Ischemic Response to Sudden Strenuous Exercise in Healthy Men

By R. James Barnard, Ph.D., Rex MacAlpin, M.D., Albert A. Kattus, M.D., and Gerald D. Buckberg, M.D.

SUMMARY

In ten healthy, asymptomatic men, intra-arterial pressure and electrocardiograms were recorded during various types of exercise. Potential subendocardial blood flow was estimated from a diastolic pressure time index (DPTI) and myocardial oxygen requirements estimated from the tension time index (TTI). The ratio DPTI/TTI provided an estimate of the supply/demand relationship. With sudden vigorous exercise without warm-up, the DPTI/TTI was below 0.35 in three men who had ischemic electrocardiograms, below 0.44 in three men with minor ST abnormalities, and above 0.44 in four men with normal ST segments. With a prior warm-up exercise, sudden exercise caused no ischemic changes, but DPTI/TTI was below 0.44 in two subjects who had minor ST abnormalities. Maximum treadmill testing produced higher heart rates and TTI than did sudden exercise, but DPTI/TTI was above 0.44 in all cases and no ST abnormalities occurred.

Abnormal electrocardiographic responses produced by sudden, vigorous exercise in normal men may represent subendocardial ischemia caused by a transient, unfavorable alteration in the subendocardial oxygen supply/demand relationship which is predictable from arterial pressure measurements.

Additional Indexing Words:
Treadmill test  Diastolic pressure time index  Tension time index

Previous investigations by Barnard et al. have shown that some normal, healthy volunteers develop ischemic electrocardiographic changes when sudden, strenuous exercise (10 to 15 sec treadmill run at 9 MPH, 30% grade) is performed without prior warm-up activity. These ischemic responses were not related to age or state of physical conditioning and could be eliminated when warm-up exercise preceded the sudden strenuous activity.

In recent studies by Buckberg et al., subendocardial ischemia was produced experimentally in dogs with patent coronary arteries and normal or elevated mean coronary blood flows. These investigators showed that the adequacy of subendocardial perfusion could be predicted from indices derived from readily obtainable blood pressure measurements. Potential subendocardial blood supply was estimated from the diastolic pressure-time index (DPTI), and myocardial oxygen demand from the tension-time index (TTI). Histochemical evidence of subendocardial ischemia was observed when the ratio of these indices (DPTI/TTI) fell below 0.70. The present studies were conducted to see how DPTI/TTI ratios correlated with electrocardiographic changes in exercising men and to determine if these ratios might provide insight into the cause of abnormal electrocardiograms.

Methods

The 10 subjects were either volunteers from the Los Angeles Fire Departments or university students. They ranged in age from 20 to 52 years and were assumed to have normal coronary arteries since they had no symptoms and their near-maximal treadmill exercise ECG was normal. Arterial blood pressure was measured by introducing a polyethylene catheter (0.045 inches I.D.) into the left brachial artery percutaneously using lidocaine (1%) anesthesia. The tip of the catheter was advanced approximately 6 inches until its tip was in the axillary artery. The catheter was connected to a Statham P23DB transducer and pressure was recorded on a Honeywell 906 Visicorder. The junction of the fourth rib and sternum was used as the zero reference

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level. Electrocardiograms (V₅-V₆R) were recorded from Sanborn exercise electrodes.

Arterial pressure and electrocardiographic recordings were obtained after a 15 min rest period while the subjects stood beside the treadmill. Without prior warm-up, the subjects ran on the treadmill for 20 sec at 10 MPH, 24% grade. Blood pressure and electrocardiographic recordings were obtained throughout the run and during the immediate 30 sec recovery period. The recordings obtained during running exercise could not be adequately evaluated because of motion artifact so that only data obtained during the first few beats in the immediate recovery period were used. When blood pressure had returned to resting levels, the subjects performed a standard multistage treadmill test, exercising for 2 min at each workload until their heart rates were near maximum for their age range. Details of the treadmill test have been described previously. Twenty minutes after the maximal treadmill test, the men again ran for 20 sec at 10 MPH, 24% grade, to test the effect of warm-up exercise on the cardiovascular responses to sudden strenuous activity. During the high-speed runs the subjects were permitted to hold on to the rail with their right hand to maintain balance.

Arterial blood pressure recordings from 3 consecutive heart beats were analyzed by planimetry to obtain an average value for TTI and DPTI. Left atrial pressure was assumed to be 5 mm Hg. The t-test was used for statistical analysis.

**Results**

**ECG**

During the progressive multistage treadmill test, all 10 subjects had normal electrocardiograms at near-maximal heart rates. After sudden, strenuous exercise without warm-up, the ECGs of 6 men were abnormal: 3 had ischemic ST segment depression, and 3 had minor ST or T wave changes. Examples are shown in figure 1. When the same sudden exercise was performed after warm-up activity, 8 subjects had normal ECG's while 2 had only minor ST or T wave changes (table 1). The duration of the abnormal ECG responses ranged from a few beats to 8 sec. None of the subjects with abnormal ECG responses experienced chest pain or other symptoms of discomfort.

![Sample ECG recordings obtained immediately after sudden strenuous exercise performed without prior warm-up activity. (Left), minor ST or T wave changes. (Right), ischemic ST segment depression.](image)

*Table 1*

<table>
<thead>
<tr>
<th>Subject</th>
<th>Heart rate</th>
<th>Diastolic pressure</th>
<th>TTI</th>
<th>DPTI</th>
<th>ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>JE</td>
<td>46</td>
<td>162</td>
<td>63</td>
<td>4908</td>
<td>ischemic</td>
</tr>
<tr>
<td>BH</td>
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<td>140</td>
<td>33</td>
<td>2688</td>
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<tr>
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<td>130</td>
<td>62</td>
<td>4630</td>
<td>normal</td>
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<tr>
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<td>180</td>
<td>62</td>
<td>68</td>
<td>normal</td>
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<tr>
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<td>171</td>
<td>89</td>
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<tr>
<td>RB</td>
<td>34</td>
<td>153</td>
<td>60</td>
<td>163</td>
<td>normal</td>
</tr>
<tr>
<td>MA</td>
<td>34</td>
<td>153</td>
<td>60</td>
<td>163</td>
<td>normal</td>
</tr>
</tbody>
</table>

*Table 1:* Cardiac responses to sudden, strenuous exercise.

*Excerpts from an article on ischemic response to exercise, published in Circulation.*
Heart Rate

Data from the various exercise conditions are given in table 2. During the final stage of the progressive treadmill test, heart rates ranged from 162 beats/min (for the 52-year-old subject BH) to 200 beats/min (for the 20-year-old subject PS). When sudden, strenuous exercise was performed without prior activity, no significant difference was observed between the heart rate response of those subjects with normal and those with abnormal ECG responses (table 3). When sudden, strenuous exercise was performed following warm-up activity, average heart rate rose from 96 to 165 beats/min. These heart rates were significantly higher than those observed without prior warm-up (table 1).

TTI

The tension time indices during the different exercise states are presented in tables 1, 2 and 3. Samples of the pressure recordings are shown in figures 2 and 3. The greatest TTI was usually recorded during the final stage of the progressive treadmill test when heart rate and blood pressure were highest. When sudden, strenuous exercise was performed without prior activity, TTI rose significantly because systolic blood pressure was increased and systolic time per minute was increased. In 7 subjects, however, it was less than that recorded during the progressive treadmill test. The mean TTI for the 6 subjects with abnormal ECG responses during sudden exercise was not significantly higher than that of the 4 subjects with normal ECG responses. Despite higher heart rates when sudden, strenuous exercise was performed following warm-up activity, 9 subjects had lower TTIs than when the same exercise was performed without warm-up (table 1). The lower TTIs following warm-up occurred because systolic pressure was lower and the systolic ejection period was shorter (table 1 and fig. 3).

DPTI

The diastolic pressure time index declined steadily during the progressive treadmill test because tachycardia shortened diastole. When sudden, strenuous exercise was performed without warm-up activity, the lowest DPTI values were observed (table 3, fig. 2) primarily because the prolonged systolic ejection times and tachycardia significantly shortened diastolic duration. Those individuals with abnormal ECG responses had mean DPTI values which were significantly lower than those recorded for the subjects with normal ECG responses (table 2). Subject JE, however, had a DPTI of 1750 mm Hg sec min⁻¹ with an ischemic response, while BH had a DPTI of 1512

Table 2

Cardiovascular Responses to Various Types of Exercise

<table>
<thead>
<tr>
<th>Condition</th>
<th>Heart rate</th>
<th>Diastolic pressure</th>
<th>Systolic pressure</th>
<th>TTI (mm Hg sec.)</th>
<th>DPTI (min⁻¹)</th>
<th>DPTI/TTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>80.9 ± 5.4</td>
<td>82.0 ± 4.5</td>
<td>135.5 ± 6.8</td>
<td>2261 ± 172</td>
<td>3557 ± 187</td>
<td>1.61</td>
</tr>
<tr>
<td>Near maximal treadmill test</td>
<td>179.6 ± 3.6</td>
<td>84.9 ± 3.6</td>
<td>185.5 ± 5.6</td>
<td>4549 ± 171</td>
<td>2319 ± 109</td>
<td>0.09</td>
</tr>
<tr>
<td>Sudden exercise without prior activity</td>
<td>158.3 ± 3.9</td>
<td>70.7 ± 4.5</td>
<td>156.0 ± 7.0</td>
<td>4147 ± 245</td>
<td>1806 ± 158</td>
<td>0.05</td>
</tr>
<tr>
<td>Sudden exercise after warm-up</td>
<td>164.8 ± 2.8</td>
<td>66.7 ± 3.8</td>
<td>139.1 ± 7.2</td>
<td>3502 ± 191</td>
<td>1949 ± 148</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Table 3

Comparison of Subjects with Normal and Abnormal ECG Responses to Sudden, Strenuous Exercise without Prior Warm-up

<table>
<thead>
<tr>
<th></th>
<th>Heart rate</th>
<th>Diastolic pressure</th>
<th>Systolic pressure</th>
<th>TTI (mm Hg sec. min⁻¹)</th>
<th>DPTI (min⁻¹)</th>
<th>DPTI/TTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal ECG</td>
<td>155.8 ± 6.8</td>
<td>75.3 ± 8.5</td>
<td>156.5 ± 16.7</td>
<td>3651 ± 372</td>
<td>2170 ± 319</td>
<td>0.59</td>
</tr>
<tr>
<td>Abnormal ECG</td>
<td>160.0 ± 5.1</td>
<td>67.7 ± 5.1</td>
<td>155.7 ± 7.3</td>
<td>4479 ± 265</td>
<td>1563* ± 67</td>
<td>0.35*</td>
</tr>
</tbody>
</table>

*Significantly different from normal group (P ≤ 0.05).
Arterial pressure recordings obtained from subject DA at rest and immediately after exercise. The stippled area was used to calculate the diastolic pressure time index (DPTI) and the clear area to calculate the tension time index (TTI). Left atrial pressure (dark area) was assumed to be 5 mm Hg.

Figure 2

Arterial pressure recordings obtained from subject DA immediately after a 20 sec run at 10 MPH, 24% grade. The cold run was performed without any prior activity. The warm-up run was performed 20 min after a multistage treadmill test. See figure 2 for explanation of stippled, clear and dark areas.

Figure 3
mm Hg sec min⁻¹ with a normal ECG response (table 1). When sudden exercise was performed following warm-up, DPTI was significantly higher (table 1). This increased DPTI value occurred despite more rapid heart rates, because systole was shorter after warm-up.

**DPTI/TTI**

During the final stage of the progressive treadmill test, all subjects had normal ECG responses and DPTI/TTI ratios above 0.44 (fig. 4). When sudden exercise was performed without warm-up, the 6 subjects with abnormal ECG responses had DPTI/TTI ratios below 0.44. Conversely, the 4 subjects with normal ECG responses had ratios higher than 0.44 (table 1). When sudden exercise was preceded by warm-up activity, 8 subjects had normal ECGs and DPTI/TTI ratios above 0.44, while the subjects with abnormal ECG responses had ratios of 0.41 and 0.43 (table 1). Each of these subjects showed more ischemic ECG responses and lower DPTI/TTI ratios when they suddenly exercised without preceding warm-up.

**Discussion**

The sudden strenuous exercise performed by our subjects was designed to simulate conditions frequently encountered by firemen. This exercise was imposed only after prior multistage near-maximal exercise tests had disclosed normal ECG responses in all subjects. This method is not recommended as a test for use under ordinary clinical conditions especially when coronary artery disease is expected.

Electrocardiographic responses observed in these studies are similar to those previously reported from our laboratory in that abnormal electrocardiograms occurred in 60 percent of apparently healthy men following sudden, vigorous exercise. These abnormal responses were not related to age or state of physical conditioning and were eliminated or reduced in severity by preliminary warm-up exercise. The abnormal responses were, however, of shorter duration when the subjects were studied while arterial catheters were in place. Without the catheter most subjects had abnormal responses which lasted from 10 to 20 sec. With the catheter in place only one subject had an abnormal response which lasted longer than 5 sec. Of the three subjects who participated in both experiments, one had a normal response with the catheter as opposed to minor ST changes without. The other two subjects had ischemic responses under both conditions; however, the duration was only half as long with the catheter in place. It is possible that placing the intra-arterial catheter may have caused apprehension which acted in part as a warm-up.

Although it is conceivable that organic coronary artery disease may have been present in some of our subjects, it seems unlikely that anatomic obstruction of the coronary lumen would account for the abnormal ECG responses to sudden exercise observed in over 60 percent of the 54 subjects in this study and our previous work.¹

Since the near-maximal treadmill ECG tests were normal in all subjects we assume that they had patent coronary arteries. If this assumption is correct the observed abnormal ECG changes must be due to a functional encroachment upon the adequacy of coronary blood supply in relation to simultaneously increased oxygen demands of exercise. We used the tension time index of Sarnoff⁴ to estimate myocardial oxygen requirements. We realize, however, that this index underestimates oxygen requirements by as much as 30 percent during isotropic stimulation.⁵

Since oxygen extraction is normally high under resting conditions, the heart increases its oxygen delivery by raising coronary blood flow in response to metabolically induced vasodilation. When maximum coronary dilatation occurs, coronary flow and oxygen delivery are determined by the coronary driving pressure and diastolic duration. This driving pressure is equal to the difference between coronary arterial diastolic pressure and impedance to coro-

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**Figure 4**

Effect of exercise on ECG and DPTI/TTI. Values are means and ranges obtained from 10 subjects immediately after the near maximal multistage treadmill test (treadmill), after sudden exercise without prior activity (cold) and from 8 subjects after sudden exercise preceded by warm-up activity (warm-up).
nary flow offered by coronary sinus pressure or left ventricular diastolic pressure, whichever is greater. If the coronary arteries are not obstructed, then coronary arterial diastolic pressure is equal to aortic diastolic pressure. Since both left ventricular diastolic pressure and coronary sinus pressure stay the same or fall with exercise, we assumed a value of 5 mm Hg and did not measure these directly. If left ventricular diastolic pressure did increase before or during the ischemic ECG changes as has been reported, then DPTI would overestimate the potential oxygen supply. Simultaneous measurement of pulmonary artery wedge pressure (Swan-Ganz catheter) would provide a more precise estimate of the coronary driving pressure (DPTI).

These pressure time events during diastole are described by the diastolic pressure time index, which has been shown to estimate diastolic and subendocardial blood supply during maximum coronary vasodilatation in experimental studies. The ratio of this index to the tension time index has been shown to provide an estimate of the oxygen supply/demand relationship. The present studies were conducted to determine how these indices, or the variables determining them, correlate with the electrocardiographic responses to various types of exercise.

The pressure recordings obtained immediately after exercise were not significantly different from those obtained during exercise. This observation precludes the possibility that major changes occurred within the first few seconds after the cessation of running. However, movement artifact observed during the run precluded any accurate analysis of the pressure tracings. In addition, our previous work demonstrated that the abnormal ECG responses were not due to the sudden cessation of exercise.

It is evident from our data that no single variable (heart rate, systolic or diastolic blood pressure, TTI or DPTI) correlated with the ECG changes observed during the different exercise conditions. For example, heart rate, systolic blood pressure, and the resultant tension time index were highest in most subjects during maximum treadmill testing, but no electrocardiographic abnormalities were observed. Conversely, arterial diastolic pressure was lowest after sudden exercise following warm-up activity and only two subjects showed minor ECG changes. When the sudden exercise was performed without preceding warm-up, arterial diastolic pressure was higher and 6 subjects showed abnormal electrocardiograms. Each of the abnormal electrocardiograms could, however, be predicted from the ratio DPTI:TTI under the various exercise states. The elimination or reduction in severity of the abnormal electrocardiographic response following warm-up was associated with an increased DPTI:TTI ratio in each subject.

Examination of the changes in the variables comprising these indices provides some insight into a possible cause of the ischemic electrocardiographic responses, as well as how preceding warm-up exercise modified them. The increase in heart rate and systolic blood pressure immediately upon starting sudden exercise suggests a massive sympathetic discharge occurred with this type of exertion. This response imposes a marked increase in cardiac oxygen requirements. If the coronary arteries do not simultaneously vasodilate to provide sufficient blood supply to meet these raised oxygen needs, then subendocardial ischemia may result.

This concept is supported by the recent experimental studies of Monroe and associates who showed that there is a delay in coronary autoregulation when oxygen demands of the heart are suddenly raised by impeding left ventricular outflow. These investigators recorded ischemic electrocardiographic patterns from intracavitary electrocardiographic leads and showed that coronary blood flow became redistributed away from subendocardial muscle at these times.

If this sequence occurred at the onset of exercise then the prolonged systolic ejection times which immediately followed sudden exertion may have been due to ischemia. Another cause for the prolonged systolic ejection period may be a lag between myocardial and peripheral catecholamine elaboration, so that enhanced contractility did not simultaneously accompany the increased venous return caused by exercise. This condition would exist if the tachycardia was due primarily to a decrease in parasympathetic tone. The prolonged systolic ejection time, from whatever cause, limits the time available for diastolic perfusion and may, therefore, potentiate ischemia.

It is also possible that the ischemia was caused by coronary vasoconstriction. Khouri, Gregg and Rayford and Erlich et al. found that coronary blood flow decreased during the first 4–6 sec of mild exercise in dogs. They suggested that the decrease in coronary flow was a result of vasoconstriction which was followed immediately by vasodilatation as metabolites accumulated in the myocardium.
The importance of immediate coronary autoregulation was emphasized by Monroe and associates\(^8\) when they administered coronary vasodilatory drugs in order to provide excessive coronary blood flow prior to suddenly increasing cardiac oxygen needs. Pretreatment with these drugs protected the heart against the abnormal electrocardiographic responses and redistribution of coronary flow which had previously accompanied sudden increases in left ventricular outflow obstruction.

It is also possible that less sympathetic discharge occurred when vigorous exertion followed warm-up. In this way, systemic blood pressure increased less after sudden exercise and cardiac oxygen requirements were lower. Thus, the normal electrocardiograms observed after warm-up perhaps occurred because oxygen delivery could more adequately meet the lower oxygen demands.

The DPTI/TTI ratios at which ischemia occurred in this study were lower than values where Buckberg et al.\(^2\) showed subendocardial ischemia in experimental animals. Recent analysis of catheterization records and metabolic data obtained from patients with aortic stenosis and patent coronary arteries showed that abnormal lactate metabolism occurred when the supply to demand ratio fell below 0.32 (unpublished observation). Monroe and associates\(^8\) observed ischemic subendocardial electrocardiographic changes while subepicardial electrocardiograms were normal, so it is possible that we underestimated the degree of ischemia in these studies.

In summary, our data indicate that the abnormal electrocardiographic responses following sudden exercise are the result of an unfavorable shift in the balance of myocardial oxygen supply and demand. Warm-up exercise preceding sudden exertion results in a more favorable supply/demand relationship. The blood pressure measurements used in our attempt to quantitate this relationship provide some insight into possible causes of the electrocardiographic abnormalities. These studies also indicate a physiologic basis for preceding sudden exertion with warm-up exercise.

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