</td>
<td>+5.3</td>
</tr>
<tr>
<td>T.A.</td>
<td>5.977</td>
<td>-2.1</td>
</tr>
<tr>
<td>Mean*</td>
<td>5.533</td>
<td>-0.2</td>
</tr>
</tbody>
</table>

*Calculated on the results of five subjects. Three other subjects (C.G., T.E., W.T.) did not exhibit ST depression of 2 mm during exercise 2 (see fig. 1).

which shows that slope of relationship varied individually.

The relationship between exercise ST-segment depression and pressure-time index was individually highly reproducible: indeed, values of pressure-time index corresponding to an ST-segment depression of exactly 2 mm show a mean difference between the two exercise periods of less than 1% (table 3). Good reproducibility is also obvious from figure 1 and table 2 since correlations were established taking into account the data of both exercise periods.

Tests were stopped because of fatigue in seven cases and for angina in subject LM; pressure-time indices at onset of pain were similar (5.323 and 5.401 mm Hg sec/min). Table 4 summarizes data collected at the endpoint of the two exercises.

In contrast to exercise, there was no correlation during recovery between magnitude of ST-segment depression and the pressure-time index (fig. 1). The morphology of ST-T segment is different during the recovery and often characterized by an inversion of the T wave, as illustrated by figure 2.

Discussion

The major finding of this study is a close correlation between magnitude of ST-segment depression during exercise and indices expressing myocardial oxygen requirements in seven of the eight subjects. Correlation was also

Table 4

<table>
<thead>
<tr>
<th>Load (watts/min)</th>
<th>HR (beats/min)</th>
<th>BP, S (mm Hg)</th>
<th>BP, M (mm Hg)</th>
<th>ET (sec)</th>
<th>ST depression (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise 1</td>
<td>131</td>
<td>129</td>
<td>185.5</td>
<td>137.5</td>
<td>0.244</td>
</tr>
<tr>
<td>Exercise 2</td>
<td>135</td>
<td>134</td>
<td>179.5</td>
<td>137</td>
<td>0.235</td>
</tr>
</tbody>
</table>

*Abbreviations as in table 2.
close with heart rate, blood pressure, and ejection time considered separately; among these factors, heart rate is the most commonly and the most highly correlated. No correlation was found during recovery.

Some data in the literature suggest that

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such a relation may exist. During atrial pacing magnitude of ST depression is related to pacing rate, and ST-segment changes consistently appear at the same rate.

Angina pectoris is closely related to level of myocardial oxygen requirements. Our data indicate that exercise ST-segment depression is also related to indices expressing myocardial oxygen requirements. Indeed, a horizontal or downsloping ST-segment depression of 2 mm occurred in each patient at a particular value of the pressure-time index specific for that patient. Furthermore, during exercise graded from submaximal to maximal intensity, seven of the eight subjects studied exhibited a close correlation between magnitude of ST-segment depression over 1 mm and myocardial oxygen requirements expressed by three indices. It is unlikely that these relations are coincidental since they were consistently observed in data collected during separate tests of maximal exercise. Furthermore, they were obtained despite acceleration of heart rate and fall in blood pressure which accompany repeated exercise. In one of the patients (W.T.), there is no correlation between exercise ST-segment depression and indices expressing the myocardial oxygen requirements. Although

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**Figure 2**

Electrocardiogram (V5) of subject L.M. during two periods of exercise and recovery. Note the deeply inverted T wave during recovery of exercise 2. Heart rate, systolic blood pressure, and ejection time were, respectively, 125, 167 mm Hg, and 0.255 sec at end of exercise 1 and 138, 168 mm Hg, and 0.233 sec at the end of exercise 2. Abbreviations: PTI = pressure-time index; W = watts/min.
the reason for this response is unknown, a possible explanation is that heart volume changed from one exercise test to another.6 Abnormal left ventricular hemodynamics resulting from dyskinesia might also account for this exception.16

Individual differences in the slopes relating exercise ST depression and pressure-time index may be related to differences in either coronary vascular disease or ventricular dimensions, but these could not be ascertained from this study.

Exercise ST-segment depression corresponds to a given and reproducible myocardial oxygen deficit, and the evolution of exercise ST depression is related to the progressive inadequacy of coronary blood flow.

During recovery, there is no correlation between indices expressing myocardial oxygen requirements and ST depression; simultaneously, the ECG often changes with the appearance of an inverted T wave. Similarly, after the two-step test, there was no correlation between pressure-time index and electrocardiographic observations.10 These data suggest an important difference in the mechanism of postexercise responses. During exertion, relationship between ST-segment depression and pressure-time index reflects an excessive hemodynamic demand on ischemic muscle, but lack of correlation during recovery may reflect inadequate perfusion at lower demand. Since coronary blood flow is not monitored, one cannot document two different mechanisms from these data. Other factors such as the slow disappearance of myocardial anaerobic metabolism11 could also play some role in the postexercise electrocardiogram. Indeed pacing-induced angina is attended by lactate myocardial production which subsides a few minutes after cessation of pacing.11 Similarly, the onset of ST-segment depression secondary to reduction of coronary blood flow is time-related to a rise in coronary sinus potassium and lactate levels.17

Our findings are of practical importance, especially for the study of the effects of a therapy and particularly of physical training in coronary patients.

Exercise training of coronary patients reduces both exercise heart rate and myocardial oxygen requirements.18,19 A diminution or a disappearance of ST-segment depression at submaximal exercise after training has been reported.20–24 These changes do not necessarily mean improvement of coronary circulation. If one compares electrocardiographic responses to exercise before and after training, for possible development of a collateral circulation, it is necessary to compare ECG findings at the same pressure-time index. Only an improvement of ST response at the same level of myocardial oxygen requirement permits the inference of improved coronary circulation.

Relationship between magnitude of exercise ST changes and the product of heart rate times the mean arterial pressure obviates a need for aortic catheterization since central and peripheral mean pressures are nearly identical25, 26; close relationship with heart rate alone allows the use of this very simple parameter as a determinant of ST-segment depression in clinical practice.

It must be emphasized that relationship between indices expressing myocardial oxygen requirements and magnitude of the ST-segment depression is modified by beta-blocking agents27, 28 and nitroglycerin29; indeed, these drugs modify either pre-load, contractile state, or after-load of the myocardium or ventricular volume, all of which are important determinants of myocardial oxygen requirements.

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