Left Ventricular Function During Sudden Strenuous Exercise

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SUMMARY Strenuous exercise without warm-up has been shown to produce ischemia-like electrocardiographic (ECG) abnormalities in 60–70% of healthy subjects. These abnormalities appeared to be related to the development of an unfavorable myocardial supply/demand balance and, in chronically instrumented dogs, to transient decreases in coronary blood flow. A mechanism involving subendocardial ischemia has been proposed to explain the response to sudden strenuous exercise (SSE). To determine whether the response to SSE included the development of changes in myocardial pump performance typical of ischemia, left ventricular (LV) function at rest, during graded exercise and during SSE was evaluated in nine young (26.6 ± 3.4 years), well-trained male volunteers using first-pass radionuclide angiography. During graded exercise, the LV ejection fraction increased from 66.9 ± 9.4% at rest to 73.0 ± 7.1% during peak exercise, and the LV ejection rate increased from 3.36 ± 0.67 sec⁻¹ at rest to 6.58 ± 1.10 sec⁻¹ during peak exercise. Segmental wall motion was normal in all studies. During SSE, the LV ejection fraction decreased in every subject, from an average 72.2 ± 8.6% at rest to 57.3 ± 8.1% during exercise. The LV ejection rate remained relatively constant (3.98 ± 0.92 sec⁻¹ at rest vs 4.33 ± 0.74 sec⁻¹ during SSE). No segmental wall motion abnormalities were observed during SSE; however, LV wall motion appeared to be diffusely hypokinetic during SSE. In contrast to previous reports, few ECG abnormalities were observed during SSE. These results support the hypothesis that subendocardial ischemia is an important mechanism in the response to SSE. However, the lack of ECG changes and segmental wall motion abnormalities and the relatively high absolute value of the LV ejection fraction suggest that if subendocardial ischemia occurs during SSE, it is attributable to physiologic rather than pathologic mechanisms.

ISCHEMIA-LIKE electrocardiographic (ECG) changes in 60–70% of apparently healthy subjects who perform severe exercise without warm-up have been reported.¹,² These subjects had normal responses during graded exercise testing and were considered free of coronary artery disease (CAD). The development of the ischemia-like ECG changes correlated well with the relative myocardial oxygen supply/demand relationship as estimated from the ratio of the diastolic pressure time index to the tension time index (DPTI/TTI).³ Because experiments with chronically instrumented animals have indicated a transiently decreased coronary blood flow during sudden strenuous exercise (SSE),⁴ Barnard et al.⁵ suggested that the ECG responses during SSE represent subendocardial ischemia. The present investigation was conducted to determine whether SSE would induce changes in LV function similar to those in patients with CAD⁶ that would support Barnard’s hypothesis of subendocardial ischemia during SSE.

Methods

Subjects

The subjects for this investigation were nine healthy men (mean age 26.6 ± 3.4 years). All were non-smokers who participated in endurance games or sports several times weekly. On the average (± sd), the subjects were 180.0 ± 7.0 cm in height, 78.3 ± 8.0 kg in weight, and 9.8 ± 2.8% fat.¹⁹ The subjects were recruited as volunteers and participated after providing informed consent.

Exercise Protocol

Subjects were studied on three separate mornings after an overnight fast. The studies were separated by approximately 1 week and the subjects were requested not to vary their lifestyle during the period of study. Additionally, they were instructed to avoid heavy exertion on the day before each laboratory visit and to avoid all exercise on the morning of each study. During the first laboratory visit, the subject was oriented to the general scope of the study, a medical history was obtained, and a symptom-limited graded exercise test (SLGXT) was performed for the purpose of screening inappropriate responses to exercise not evident from the subject’s history. Exercise was performed on a mechanically braked bicycle ergometer (Monarch) with the pedal frequency fixed at 60 rpm. The initial work load was 30 W and was increased by 15 W every minute until the subject could no longer continue. Strong verbal encouragement was given to

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ensure a maximal effort. A 12-lead ECG was obtained at rest and during each minute of the test; blood pressure was measured every third minute. ECG tracings and blood pressure were obtained at 1 and 5 minutes of recovery.

During the second laboratory visit, each subject again performed a symptom-limited graded exercise test. During this test, LV function was measured using first-pass radionuclide angiography (RN-SLGXT). Exercise was performed on an electrically braked bicycle ergometer (W. E. Collins, Inc.) with a pedal frequency of 60 rpm. The initial work load was 25 W and was increased by 25 W every 2 minutes until the subject could not continue. Strong verbal encouragement was again given to ensure maximal effort. The ECG (lead V6) was recorded during each minute of the test and the blood pressure was obtained every second minute. LV function was measured before exercise and during the last 15 seconds of exercise. The ECG and blood pressure were monitored during the first 5 minutes of recovery.

During the third laboratory visit, each subject performed SSE on the electrically braked ergometer (RN-SSE). The work load on the ergometer was set at 400 W as the subject began pedaling at about 80 rpm. Exercise was discontinued after 30 seconds. LV function was measured before the study and during the last 15 seconds of exercise. A practice trial after RN-SLGXT had been performed to acquaint the subject with the skill of starting the ergometer against the torque imposed by the high work load. The ECG (lead V6) was monitored continuously during rest, exercise and recovery. The blood pressure was measured at rest, at peak exercise and during the first 5 minutes of recovery.

Radionuclide Technique

First-pass radionuclide angiograms were obtained with a computerized multicyrystal scintillation camera (Cordis-Baird System 77). An 18-gauge, 2½-inch polyethylene catheter was placed in a right antecubital vein for radionuclide injection. All studies were performed with the subject upright and in the 30° right anterior oblique position. The subject’s position relative to the camera was maintained with a foam wedge. During the studies, an assistant stabilized the subject’s chest against the wedge. The resting studies were performed immediately before either RN-SLGXT or RN-SSE with the subject sitting on the ergometer in a position identical to that used during the subsequent exercise study. All exercise studies were performed during peak exercise. Technetium-99m pertechnetate was used for all studies and was given as a bolus of 15 mCi at a concentration of 30 mCi/ml with a 20-ml saline push. Counts were obtained over the precordium at a high framing rate (30 msec) using 1.5-inch, parallel-hole collimation.

Radionuclide Data Processing

The serial passage of the isotope was followed through the heart, a LV region of interest was identified and flagged, and a time-activity curve was generated. After appropriate background subtraction, a representative cycle was created from four to eight beats of the LV time-activity curve. The LV ejection fraction (LVEF) was calculated as: total end-diastolic counts minus total end-systolic counts divided by total end-diastolic counts. The mean normalized LV ejection rate (LVER) was computed from the individual beats that constituted the representative cycle by using a least-squares curve fitting technique as outlined by Marshall et al. Segmental wall motion was evaluated by two experienced observers using both the end-systolic image circumscribed by the end-diastolic perimeter and the regional distribution of ejection fraction image. This functional image represents the stroke volume divided by the end-diastolic image and gives a three-dimensional concept of wall motion.

Statistical Methods

The data were analyzed using Dunn’s multiple comparison procedure, which is similar to a paired t test but with appropriate adjustment of the confidence interval for multiple usage. A p value of 0.05 or less was considered statistically significant.

Results

All subjects completed three exercise protocols without chest discomfort, inappropriate blood pressure response or other clinical indications of an inappropriate response to exercise. The mean responses during the three protocols are presented in table 1.

During RN-SLGXT, the heart rate increased to 177.2 beats/min, which represents 92% of the age-predicted maximal heart rate for the subjects. The lower work load and heart rate obtained during RN-SLGXT as compared to the diagnostic SLGXT is indicative of the difficulty of pedaling the ergometer while sitting in front of the scintillation camera. The heart rate and double product during RN-SSE were significantly less than those during RN-SLGXT.

During both SLGXT and RN-SLGXT, all subjects had normal ECG patterns. During RN-SSE, one subject had inverted T waves during the first minute of recovery. No other ECG abnormalities were noted during or after SSE. The LVEF increased during RN-SLGXT from a mean of 66.9% at rest to 73.0% during exercise. In the only subject who failed to increase LVEF during RN-SLGXT, the LVEF decreased from 85% to 83%. During RN-SSE, the LVEF decreased in every subject from a mean 72.7% at rest to 57.3% during SSE. The LVEF response to RN-SSE was significantly different from the response to RN-SLGXT (fig. 1).

The LVER increased during RN-SLGXT from rest to exercise (3.36 to 6.58 sec−1) and was largely unchanged during SSE (3.98 to 4.33 sec−1). The change in LVER during RN-SLGXT and RN-SSE was significantly different (fig. 1).

Segmental wall motion was normal during all
Table 1. Mean (± sd) Responses During the Three Exercise Protocols

<table>
<thead>
<tr>
<th></th>
<th>SLGXT</th>
<th>RN-SLGXT</th>
<th>RN-SSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Work load (W)</td>
<td>300.0 ± 44.7*</td>
<td>238.9 ± 28.3</td>
<td>400.0 ± 0.0*</td>
</tr>
<tr>
<td>Resting HR (beats/min)</td>
<td>62.4 ± 9.9</td>
<td>66.7 ± 15.4</td>
<td>74.2 ± 16.0</td>
</tr>
<tr>
<td>Max HR (beats/min)</td>
<td>184.6 ± 8.9*</td>
<td>177.2 ± 11.0</td>
<td>149.7 ± 13.6*</td>
</tr>
<tr>
<td>Maximal double product (mm Hg × beats/min)</td>
<td>33.1 ± 3.9 × 10³</td>
<td>33.3 ± 2.4 × 10³</td>
<td>24.2 ± 2.9 × 10³</td>
</tr>
<tr>
<td>Resting LVEF (%)</td>
<td>--</td>
<td>66.9 ± 9.4</td>
<td>72.2 ± 8.6</td>
</tr>
<tr>
<td>Exercise LVEF (%)</td>
<td>--</td>
<td>73.0 ± 7.1</td>
<td>57.3 ± 8.1*</td>
</tr>
<tr>
<td>Resting LVER (sec⁻¹)</td>
<td>--</td>
<td>3.36 ± 0.67</td>
<td>3.98 ± 0.98</td>
</tr>
<tr>
<td>Exercise LVER (sec⁻¹)</td>
<td>--</td>
<td>6.58 ± 1.10</td>
<td>4.33 ± 0.78</td>
</tr>
</tbody>
</table>

*Significantly different than RN-SLGXT, p < 0.05.

Abbreviations: SLGXT = symptom-limited graded exercise test; RN-SLGXT = symptom-limited graded exercise test with radionuclide measurement of left ventricular function; RN-SSE = sudden strenuous exercise with radionuclide measurement of left ventricular function; LVEF = left ventricular ejection fraction; LVER = mean normalized left ventricular ejection rate.

However, during RN-SSE there was a tendency for the development of diffuse symmetric hypokinesis and for a modest degree of LV dilatation (fig. 2).

Discussion

Exercise-induced myocardial ischemia in patients with CAD produces an array of responses, including ST-segment depression, decreased LVEF, small or no increase in LVER, the development of segmental wall motion abnormalities and LV dilatation. Barnard et al. have presented evidence of ischemia-like ST segment depression (1 mm horizontal or downsloping) in a significant proportion of apparently healthy subjects who performed SSE. Because this response was similar to the ECG response of patients with CAD,
and because subsequent experiments in both human and animal models suggest abnormalities of coronary blood supply during SSE, the present study was conducted to determine whether SSE might induce changes in LV function consistent with a hypothesis of subendocardial ischemia in healthy subjects during SSE.

The subendocardium is thought to be the portion of the myocardium most susceptible to limitations of coronary blood flow. Factors acting to reduce either the diastolic filling time or pressure are thought to produce relative subendocardial ischemia, and have been shown to contribute to a compromised endocardial contractility. The consistently decreasing LVEF and inappropriately low LVER observed in the present investigation are consistent with the mild LV dysfunction that would be expected if the response to SSE includes subendocardial ischemia. Likewise, the diffusely hypokinetic LV wall motion and mild LV dilatation is consistent with the result expected from LV dysfunction secondary to subendocardial ischemia.

The lack of segmental wall motion abnormalities during RN-SSE represents a departure from the expected results if SSE-induced ischemia is functionally equivalent to ischemia in patients with the localized coronary artery blood flow disturbances characteristic of CAD. It is, however, generally consistent with the results that might be predicted for global subendocardial ischemia. Similarly, the lack of ischemia-like ECG changes during SSE is a departure from previous results in which ST-segment changes were observed in 60–70% of healthy subjects during SSE. There are several possible causes for this discrepancy. The electrocardiographic arrangement in this study (V5) and that used by Barnard et al. (transthoracic V5-V6R) are approximately equivalent in terms of inherent sensitivity. However, Barnard et al. showed that the transthoracic ECG is comparatively insensitive in detecting subendocardial ischemia. Thus, very small differences in either the degree of ischemia or the sensitivity of the instrumentation may be reflected as significant differences in the incidence of abnormal ECG responses. Barnard et al. noted that the severity
and duration of abnormal ECG findings were reduced during studies in which arterial catheters were in place. They have suggested that the apprehension associated with placement of arterial catheters may have effectively acted as a warm-up. Although considerable care was taken to ensure that our subjects were in the resting state, a similar argument can be proposed to account for the relative absence of abnormal ischemia-like ECG findings during RN-SSE. The small discomfort of placing the venous catheter, the effort involved in positioning the subject next to the scintillation camera, the cardiovascular effects of the resting cardiac dynamic study, and the anticipation of the impending exercise may have worked together to produce an effect similar to warm-up and diminished the severity of any ischemia during RN-SSE. The numerically, but not statistically, higher resting heart rate, LVEF and LVER during RN-SSE compared with RN-SLGXT support this explanation. Barnard et al., reported evidence that the ischemia-like ECG changes during SSE may be normalized if the exercise is continued for approximately 1 minute. The duration of RN-SSE in this study (30 seconds) was longer than used by Barnard et al. (10–20 seconds). This small increase in duration, used because of the technical requirements of the radionuclide technique, may also have contributed to the relatively normal ECG findings in this investigation. Thus, although the primary findings of Barnard et al. were not duplicated during this investigation, our results may be accounted for in several ways that tend to minimize the importance of differences between our findings and theirs.

The results of the present study indicate that LV behavior is abnormal during SSE. These abnormalities are in some respects similar to the abnormalities of LV function during exercise in patients with CAD. Thus the data support the hypothesis of subendocardial ischemia during SSE. However, the relatively high absolute values of LVEF and the absence of segmental wall motion abnormalities suggest that the LV response to SSE is in some important aspects different from that during graded exercise in patients with CAD.

The mechanism for the abnormal response to SSE remains unclear. The abnormal response to SSE is in some respects similar to the LV response to abrupt pressure loading first described in 1912 by Knowlton and Starling and by von Anrep. Reports from several laboratories suggest that the positive inotropic state that characterizes the Anrep effect represents the recovery from an ischemic insult occurring at the time of abruptly increasing LV systolic pressure. However, the lack of direct data regarding intraventricular pressures in the present study makes evaluation of this hypothesis impossible. Further, because these reports were largely compiled in animal preparations by dramatic increases in ventricular afterload (though aortic constriction), the applicability to SSE, in which the hemodynamic state is much more complicated, is uncertain.

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