Impaired Maximal Exercise Performance with Hypertensive Cardiovascular Disease

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SUMMARY

Responses to a multistage treadmill test of maximal exercise were studied in 61 hypertensive patients: 13 had uncomplicated hypertension; 15 had associated retinopathy; 22 had left ventricular hypertrophy; and 11 also had coronary heart disease. Because of significant differences with aging normally, and differences in ages of these subgroups, responses were compared with those of normotensive persons matched for age and sex.

With only elevated blood pressure there was no impairment of exercise performance and no increase in S-T segment depression. With ventricular hypertrophy and particularly with retinopathy, maximal exercise duration was shortened. Prevalence of postexercise myocardial ischemia, manifested by S-T segment depression, was increased threefold in those with hypertrophy of the left ventricle.

Even greater impairment of exercise duration, maximal heart rate, and systolic pressure was observed in patients with coronary heart disease and hypertension. Prevalence of S-T segment depression was sevenfold greater.

This ECG manifestation of myocardial ischemia may represent either an augmented contractile force or a significantly restricted coronary blood supply to limit myocardial perfusion. Differences in duration of exercise and circulatory responses, particularly the product of maximal heart rate and maximal systolic pressure/100, indicate these variations in pathophysiological mechanisms.

Additional Indexing Words:
Retinopathy  Myocardial ischemia  Left ventricular hypertrophy
Coronary heart disease  S-T segment depression

DEMANDS for circulatory transport of oxygen to skeletal muscles and myocardium increase with exercise, but the amounts supplied by the peripheral and the coronary circulations may be limited by cardiovascular disease. Sustained hypertension accentuates hemodynamic stress on the left ventricle, initiates myocardial hypertrophy, and aggravates coronary atherosclerosis. The relative importance of various manifestations of hypertensive cardiovascular disease is more clearly revealed by quantitative effects on exercise capacity and myocardial ischemia. In ambulatory patients these effects may be appraised by a multistage test of maximal exercise. Inasmuch as both severity of disease and maximal limits of exercise vary inversely with aging, a critical study of this clinical model requires comparison with age-matched healthy persons.

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Methods

Sixty-one ambulatory patients (38 males and 23 females) from 16 to 67 years of age were selected for study because of persistently elevated resting systolic pressure of 160 mm Hg or more or diastolic pressure of 95 mm Hg or more, or both. Of these 61 hypertensive patients 13 had no other clinical findings, 15 had hypertensive retinopathy (without hemorrhages, exudate, or papilledema), 22 had radiological evidence of enlargement or electrocardiographic signs of hypertrophy of the left ventricle, or both, and 11 had associated coronary heart disease with angina pectoris or healed myocardial infarction. Diagnosis of myocardial infarction required evidence of transient elevation of enzyme levels. Diagnosis of angina pectoris required a history of recurrent episodes of typical chest pain with exertion or emotion and prompt relief from nitroglycerin taken sublingually. Three patients with both retinopathy and hypertrophy of the left ventricle were classified in the subgroup of hypertrophy. Of the 50 patients without coronary heart disease, none had angina pectoris, two had a history of heart failure, one had atrial fibrillation, and five were treated with digitalis. None had encephalopathy or uremia. Of 29 who were under treatment with antihypertensive agents, 17 showed some clinical improvement prior to this study.

Blood pressure was measured in the upright position, with an aneroid sphygmomanometer on the arm, before and immediately after maximal exercise. Heart rates just before, during, and after exercise were determined from the electrocardiogram.

Exercise in the upright posture was standardized with the multistage treadmill test of maximal exercise. Exertional effort at the prescribed speeds and grades was increased every 3 min to a self-determined limit of maximally tolerated fatigue, dyspnea, or chest pain. Maximal oxygen intake in milliliters per kilogram of body weight per minute is highly correlated with duration of this multistage exercise test ($r = 0.9, P < 0.001$); it was estimated from the regression on duration. A bipolar precordial CB$_5$ electrocardiogram (from V$_6$ position to inferior tip of the right scapula) was monitored continuously. Appearance of three or more consecutive ventricular premature beats was an indication for stopping exertion, whereas S-T depression in the absence of symptoms was not an indication for stopping. An abnormal S-T response was defined as segment depression of 1 mm or more ($\leq -0.1$ mV) of 0.06 duration of the S-T interval, in relation to the P-R isoelectric reference level, in consecutive heart beats which appeared after maximal exertion. This included upsloping, horizontal, or downsloping S-T seg-

ments, but not merely an initial junctional depression with a rapidly rising segment.

Results

Age Distribution and Mean Exercise Duration

Mean ages for 61 ambulatory hypertensive patients who were classified according to clinical findings are shown in table 1 and figure 1. The average age of 13 patients with elevated blood pressure only was 36 ± 13 years. Those with either retinopathy or ventricular hypertrophy as additional evidence of hypertensive vascular disease were significantly older ($P < 0.01$) with an average age of 48 ± 12 years. The 11 patients with
Clinical evidence of coronary heart disease were still older, with a mean age of 54 ± 9 years.

Mean durations of maximal exercise in relation to averages for equal numbers of normals matched for age and sex are shown in table 1 and figure 2. Whereas there was no significant difference in the younger patients with only elevated blood pressure, duration of exercise was significantly reduced in older hypertensive patients who exhibited cardiac enlargement, retinopathy, or coronary heart disease. Duration, which averaged 9.9 min for those with only elevated blood pressure, was significantly reduced to 7.7, 5.3, and 3.7 min (P < 0.001) for the older patients with both

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**Table 1**

Hemodynamic Characteristics and Exercise Performance in Comparison with Observations in Controls (Mean ± Standard Deviations)

<table>
<thead>
<tr>
<th></th>
<th>Hypertension</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alone</td>
<td>With retinopathy</td>
<td>With LVH</td>
<td>With CHD</td>
</tr>
<tr>
<td>No. in each group</td>
<td>13</td>
<td>15</td>
<td>22</td>
<td>11</td>
</tr>
<tr>
<td>Patients</td>
<td>36 ± 13</td>
<td>47 ± 9</td>
<td>48 ± 12</td>
<td>54 ± 9</td>
</tr>
<tr>
<td>Controls</td>
<td>35 ± 12</td>
<td>47 ± 9</td>
<td>48 ± 12</td>
<td>53 ± 8</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>172 ± 24*</td>
<td>165 ± 23*</td>
<td>180 ± 42*</td>
<td>158 ± 27†</td>
</tr>
<tr>
<td>Patients</td>
<td>130 ± 11</td>
<td>128 ± 11</td>
<td>125 ± 13</td>
<td>131 ± 18</td>
</tr>
<tr>
<td>Controls</td>
<td>104 ± 19*</td>
<td>101 ± 14*</td>
<td>107 ± 31*</td>
<td>100 ± 11†</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>81 ± 8</td>
<td>83 ± 7</td>
<td>83 ± 9</td>
<td>80 ± 15</td>
</tr>
<tr>
<td>Maximal SBP (mm Hg)</td>
<td>201 ± 34</td>
<td>202 ± 40</td>
<td>235 ± 37</td>
<td>194 ± 32</td>
</tr>
<tr>
<td>Patients</td>
<td>186 ± 43</td>
<td>166 ± 31</td>
<td>174 ± 30</td>
<td>187 ± 35</td>
</tr>
<tr>
<td>Controls</td>
<td>97 ± 28†</td>
<td>103 ± 17*</td>
<td>107 ± 31*</td>
<td>104 ± 22†</td>
</tr>
<tr>
<td>Maximal HR</td>
<td>70 ± 21</td>
<td>77 ± 14</td>
<td>78 ± 18</td>
<td>74 ± 15</td>
</tr>
<tr>
<td>Max SBP × Max HR/100</td>
<td>353 ± 63</td>
<td>322 ± 80</td>
<td>387 ± 70†</td>
<td>259 ± 56‡</td>
</tr>
<tr>
<td>Patients</td>
<td>344 ± 94</td>
<td>283 ± 65</td>
<td>301 ± 70</td>
<td>324 ± 68</td>
</tr>
<tr>
<td>Duration of Max exercise (sec)</td>
<td>595 ± 201</td>
<td>313 ± 193*</td>
<td>461 ± 166*</td>
<td>223 ± 155*</td>
</tr>
<tr>
<td>Controls</td>
<td>559 ± 218</td>
<td>510 ± 144</td>
<td>610 ± 95</td>
<td>559 ± 115</td>
</tr>
</tbody>
</table>

* P < 0.001.
† P < 0.01.
‡ P < 0.05.
§ Nondigitalized patients.
** X² = 5.65, 1 df, P < 0.05.

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hypertension and cardiac hypertrophy, retinopathy, or coronary heart disease, respectively. Mean estimated maximal oxygen intakes ranged from 34.6, 29.7, 23.3, to 18.3 ml/kg of body weight/min or averaged 106, 78, 74, and 39% of maximal oxygen intakes for normal subjects matched for age and sex. It should be noted that patients with vascular disease manifested by hypertensive retinopathy had greater impairment of exercise capacity than those with left ventricular hypertrophy.

Circulatory Responses

Systolic and diastolic pressures immediately after maximal exertion were significantly elevated ($P < 0.001$) (table 1). In 50 patients without coronary heart disease, maximal systolic pressure was 42 mm Hg (24%) higher than the corresponding pressure in normotensive controls. Despite this trend, two patients exhibited only a 5 mm Hg rise and another had a 13 mm Hg fall with maximal exercise. The average change in systolic pressure from rest to maximal exercise was 29 mm Hg ($P < 0.05$) in 13 younger patients with only elevated pressure and 47 mm Hg ($P < 0.01$) in 37 older patients with other clinical manifestations of hypertensive disease. In 11 patients with both hypertensive and coronary heart disease, change in systolic pressure with maximal exercise was 19 to 20 mm Hg less than that observed in hypertensive patients with ventricular hypertrophy or normotensive controls of comparable age ($P < 0.01$).

Only 13 younger patients with uncomplicated hypertension showed the expected slight decrease in diastolic pressure from vasodilation in exercising skeletal muscles. The remaining 37 patients without coronary disease maintained diastolic pressure, while 11 patients with coronary disease showed a slight rise in diastolic pressure.

Pulse pressure increased from 69 to 113 mm Hg (64%) in 50 hypertensive patients and from 58 to 90 mm Hg (55%) in 11 patients with both hypertensive and coronary heart disease. Values in the corresponding normotensive controls were 45 to 98 mm Hg (118%) and 51 to 113 mm Hg (102%) respectively.

Maximal heart rate was only 11 beats/min slower ($-6\%$) in 50 hypertensive patients than in their matched controls. In 11 older patients with both hypertensive and coronary heart disease, maximal heart rate was 40 beats/min ($-22\%$) slower than in their matched controls. The difference between maximal and resting heart rates just before exercise was only slightly reduced by uncomplicated hypertension, but significantly ($P < 0.01$) reduced by ventricular hypertrophy and especially by coronary heart disease ($P < 0.001$).

![Figure 3](image)

**Figure 3**

Comparison of products of maximal systolic pressure and maximal heart rate (means and standard deviations) per 100 in four groups of hypertensive patients. Only patients with coronary heart disease exhibit lower products than the controls, indicating that exercise impairment is not due to greater hemodynamic stress on the left ventricle. Accordingly, restricted coronary circulation is inferred to be the major limiting factor.

Prevalence of ST Segment Depression after Maximal Exercise

![Figure 4](image)

**Figure 4**

Comparative prevalence of S-T segment depression of more than 1 mm ($<-0.10$ me) after exercise in hypertensive patients. Only patients with ventricular hypertrophy and particularly those with coronary heart disease show this abnormal response after maximal exercise more frequently than controls matched for age.
Maximal heart rate for the lowest work load, stage I of the multistage exercise test, averaged 33 and 56% of maximal heart rates for normal males and females, respectively. Corresponding values for 50 hypertensive males and females were 49 and 69%.

The product of heart rate and systolic blood pressure and maximal exercise, divided by 100 (an index of the hemodynamic stress imposed on the left ventricle) was insignificantly increased in all three groups of hypertensive patients without coronary disease (fig. 3). Nevertheless it was significantly lower \( (P < 0.05) \) in patients with both coronary and hypertensive heart disease.

**S-T Segment Depression in Postexercise ECG**

Altogether, 23 of 61 (38%) hypertensive patients exhibited significant S-T segment depression (≥1 mm or ≤−0.1 mv) after maximal exercise. When five patients who were taking digitalis (which frequently initiates or accentuates this response) were omitted, the prevalence in 18 of the 56 patients was 32%. Only five (8%) normotensive controls, showed this S-T response to maximal exercise. Of 19 hypertensive patients with left ventricular hypertrophy who were not treated with digitalis, eight (42%) showed S-T segment depression after maximal exertion (table 1 and fig. 4). Seven of 11 (63%) patients with both hypertensive and coronary heart disease exhibited this response.

**Discussion**

Variations in regional manifestations of vascular disease associated with hypertension provide a basis for observation of the effects of augmented hemodynamic stress on, and restricted coronary blood supply to, the left ventricular myocardium. Stressing the heart to maximally tolerated symptomatic limits of exercise reveals differences which are not apparent at rest. Since estimated maximal oxygen intakes either were in accord with, or exceeded, those reported in other studies of maximal exercise, the hypertensive patients in this study probably exercised to their maximal capacity. In the absence of clinical signs of vascular or cardiac disease, duration of exercise, estimated maximal oxygen intake, and maximal heart rate were not diminished, and the prevalence of postexertional S-T segment depression of possible myocardial ischemia was not increased. Possibly this group represented individuals with a hyperkinetic circulation, but in the absence of measurements of cardiac output and estimates of peripheral resistance this could not be assessed.

Patients with clinical manifestations of hypertensive cardiovascular disease were significantly older than those with only elevated blood pressure. Although exercise capacity and cardiovascular performance normally diminish with aging, the effects of disease were more clearly revealed by comparison with normotensive individuals who were closely matched for age as well as sex. Hypertensive patients with left ventricular hypertrophy showed less, and those with coronary disease showed more, impairment of maximal exercise capacity than patients with retinal vascular disease. This suggested the possibility of compensatory adaptation of the myocardium in the former, and restricted coronary perfusion in the latter individuals. Greater change in systolic pressure and pulse pressure from rest to maximal exercise indicated enhanced contractile force in patients with hypertrophy. Lesser measurements in systolic pressure and a significant reduction in maximal heart rate in the coronary patients were consistent with myocardial ischemia from coronary insufficiency. Accordingly, the product of maximal heart rate and systolic pressure was significantly greater in patients with hypertrophy and significantly less in patients with coronary disease, despite any hypertrophy they might have had.

Greater hemodynamic stress on the left ventricle of those hypertensive patients was evident, even at submaximal exercise (stage I of the multistage test), by the higher percentage of maximal heart rate, particularly in women. Whereas normally aging does not affect the relative work load on the heart for submaximal exertion, hypertensive cardiovascular disease imposes a greater pressure
load on the heart at all levels of exercise and a greater relative heart rate for only moderate exertion. Since duration of exertion was twice as long in hypertensive patients with hypertrophy, the cumulative hemodynamic stress on the myocardium was greater than that observed in either normotensive controls or hypertensive coronary patients. Yet maximal exercise was less impaired in the former than the latter subgroups.

The prevalence of S-T segment depression in hypertensive patients was threefold greater with ventricular hypertrophy and sevenfold greater with coronary disease than in normotensive, age-matched controls. Presumably myocardial ischemia was due to augmented contractile force, at faster heart rates and for a longer duration of exercise in the former group. In the latter group restricted coronary perfusion was the major factor, despite the lower heart rate, lesser contractile force, and shorter duration of exertional hemodynamic stress. In another study of 1,346 healthy middle-aged Chinese men from a population that rarely manifests coronary heart disease, the less frequent occurrence of S-T segment depression after maximal exercise was a graded response primarily dependent upon age and maximal systolic pressure, even in the normotensive range. Neither exercise capacity nor maximal heart rate was restricted or associated with this response. Therefore, interpretation of the pathophysiological causes of postexertional S-T segment depression depends upon the associated findings, including duration of effort, heart rate, and systolic pressure with maximal exercise.

In conclusion, the major factors for impaired exercise capacity and restricted circulatory transport of oxygen to skeletal muscles in these hypertensive patients were the clinical manifestations of increased peripheral vascular resistance and either augmented contractile force or more importantly, restricted coronary supply which limited myocardial perfusion and initiated ischemic electrocardiographic responses.

References


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