

# Exercise-Induced Hypotension in a Male Population

## Criteria, Causes, and Prognosis

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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<sup>1,2</sup> or high-risk coronary angiographic disease.<sup>3</sup> 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.<sup>4</sup> In addition, EIH has been associated with cardiac complications during exercise testing<sup>5</sup> and appears to be corrected by coronary artery bypass graft surgery.<sup>6</sup> 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<sup>7</sup> despite uncertainty regarding its etiology,<sup>8</sup> the use of several different definitions or criteria, reproducibility limitations, and controversy regarding its predictive

power.<sup>9</sup> 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

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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.<sup>10</sup> Blood pressure measurements were taken during each stage and also when any electrocardiographic changes or symptoms occurred. Standard sphygmomanometry measurements were made by the physician monitoring the test. In addition, heart rate, Borg scale, and electrocardiographic changes were recorded for each stage. Maximum symptom-limited tests were performed by all patients except those tested before discharge after an 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  $\beta$ -blockers, or heart rate greater than 130 beats/min if not on  $\beta$ -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 BMDPMR.<sup>11</sup>

## 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.  $\beta$ -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

	Recent MI	Old MI	No MI	Total
<b>Patients (n)</b>				
All	191 (9.4%)	400 (19.8%)	1,431 (70.0%)	2,022
With EIHBR	16 (17%)	38 (40%)*	40 (42%)	94
With EIH20	3 (13%)*	5 (21.7%)*	15 (65%)	23
<b>Age</b>				
All	60±10	59±8	58±10	58±10
With EIHBR	65±10	62±5	64±9	64±8
With EIH20	50±8	63±5	59±7	58±8
<b>Previous CABG</b>				
All	9% (18)	27% (109)	10% (142)	13% (269)
With EIHBR	25% (4)	26% (10)	5% (2)	17% (16)
With EIH20	0% (-)	20% (1)	13% (2)	13% (3)
<b>Medications</b>				
<b>β-Blockers</b>				
All	49% (93)	46% (184)	25% (354)	31% (631)
With EIHBR	50% (8)	42% (16)	30% (12)	38% (36)
With EIH20	33% (1)	20% (1)	13% (2)	17% (4)
<b>Digoxin</b>				
All	12% (23)	11% (45)	7% (96)	8% (164)
With EIHBR	13% (2)	21% (8)	5% (2)	13% (12)
With EIH20	0% (-)	0% (-)	0% (-)	0% (-)
<b>Calcium antagonists</b>				
All	35% (68)	41% (162)	16% (228)	23% (458)
With EIHBR	44% (7)	45% (17)	15% (6)	32% (30)
With EIH20	66% (2)	40% (2)	27% (4)	35% (8)

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  $\chi^2$  with Yates' continuity correction.<sup>12</sup> 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

	Recent MI	Old MI	No MI	Total
<b>MET</b>				
All	5.2±2.1	7.2±2.9	8.2±3.5	7.7±3.4
With EIHBR	4.6±1.8	6.3±2.2	5.3±2.6	5.6±2.4*
With EIH20	4.3±0.5	7.9±2.1	9.1±3.1	8.2±3.1*
<b>MHR</b>				
All	115±22	127±23	137±25	133±25
With EIHBR	108±18	122±24	120±20	117±22*
With EIH20	132±9	140±13	150±18	146±18
<b>SBP<sub>max</sub></b>				
All	145±28	160±29	175±28	170±29
With EIHBR	110±16	123±20	131±25	124±33*
With EIH20	120±14	146±15	160±24	152±25
<b>No ischemia</b>				
All	57% (109/191)	52% (209/400)	68% (972/1,431)	64% (1,290/2,022)
With EIHBR	44% (7/16)	32% (12/38)	35% (14/40)	35% (33/94)
With EIH20	66% (2/3)	40% (2/5)	27% (4/15)	35% (8/23)
<b>Angina pectoris (with or without ST changes)</b>				
All	19%	29%	15%	18%
With EIHBR	19%	47%	33%	35%
With EIH20	33%	40%	27%	35%
<b>Silent ischemia</b>				
All	24%	19%	17%	18%
With EIHBR	38%	21%	33%	29%
With EIH20	0%	20%	47%	35%

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.<sup>13</sup> 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.<sup>13</sup> 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,<sup>2,3,6</sup> valvular heart disease,<sup>14</sup> or cardiomyopathies.<sup>1</sup> Occasionally, patients without clinically significant heart disease will exhibit EIH during exercise because of antihypertensive therapy,<sup>3</sup> unusually prolonged strenuous exercise,<sup>15</sup>

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

	Recent MI	Old MI	No MI	Total
All	14% (27/191)	5% (20/400)	4% (53/1,431)	5% (100/2,022)
With EIHBR	31% (5/16)	13% (5/38)	10% (4/40)	15% (14/94)
With EIH20	0% (-/3)	0% (-/5)	0% (-/15)	0% (-/23)*

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 without 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**

Deaths	Recent MI	Old MI	No MI	Total
<b>No ischemia</b>				
All without	13% (13/102)	4% (8/197)	3% (30/958)	4% (51/1,257)
With EIHBR	29% (2/7)	17% (2/12)	0% (-/14)	12% (4/33)
Odds ratio	2.7×	4.7×	...	3.3×
<b>Angina pectoris (with or without ST changes)</b>				
All without	15% (5/33)	1% (1/96)	3% (6/207)	4% (12/336)
With EIHBR	0% (0/3)	6% (1/18)	23% (3/13)	12% (4/34)
Odds ratio	...	5.6×	10×*	3.6×
<b>Silent ischemia</b>				
All without	15% (6/40)	10% (7/69)	4% (8/226)	6% (21/335)
With EIHBR	17% (1/6)	25% (2/8)	8% (1/13)	15% (4/27)
Odds ratio	1.1×	3.0×	2.3×	2.6×
<b>Total</b>				
All without	14% (24/175)	4% (16/362)	3% (44/1,391)	4% (84/1,928)
With EIHBR	19% (3/16)	13% (5/38)	10% (4/40)	13% (12/94)
Odds ratio	1.5×	3.3×†	3.4×‡	3.2×§

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,<sup>2,3,6</sup> valvular heart disease,<sup>14</sup> or cardiomyopathies.<sup>1</sup> Occasionally, patients without clinically significant heart disease will exhibit EIH during exercise because of antihypertensive therapy,<sup>3</sup> unusually prolonged strenuous exercise,<sup>15</sup> or it can occur in normal women.<sup>16</sup> 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.<sup>1</sup> EIH has also been reported to be reversed by coronary artery bypass graft surgery.<sup>9</sup> 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 impor-

tant 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<sup>3</sup> defined EIH as systolic blood pressure failing to rise 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,<sup>18</sup> and others have used a 10 mm Hg drop after an initial rise.<sup>8,17,19</sup> Thompson and Kelemen<sup>9</sup> and Morris et al<sup>17</sup> 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**

	All patients	With EIHBR	With EIH20
Studies (n)	389	31	11
<b>Vessel disease</b>			
None	11% (41/389)	0% (0/31)	0% (0/11)
One vessel	17% (68/389)	13% (4/31)	27% (3/11)
Two vessel	27% (105/389)	26% (8/31)	46% (5/11)
Three vessel (only)	36% (141/389)	48% (15/31)	27% (3/11)
Left main occlusion	9% (34/389)	13% (4/31)	0% (0/11)
Ejection fraction	59±15	56±14	61±17

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

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

	Definition	Prevalence of EIH	Prevalence of LM/3VD	Predictive value of EIH for LM/3VD	Subgroups at high risk	EIH reversed by revascularization	Mortality	
							MED	CABG/PTCA
Dubach et al	Drop in SBP below rest	5% (94/2,022)	45%	61%	No deaths in those with either ischemia or MI	18/22	12/95	0/22
Hammermeister <sup>1</sup>	SBP drop below rest	7% (93/1,241)	25%	50%	Angina, poor exercise capacity, LM/3VD with low EF			
Weiner <sup>2</sup>	Drop in SBP below rest	11% (47/436)	28%	55%	Ischemia, PVCs, poor exercise capacity		2/24	1/23
SanMarco et al <sup>3</sup>	Failure of SBP to rise 10 mm Hg in 1st min; or 20 mm Hg drop	24% (90/378)	39%	70%	None found			
Li et al <sup>6</sup>	SBP equal to or drop below rest	23% (55/234)	100%	100%		33/37		
Hakki et al <sup>8</sup>	Decrease of SBP by 10 mm Hg	7% (127/1,800)			3VD and LV dysfunction			
Thompson and Keleman <sup>9</sup>	SBP drop below rest	100% (17/17)	100%	100%		6/6	2/9	0/6
Levites et al <sup>16</sup>	SBP drop below rest	3% (30/1105)	20%	20%	(Women were false-positive.)			
Morris et al <sup>17</sup>	Decrease of SBP by 10 mm Hg	5% (23/438)	24%	78%	None found	6/6		0/12
Mazzotta et al <sup>18</sup>	Decrease of SBP by 5 mm Hg	20% (44/224)			None found			
Gibson et al <sup>19</sup>	Decrease in SBP by 10 mmHg	3% (27/820)	...	...	Age, LM, 3VD, LV dysfunction	...	...	...

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 al<sup>3</sup> also mentioned a vasovagal discharge and  $\beta$ -blocker therapy as possible causes. Recently, Rich et al<sup>20</sup> 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  $\beta$ -blocker therapy and EIH. Our results therefore suggest that factors other than those mentioned 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 predictors, 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, medication 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,<sup>2</sup> Thompson and Kelemen,<sup>9</sup> and Morris et al<sup>17</sup> 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 suggest that percutaneous transluminal coronary angioplasty 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,<sup>6</sup> Thompson and Kelemen,<sup>9</sup> and Morris et al<sup>17</sup> 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 Ehsani<sup>21</sup> 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 premature ventricular contractions.<sup>1,2,7,19</sup> Some investigators<sup>1,8,19</sup> 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 following: 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 radionuclide ventriculography. Thus, left ventricular function 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 interventions, so conclusions regarding the impact of revascularization 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, prognosis, 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 association 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.

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KEY WORDS • exercise-induced hypotension • treadmill test  
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