Exercise-Induced Hypotension in a Male Population
Criteria, Causes, and Prognosis
Paul Dubach, MD, Victor F. Froelicher, MD, Jacob Klein, MD, David Oakes, MD, Maleah Grover-McKay, MD, and Robert Friis, PhD

The objective of this study was to demonstrate the causes, optimal definition, and predictive value of exercise-induced hypotension occurring during treadmill testing. This study included all patients referred for clinical reasons to the Long Beach Veterans Administration Medical Center treadmill laboratory and then followed for a 2-year period for cardiac events. The population consisted of 2,036 patients who underwent testing from April 4, 1984, to May 7, 1987, 131 of whom exhibited exercise-induced hypotension (6.4%). We found that exercise-induced hypotension is usually related to myocardial ischemia or myocardial infarction, is best defined as a drop in systolic blood pressure during exercise below the standing preexercise value, and indicates a significantly increased risk for cardiac events (3.2-fold, \( p < 0.005 \)). This increased risk was not found in those having no previous myocardial infarction or no signs or symptoms of ischemia during the exercise test, and the increased risk was also not found in those undergoing a treadmill test within 3 weeks after a myocardial infarction. Exercise-induced hypotension appeared to be reversed by revascularization procedures, but confirmation of a beneficial effect on survival requires a randomized trial. The clinical importance of this study is that we have demonstrated that a drop in systolic blood pressure below standing preexercise values during treadmill testing indicates an increased risk for cardiac events except in certain subsets of patients. (Circulation 1988;78:1380–1387)

Exercise-induced hypotension (EIH) has been demonstrated in most studies to predict either a poor prognosis or high-risk coronary angiographic disease. Although the prognosis of EIH has not been specifically examined in patients after myocardial infarction, an abnormal systolic blood pressure response has been found to indicate an increased risk for cardiac events in this population. In addition, EIH has been associated with cardiac complications during exercise testing and appears to be corrected by coronary artery bypass graft surgery. It has been accepted as a high-risk exercise test response by the American Heart Association/American College of Cardiology Task Force on cardiovascular procedures despite uncertainty regarding its etiology, the use of several different definitions or criteria, reproducibility limitations, and controversy regarding its predictive power. To further demonstrate its causes, definition, and predictive power, we have analyzed the experience in our exercise laboratory.

Patients and Methods

Population
From April 4, 1984, to May 7, 1987, 2,036 patients underwent exercise testing for clinical reasons in the Long Beach Veterans Administration Medical Center exercise testing laboratory, Long Beach, California. EIH was defined as 1) an initial increase in systolic blood pressure during exercise with a subsequent 20 mm Hg or more decrease without a drop below the standing rest value and 2) a decrease in systolic blood pressure during exercise below the standing rest value. One hundred thirty-one patients exhibited EIH, six on multiple occasions. Fourteen patients with EIH were excluded: four because they were women, nine because of primary valvular heart disease, and one patient because of a cardiomyopathy. One hundred seventeen patients remained, 64 of whom were tested once and 53 who were tested multiple times for clinical reasons. Of those tested multiple times, 31 did not receive any intervention, whereas...
nine underwent percutaneous transluminal coronary angioplasty, and 13 underwent coronary artery bypass surgery. Average length of follow-up was 2 years with a minimum follow-up of 235 days except for patients who had earlier events.

Exercise Testing

Exercise tests were performed and data gathered in a standardized manner. Supine and standing measurements were recorded before testing without hyperventilation. A progressive continuous treadmill protocol was used with the maximum workload reported in estimated METs. Blood pressure measurements were taken during each stage and also after discharge following acute myocardial infarction. The endpoint for the submaximal tests was whichever of the following came first: 5 MET, a Borg scale of 16, signs or symptoms of ischemia, heart rate greater than 110 beats/min if on β-blockers, or heart rate greater than 130 beats/min if not on β-blockers. Endpoints for the maximal test included: 1) severe angina; 2) 4-mm ST depression; 3) serious dysrhythmias; 4) a hypertensive response defined as a systolic blood pressure greater than 220 mm Hg; or 5) exhaustion. Neither heart rate, MET level, nor systolic blood pressure drop without signs or symptoms was used as an endpoint for the maximal test.

Coronary Angiography

Coronary angiography was performed with the standard Judkins technique on the 389 patients who were selected for the procedure for clinical reasons. Angiograms were interpreted visually with significant disease defined as 75% or greater luminal occlusion. The number of vessels involved was calculated as follows: right coronary artery = 1, left circumflex coronary artery and/or marginal = 1, and left anterior descending coronary artery and/or diagonal = 1 for a maximal sum of 3. A 50% or greater lesion in the left main trunk was considered significant.

Data Management and Follow-up

All patients were entered into the centralized hospital computer data base where their files were updated for subsequent admissions and deaths. The computer files were reviewed for death and myocardial infarction on December 30, 1987, resulting in an average follow-up of 767 days with a minimum follow-up of 235 days. Statistical analysis with BMDP was performed and included BMDPLR, BMDP4F, and BMDPRM.

Results

Table 1 describes the demographics of the entire population. All patients were men ranging in age from 20 to 95 years with a mean age of 58 years. Subgroups were tabulated relative to myocardial infarction status for all patients, for those with a drop in systolic blood pressure below resting, and for those with a drop of 20 mm Hg after a rise without a fall below rest (EIH20). The prevalence of EIH below resting in patients with a recent myocardial infarction (8%; 16 of 191 patients) and in patients with an old myocardial infarction (9.5%; 38 of 400 patients) was more than twice that found in those with no myocardial infarction (2.8%; 40 of 1,431 patients) (p<0.001). There were no differences relative to age, or before coronary artery bypass graft surgery or resting electrocardiographic abnormalities except the expected difference in Q waves between the groups. β-Blockers, calcium antagonists, and nitroglycerin were being taken less frequently by the patients without a history of myocardial infarction, but there were no significant differences in drug administration within subgroups between those with or without exertional hypotension.

BMDPLR stepwise logistic regression was used to determine the predictors of exertional hypotension. Of the eight variables in Table 1 only "no MI" and "age" were statistically significant (p<0.01) for predicting who would have EIH below resting. "No MI" was negatively correlated, and "age" was positively correlated with EIH. These two variables explained 28% of the variance.

Table 2 describes the treadmill test hemodynamic responses in the total group and by subgroups. The lower average MET level in the recent myocardial infarction group is a result of the patients performing submaximal tests. Overall, the average MET, maximal heart rate, and maximal systolic blood pressure were lower in those with EIH below resting compared with those with a drop of 20 mm Hg after a rise without a fall below resting and the total group (p<0.01).

Table 2 also describes the number of patients with no ischemia, those with angina with or without ST segment depression, and those with silent ischemia (ST depression without angina) during treadmill testing. Patients in the group without previous myocardial infarction had slightly less ischemia of any kind (p<0.001), but no particular pattern of ischemia was more prevalent in those with EIH.

Neither death nor infarction occurred in the patients who had only a drop of 20 mm Hg in systolic blood pressure that did not drop below the standing baseline value compared with 14 events out of 94 patients in the group with EIH below resting (p=0.05) (Table 3). Table 4 shows the deaths only in those patients with a drop in systolic blood pressure below resting values. The deaths were classified according to myocardial infarction and ischemia status, and odds ratios were calcu-
TABLE 1. Clinical Characteristics and Medical Status of the Study Population

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>Recent MI</th>
<th>Old MI</th>
<th>No MI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>191 (9.4%)</td>
<td>400 (19.8%)</td>
<td>1,431 (70.0%)</td>
<td>2,022</td>
</tr>
<tr>
<td>With EIHBR</td>
<td>16 (17%)</td>
<td>38 (40%)*</td>
<td>40 (42%)</td>
<td>94</td>
</tr>
<tr>
<td>With EIH20</td>
<td>3 (13%)*</td>
<td>5 (21.7%)</td>
<td>15 (65%)</td>
<td>23</td>
</tr>
</tbody>
</table>

Age

<table>
<thead>
<tr>
<th>All</th>
<th>60±10</th>
<th>59±8</th>
<th>58±10</th>
<th>58±10</th>
</tr>
</thead>
<tbody>
<tr>
<td>With EIHBR</td>
<td>65±10</td>
<td>62±5</td>
<td>64±9</td>
<td>64±8</td>
</tr>
<tr>
<td>With EIH20</td>
<td>50±8</td>
<td>63±5</td>
<td>59±7</td>
<td>58±8</td>
</tr>
</tbody>
</table>

Previous CABG

<table>
<thead>
<tr>
<th>All</th>
<th>9% (18)</th>
<th>27% (109)</th>
<th>10% (142)</th>
<th>13% (269)</th>
</tr>
</thead>
<tbody>
<tr>
<td>With EIHBR</td>
<td>25% (4)</td>
<td>26% (10)</td>
<td>5% (2)</td>
<td>17% (16)</td>
</tr>
<tr>
<td>With EIH20</td>
<td>0% (−)</td>
<td>20% (1)</td>
<td>13% (2)</td>
<td>13% (3)</td>
</tr>
</tbody>
</table>

Medications

β-Blockers

<table>
<thead>
<tr>
<th>All</th>
<th>49% (93)</th>
<th>46% (184)</th>
<th>25% (354)</th>
<th>31% (631)</th>
</tr>
</thead>
<tbody>
<tr>
<td>With EIHBR</td>
<td>50% (8)</td>
<td>42% (16)</td>
<td>30% (12)</td>
<td>38% (36)</td>
</tr>
<tr>
<td>With EIH20</td>
<td>33% (1)</td>
<td>20% (1)</td>
<td>13% (2)</td>
<td>17% (4)</td>
</tr>
</tbody>
</table>

Digoxin

<table>
<thead>
<tr>
<th>All</th>
<th>12% (23)</th>
<th>11% (45)</th>
<th>7% (96)</th>
<th>8% (164)</th>
</tr>
</thead>
<tbody>
<tr>
<td>With EIHBR</td>
<td>13% (2)</td>
<td>21% (8)</td>
<td>5% (2)</td>
<td>13% (12)</td>
</tr>
<tr>
<td>With EIH20</td>
<td>0% (−)</td>
<td>0% (−)</td>
<td>0% (−)</td>
<td>0% (−)</td>
</tr>
</tbody>
</table>

Calcium antagonists

<table>
<thead>
<tr>
<th>All</th>
<th>35% (68)</th>
<th>41% (162)</th>
<th>16% (228)</th>
<th>23% (458)</th>
</tr>
</thead>
<tbody>
<tr>
<td>With EIHBR</td>
<td>44% (7)</td>
<td>45% (17)</td>
<td>15% (6)</td>
<td>32% (30)</td>
</tr>
<tr>
<td>With EIH20</td>
<td>66% (2)</td>
<td>40% (2)</td>
<td>27% (4)</td>
<td>35% (8)</td>
</tr>
</tbody>
</table>

Recent MI, myocardial infarction (MI) within 3 weeks; old MI, MI older than 3 weeks; no MI, no history of MI; CABG, coronary artery bypass graft surgery; EIHBR, systolic blood pressure drop below resting; EIH20, systolic blood pressure drop of 20 mm Hg after initial rise not falling below rest.

*p<0.001.

lated with BMDP4F. The death rate was 14% (27 of 191) in the recent myocardial infarction group and 7% (25 of 362) in the silent ischemia group compared with 3% (48 of 1,431) in the group with no previous myocardial infarction and 5% (21 of 400) in the group with old myocardial infarction (p<0.001).

The death rate was lowest in those with no previous myocardial infarction and no ischemia (3%, 30 of 972) where no deaths occurred in the 14 patients in the subgroup with EIH below resting. There were no significant differences in the death rates of the groups as determined by ischemia status (55 of 1,290 for the group with no previous ischemia compared with 16 of 370 for the angina pectoris group, compared with 25 of 362 for the silent ischemia group, and compared with 96 of 2,022 for the total group).

In the total group (3.2-fold, p<0.0005) and in the no myocardial infarction–angina pectoris group (p=0.0045), those who had a drop in systolic blood pressure below rest were at increased risk as determined by χ² with Yates’ continuity correction.12 Borderline significance was found for the groups with old and without myocardial infarctions. Regarding medication status, EIH below resting generated a significant odds ratio only in those taking digoxin in the silent ischemia subgroup (p=0.0125) and in those taking digoxin in the total group (p=0.01).

Table 5 lists the cardiac catheterization data for those patients in whom catheterization was available (389 of the total 2,022 and 42 of 117 with EIH).

Three-vessel and left main trunk disease were more prevalent in those with EIH below resting (48% and 13%, respectively) but not in those with a drop of 20 mm Hg after a rise without a fall below resting (27% and 0%, respectively) compared with those without EIH (32% and 8%, respectively). There was no significant difference in these angiographic findings nor in the ejection fraction.

We analyzed the reasons for performing multiple tests and their outcome. Twenty-two of the 53 patients with multiple tests had an intervention between the first and the last test. In 18 of the 22 patients (11 after coronary artery bypass graft surgery and seven after percutaneous transluminal coronary angioplasty), EIH was no longer present, but in four patients (two after coronary artery bypass graft surgery and two after percutaneous transluminal coronary angioplasty), EIH was present only after the intervention. In two patients, EIH no longer occurred after a myocardial infarction,
TABLE 2. Hemodynamic and Ischemic Responses to the Treadmill Test

<table>
<thead>
<tr>
<th></th>
<th>Recent MI</th>
<th>Old MI</th>
<th>No MI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MET</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>5.2±2.1</td>
<td>7.2±2.9</td>
<td>8.2±3.5</td>
<td>7.7±3.4*</td>
</tr>
<tr>
<td>With EIHBR</td>
<td>4.6±1.8</td>
<td>6.3±2.2</td>
<td>5.3±2.6</td>
<td>5.6±2.4*</td>
</tr>
<tr>
<td>With EIH20</td>
<td>4.3±0.5</td>
<td>7.9±2.1</td>
<td>9.1±3.1</td>
<td>8.2±3.1*</td>
</tr>
<tr>
<td><strong>MHR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>115±22</td>
<td>127±23</td>
<td>137±25</td>
<td>133±25</td>
</tr>
<tr>
<td>With EIHBR</td>
<td>108±18</td>
<td>122±24</td>
<td>120±20</td>
<td>117±22*</td>
</tr>
<tr>
<td>With EIH20</td>
<td>132±9</td>
<td>140±13</td>
<td>150±18</td>
<td>146±18</td>
</tr>
<tr>
<td><strong>SBP&lt;sub&gt;max&lt;/sub&gt;</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>145±28</td>
<td>160±29</td>
<td>175±28</td>
<td>170±29*</td>
</tr>
<tr>
<td>With EIHBR</td>
<td>110±16</td>
<td>123±20</td>
<td>131±25</td>
<td>124±33*</td>
</tr>
<tr>
<td>With EIH20</td>
<td>120±14</td>
<td>146±15</td>
<td>160±24</td>
<td>152±25</td>
</tr>
</tbody>
</table>

Recent MI, myocardial infarction (MI) within 3 weeks; old MI, MI older than 3 weeks; no MI, no history of MI; MET, metabolic equivalent (3.5 ml oxygen consumption per kilogram of body weight); MHR, maximal heart rate achieved; SBP<sub>max</sub>, systolic blood pressure at maximal exercise; EIHBR, systolic blood pressure drop below resting; EIH20, systolic blood pressure drop of 20 mm Hg after initial rise not falling below rest.

*p<0.01.

and in eight patients, EIH occurred only after a myocardial infarction.

The clinical data in those with interventions, in those who died, and in all others with EIH were compared. In the group of patients who died, there was a higher prevalence of anterior and lateral Q waves, and those patients achieved a lower mean MET level, whereas in the group that received interventions, there was a higher prevalence of angina pectoris and ischemia (p = 0.008) and a lower mean ejection fraction compared with all others.

**Discussion**

The normal blood pressure response to dynamic upright exercise consists of a progressive increase in systolic blood pressure, a decrease in diastolic blood pressure, and a widening of the pulse pressure. Even when tested to exhaustion, normal male individuals do not exhibit a drop of 20 mm Hg systolic blood pressure after a rise or a drop in systolic blood pressure below baseline. Normally, after exercise, there is a drop in both systolic and diastolic pressure. Exercise-induced decreases in systolic blood pressure can occur in patients with coronary artery disease, valvular heart disease, or cardiomyopathies. Occasionally, patients without clinically significant heart disease will exhibit EIH during exercise because of antihypertensive therapy, unusually prolonged strenuous exercise,

TABLE 3. Endpoints (Death, Myocardial Infarction) in the Study Population According to Systolic Blood Pressure Response and Myocardial Infarction Status

<table>
<thead>
<tr>
<th></th>
<th>Recent MI</th>
<th>Old MI</th>
<th>No MI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>14% (27/191)</td>
<td>5% (20/400)</td>
<td>4% (53/1,431)</td>
<td>5% (100/2,022)</td>
</tr>
<tr>
<td>With EIHBR</td>
<td>31% (5/16)</td>
<td>13% (5/38)</td>
<td>10% (4/40)</td>
<td>15% (14/94)</td>
</tr>
<tr>
<td>With EIH20</td>
<td>0% (0/3)</td>
<td>0% (0/5)</td>
<td>0% (0/15)</td>
<td>0% (0/23)</td>
</tr>
</tbody>
</table>

Recent MI, myocardial infarction (MI) within 3 weeks; old MI, MI older than 3 weeks; no MI, no history of MI; EIHBR, systolic blood pressure drop below resting; EIH20, systolic blood pressure drop of 20 mm Hg after initial rise not falling below rest.

*p<0.05.
TABLE 4  Tabulation of Deaths by Myocardial Infarction and Ischemia Status for Patients With an Exercise-Induced Drop in Systolic Blood Pressure Below Standing Rest Compared With Those Without Such a Response for Calculation of Odds (Risk) Ratio

<table>
<thead>
<tr>
<th>Deaths</th>
<th>Recent MI</th>
<th>Old MI</th>
<th>No MI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ischemia</td>
<td>13% (13/102)</td>
<td>4% (8/197)</td>
<td>3% (30/958)</td>
<td>4% (51/1,257)</td>
</tr>
<tr>
<td>With EIHBR</td>
<td>29% (2/7)</td>
<td>17% (2/12)</td>
<td>0% (0/14)</td>
<td>12% (4/33)</td>
</tr>
<tr>
<td>Angina pectoris (with or without ST changes)</td>
<td>2.7×</td>
<td>4.7×</td>
<td>...</td>
<td>3.3×</td>
</tr>
<tr>
<td>Silent ischemia</td>
<td>15% (5/33)</td>
<td>1% (1/96)</td>
<td>3% (6/207)</td>
<td>4% (12/336)</td>
</tr>
<tr>
<td>With EIHBR</td>
<td>0% (0/3)</td>
<td>6% (1/18)</td>
<td>23% (3/13)</td>
<td>12% (4/34)</td>
</tr>
<tr>
<td>Silent ischemia</td>
<td>15% (6/40)</td>
<td>10% (7/69)</td>
<td>4% (8/226)</td>
<td>6% (21/335)</td>
</tr>
<tr>
<td>With EIHBR</td>
<td>17% (1/6)</td>
<td>25% (2/8)</td>
<td>8% (1/13)</td>
<td>15% (4/27)</td>
</tr>
<tr>
<td>Total</td>
<td>14% (24/175)</td>
<td>4% (16/362)</td>
<td>3% (44/1,391)</td>
<td>4% (84/1,928)</td>
</tr>
<tr>
<td>With EIHBR</td>
<td>19% (3/16)</td>
<td>13% (5/38)</td>
<td>10% (4/40)</td>
<td>13% (12/94)</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>1.1×</td>
<td>3.0×</td>
<td>2.3×</td>
<td>2.6×</td>
</tr>
</tbody>
</table>

Recent MI, myocardial infarction (MI) within 3 weeks; old MI, MI older than 3 weeks; no MI, no history of MI; EIHBR, systolic blood pressure drop below resting.

*p=0.0045; †p=0.055; ‡p=0.054; §p<0.005.

systolic blood pressure can occur in patients with coronary artery disease, or cardiomyopathies. Occasionally, patients without clinically significant heart disease will exhibit EIH during exercise because of antihypertensive therapy, unusually prolonged strenuous exercise, or it can occur in normal women. EIH in patients with known or suspected coronary artery disease in the absence of other forms of heart disease has been reported to be a specific but insensitive indicator of significant left main trunk or three-vessel coronary artery disease. EIH has also been reported to be reversed by coronary artery bypass graft surgery. Pathophysiologically, EIH could be due to chronic ventricular dysfunction, exercise-induced ischemia causing left ventricular dysfunction or papillary muscle dysfunction and mitral regurgitation.

Numerous studies have addressed the diagnostic and prognostic implications of EIH. Their important findings regarding definition, prevalence, high-risk subgroups, intervention, and mortality are summarized in Table 6. One difficulty encountered in interpreting these previous studies is that although EIH has been related to coronary artery disease and a poor prognosis, various criteria have been used to define it. SanMarco et al defined EIH as systolic blood pressure falling to 10 mm Hg in the 1st minute of exercise or dropping 20 mm Hg or more during the test or both. Some investigators have defined EIH as an exercise-induced drop in systolic blood pressure of 5 mm Hg, and others have used a 10 mm Hg drop after an initial rise. Thompson and Kelemen and Morris et al stressed possible technical difficulties in the measurements of the blood pressure during treadmill testing.

To clarify the uncertainty regarding the definition of EIH, we applied the following criteria: 1) a drop of 20 mm Hg or more after an initial rise but without

TABLE 5  Cardiac Catheterization Results in Patients Who Were Chosen for Clinical Reasons to Undergo Invasive Evaluation

<table>
<thead>
<tr>
<th>Vessel disease</th>
<th>All patients</th>
<th>With EIHBR</th>
<th>With EIHBR20</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>11% (41/389)</td>
<td>0% (0/31)</td>
<td>0% (0/11)</td>
</tr>
<tr>
<td>One vessel</td>
<td>17% (68/389)</td>
<td>13% (4/31)</td>
<td>27% (3/11)</td>
</tr>
<tr>
<td>Two vessel</td>
<td>27% (105/389)</td>
<td>26% (8/31)</td>
<td>46% (5/11)</td>
</tr>
<tr>
<td>Three vessel (only)</td>
<td>36% (141/389)</td>
<td>48% (15/31)</td>
<td>27% (3/11)</td>
</tr>
<tr>
<td>Left main occlusion</td>
<td>9% (34/389)</td>
<td>13% (4/31)</td>
<td>0% (0/11)</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>59±15</td>
<td>56±14</td>
<td>61±17</td>
</tr>
</tbody>
</table>

Vessel disease, number vessels diseased with >75% occlusion; Left main occlusion of 50% or greater.
Dubach et al  

Exercise-Induced Hypotension

Table 6. Results of Major Studies Examining Relation Between Exercise-Induced Hypotension and Coronary Artery Disease

<table>
<thead>
<tr>
<th>Definition</th>
<th>Prevalence of EIH</th>
<th>Prevalence of LM/3VD</th>
<th>Predictive value of EIH for LM/3VD</th>
<th>Subgroups at high risk</th>
<th>EIH reversed by revascularization</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dubach et al</td>
<td>Drop in SBP below rest</td>
<td>5% (94/2,022)</td>
<td>45%</td>
<td>61%</td>
<td>No deaths in those with either ischemia or MI</td>
<td>18/22</td>
</tr>
<tr>
<td>Hammermeister</td>
<td>SBP drop below rest</td>
<td>7% (93/1,241)</td>
<td>25%</td>
<td>50%</td>
<td>Angina, poor exercise capacity, LM/3VD with low EF</td>
<td>None found</td>
</tr>
<tr>
<td>Weiner</td>
<td>Drop in SBP below rest</td>
<td>11% (47/436)</td>
<td>28%</td>
<td>55%</td>
<td>Ischemia, PVCs, poor exercise capacity</td>
<td>None found</td>
</tr>
<tr>
<td>SanMarco et al</td>
<td>Failure of SBP to rise 10 mm Hg in 1st min; or 20 mm Hg drop</td>
<td>24% (90/378)</td>
<td>39%</td>
<td>70%</td>
<td>None found</td>
<td></td>
</tr>
<tr>
<td>Li et al</td>
<td>SBP equal to or drop below rest</td>
<td>23% (55/234)</td>
<td>100%</td>
<td>100%</td>
<td>None found</td>
<td></td>
</tr>
<tr>
<td>Hakki et al</td>
<td>Decrease of SBP by 10 mm Hg</td>
<td>7% (127/1,800)</td>
<td>100%</td>
<td>100%</td>
<td>3VD and LV dysfunction</td>
<td>6/6</td>
</tr>
<tr>
<td>Thompson and Keleman</td>
<td>SBP drop below rest</td>
<td>100% (17/17)</td>
<td>100%</td>
<td>100%</td>
<td>None found</td>
<td></td>
</tr>
<tr>
<td>Levites et al</td>
<td>SBP drop below rest</td>
<td>3% (30/1105)</td>
<td>20%</td>
<td>20%</td>
<td>(Women were false-positive.)</td>
<td></td>
</tr>
<tr>
<td>Morris et al</td>
<td>Decrease of SBP by 10 mm Hg</td>
<td>5% (23/438)</td>
<td>24%</td>
<td>78%</td>
<td>None found</td>
<td></td>
</tr>
<tr>
<td>Mazzotta et al</td>
<td>Decrease of SBP by 5 mm Hg</td>
<td>20% (44/224)</td>
<td>None found</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gibson et al</td>
<td>Decrease in SBP by 10 mmHg</td>
<td>3% (27/820)</td>
<td>None found</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

EIH, exercise-induced hypotension; LM/3VD, left main trunk or three-vessel coronary artery disease; MED, medically treated; CABG/PTCA, patients treated with revascularization; SBP, systolic blood pressure; LV, left ventricular; MI, myocardial infarction; predictive value, percentage with EIH who had three-vessel disease or left main trunk disease; PVCs, premature ventricular contractions.

A fall below rest; and 2) a drop of the systolic blood pressure below standing rest value. A drop of 20 mm Hg should be sufficient to avoid the technical limitations of determining blood pressure changes during treadmill testing. We were able to demonstrate that in our population the definition of a drop below rest was clearly a better criterion than a drop of 20 mm Hg for predicting increased risk for deaths and myocardial infarction (p = 0.05) (Table 5). Therefore, we calculated the odds (risk) ratio of EIH for death (Table 4) by using only the criterion of a systolic blood pressure drop below rest. Although other cut-off points for an inadequate systolic blood pressure response to exercise were found to generate odds ratios, particularly in patient subsets, only the results for the conventional criteria for exertional hypotension are presented.

The average prevalence of EIH among the studies cited in Table 6 was 8% (553 of 6,693), whereas the prevalence in our study was 5%. The prevalence and predictive value for left main trunk and three-vessel disease together ranged from 20% to 100% with an average of 48% for the prevalence and an average of 68% for the predictive value. In our study, the prevalence was 45%, and the predictive value was 61%. The wide scatter of prevalences of EIH and of left main trunk and three-vessel disease, and consequently in the predictive value of EIH, is the result of the variability in patient selection and methodologies used in the studies. In the reported studies, varying percentages of patients underwent cardiac catheterization, and it was not always possible to distinguish between left main trunk and three-vessel disease or whether the right coronary artery was also involved when left main trunk disease was present. Patients with valvular heart disease or cardiomyopathy and women were not consistently excluded. Despite the above limitations, a consistent finding was that slightly more than half of the patients with known or suspected coronary artery disease and EIH had left main trunk or three-vessel disease.

EIH can be due to left ventricular dysfunction or ischemia. SanMarco et al3 also mentioned a vaso-vagal discharge and β-blocker therapy as possible causes. Recently, Rich et al20 described a patient in whom EIH was found to be due to right ventricular ischemia. Fifteen percent of our patients with EIH had neither a history of myocardial infarction nor an ischemic response during treadmill testing. There
was no bradycardia as is usually associated with a
vasovagal reaction, nor could we find a relation
between β-blocker therapy and EIH. Our results
therefore suggest that factors other than those men-
tioned above can cause EIH, such as an abnormal
peripheral vasodilation during exercise or exercise-
induced mitral regurgitation.

Interestingly, all of our patients with EIH who
died had either a history of myocardial infarction or
an ischemic response during the exercise test or
both (Table 4). Because no deaths occurred in
patients with EIH who had neither a previous
myocardial infarction nor ischemia, there could be
two hypothetical mechanisms for EIH: 1) a primary
cardiac cause due to left ventricular dysfunction or
ischemia, or both, that is associated with an
increased risk of death; and 2) an unknown, non-
cardiac cause probably due to an abnormal but
benign peripheral vascular response.

Patients with EIH have an increased risk of
death. In all subgroups in the present study, the risk
of death was at least two times greater in patients
with EIH compared with those without EIH, with
the exception of patients recovering from a recent
myocardial infarction. The patients recovering from
a recent myocardial infarction had the highest death
rate, suggesting that the degree of left ventricular
dysfunction must predominate over other predic-
tors, including EIH. The patients tested multiple times were at higher
risk to have an intervention or event compared with
the patients tested only once. Twenty-two of the 53
patients tested multiple times had an intervention,
but none of the 64 patients tested only once had an
intervention. In comparing these three subgroups,
no differences were found in regard to age, medica-
tion status, myocardial infarction status, and treadmill or cardiac catheterization results. Because no
patient died in the intervention group, whereas 12
patients died in the nonintervention group, we looked
for possible differences between the intervention
group, those who died, and those who did not
receive an intervention. No differences were found.

These results are supported by other studies.
Weiner et al.,2 Thompson and Kelemen,9 and Morris
et al17 found a lower mortality in patients with EIH
who received an intervention compared with those
who were medically treated. The average death rate
in the medically treated group of all studies was four
of 33 and one of 41 in the intervention group (Table
6). Our results are even more striking: 12 deaths in
95 medically treated patients and no deaths in 22
patients who had an intervention. This would sug-
gest that percutaneous transluminal coronary angio-
plasty or coronary artery bypass graft surgery in
patients with EIH can reduce mortality. However,
the patients were not randomized to surgery in any
of those studies. Li et al.,6 Thompson and Kelemen,9
and Morris et al17 reported a reversing of EIH with
coronary artery bypass graft surgery. Eighteen of
our patients had EIH that was reversed by revascu-
larization. Martin and Ehsani21 recently described a
reversal of EIH in 16 patients after a year of intense
exercise training.

Our study did not corroborate other studies that
found a relation between the prevalence of EIH and
the amount and duration of ST depression, exercise
capacity, or prevalence of angina pectoris, or pre-
mature ventricular contractions.1,2,7,19 Some
investigators1,8,19 described an association between
left ventricular dysfunction, three-vessel disease,
left main trunk disease and the prevalence of EIH.
The limitations of our study include the follow-
ing: measurements were not made during exercise
to clarify the causes of EIH; the reproducibility of
EIH was not evaluated; and inadequate numbers of
patients had ventricular function data from cardiac
catheterization and echocardiographic or radionu-
clide ventriculography. Thus, left ventricular func-
tion was only indirectly assessed by a history of
myocardial infarction. Also, thallium scintigraphy
was not available to confirm silent ischemia. Finally,
patients with EIH were not randomized to interven-
tions, so conclusions regarding the impact of revas-
cularization on survival can only be conjectural and
need to be confirmed by a randomized trial.

The results of this study are in accordance with
previous studies in regard to the prevalence, progno-
sis, and predictive value of EIH. The following aspects
of our study are considered of particular importance:

**Definition of Exercise-Induced Hypotension**

The definition of EIH is of crucial importance in
the evaluation of the exercise test response. We
have demonstrated that a drop in systolic blood
pressure below preexercise values is the most
important criterion, whereas a drop of 20 mm Hg
or more without a fall below preexercise values
has little if any predictive value.

**Causes of Exercise-Induced Hypotension**

We have demonstrated that EIH can be due to
either left ventricular dysfunction (as reflected by
myocardial infarction status) or ischemia. In the
10% of patients in which EIH occurs without asso-
ciation with either of these two factors, EIH appears
to be benign. Though speculative, other potential
mechanisms of EIH deserve further investigation,
such as exercise-induced mitral regurgitation and a
(noncardiac) peripheral vasodilatory mechanism.

**Prognostic Value of Exercise-Induced
Hypotension**

Though the risk of death was increased in patients
with EIH, two subgroups did not show this. EIH
was not associated with an increased risk in those
tested within 3 weeks after myocardial infarction or
in those without a previous myocardial infarction or
ischemia during the exercise test.
References


KEY WORDS • exercise-induced hypotension • treadmill test • myocardial ischemia • systolic blood pressure
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