Blood Pressure Response During Treadmill Testing as a Risk Factor for New-Onset Hypertension

The Framingham Heart Study

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Background—Although systolic blood pressure (SBP) response to exercise has been shown to predict subsequent hypertension in small samples of men, this association has not been studied in a large population-based sample of middle-aged men and women. The purpose of this study was to examine, in normotensive subjects, the relations of SBP and diastolic blood pressure (DBP) during the exercise and recovery periods of a graded treadmill test to the risk of developing new-onset hypertension.

Methods and Results—BP data from exercise testing in 1026 men and 1284 women (mean age, 42 ± 10 years; range, 20 to 69 years) from the Framingham Offspring Study who were normotensive at baseline were related to the incidence of hypertension 8 years later. New-onset hypertension, defined as an SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg or the initiation of antihypertensive drug treatment, occurred in 228 men (22%) and 207 women (16%). Exaggerated SBP (Ex-SBP 2) and DBP (Ex-DBP 2) response and delayed recovery of SBP (R-SBP 3) and DBP (R-DBP 3) were defined as an age-adjusted BP greater than the 95th percentile during the second stage of exercise and third minute of recovery, respectively. After multivariable adjustment, Ex-DBP 2 was highly predictive of incident hypertension in both men (OR, 4.16; 95% CI, 2.15, 8.05) and women (OR, 2.17; CI, 1.19, 3.96). R-SBP 3 was predictive of hypertension in men in a multivariable model that included exercise duration and peak exercise BP (OR, 1.92; CI, 1.00, 3.69). Baseline resting SBP ($\chi^2$, 23.4 in men and 34.7 in women) and DBP ($\chi^2$, 11.3 in men and 13.1 in women) had stronger associations with new-onset hypertension than exercise DBP ($\chi^2$, 16.4 in men and 6.1 in women) and recovery SBP ($\chi^2$, 6.5 in men and 2.1 in women) responses.

Conclusions—An exaggerated DBP response to exercise was predictive of risk for new-onset hypertension in normotensive men and women. An elevated recovery SBP was predictive of hypertension in men. These findings may reflect subtle pathophysiological features in the preclinical stage of hypertension. (Circulation. 1999;99:1831-1836.)

Key Words: tests ■ hypertension ■ trials

Hypertension, a key risk factor for cardiovascular disease morbidity and mortality,1 is a highly prevalent condition in the adult population of the United States.2,3 Given the health costs and potential importance of early detection of hypertension, several studies have examined the role of blood pressure (BP) response to exercise as a risk factor for the development of hypertension.4–10 Most studies addressing this issue have focused on systolic BP response4,5,8,9 and examined either young subjects4,5,7–10 or small groups of men at risk for hypertension8–10 or small groups of women at risk for hypertension11–8,10 and have not looked at a large, unselected sample of middle-aged men and women. Other aspects of the dynamic behavior of BP response, such as exercise-induced changes in diastolic BP and recovery BP after exercise and their association with hypertension risk, have not been examined.

The purpose of this study was to (1) examine the BP responses during exercise and early recovery period of a standard exercise test in normotensive men and women and determine their association with risk of developing hypertension during an 8-year follow-up and (2) define the strength and independence of these associations after adjustment for other risk factors.

Methods

The Framingham Heart Study is a prospective epidemiological study established in 1948 to evaluate potential risk factors for coronary
Subjects for this investigation were Framingham Offspring Study subjects who had an exercise treadmill test between 1979 and 1983 during a routine, scheduled examination at the Framingham Heart Study clinic. Subjects were excluded if they met any of the following criteria: (1) history or clinical evidence of coronary heart disease, congestive heart failure, or valvular or congenital heart disease; (2) hypertension, defined as the current use of antihypertensive medications or a resting BP of ≥140 mm Hg systolic or 90 mm Hg diastolic at the index examination; (3) use of cardiac medication; and (4) age <20 or >69 years. All subjects entered at least the second stage of the standard Bruce protocol.14

The diagnoses of myocardial infarction and congestive heart failure were established by a committee of 3 physicians in accordance with published criteria.15 At the index examination, body height and weight measurements, medical history, physical examination, 12-lead resting ECG, and treadmill testing were routinely performed.

Exercise Treadmill Methods
All participants were studied with a multistage exercise treadmill test according to the Bruce protocol.14 Subjects remained on the treadmill for up to five 3-minute stages. Systolic and diastolic BPs were recorded by cuff when the subject was standing immediately before testing and during the last minute of each 3-minute exercise stage. Subjects exercised until reaching an age-specific target heart rate or the development of symptoms necessitating termination of the test. The recovery phase was 4 minutes, with BP and heart rate recorded in the upright (sitting) position at the end of each minute.

BP Measurements
At each routine examination at baseline and at 4-year intervals thereafter, resting BP was obtained in the left arm twice in the seated position by an examining physician using a mercury column sphygmomanometer. The averaged values were then used to derive the respective examination systolic and diastolic BP. The index examination was the one performed at the time of the treadmill testing. BP obtained 8 years after the index examination was used to identify new-onset hypertension.

Definitions of BP Responses
1. Exaggerated exercise systolic BP (Ex-SBP, stage 2): Sex-specific, age-predicted systolic BP ≥95th percentile during the second stage of exercise.
2. Exaggerated exercise diastolic BP (Ex-DBP, stage 2): Sex-specific, age-predicted diastolic BP ≥95th percentile during the second stage of exercise.
3. Elevated recovery systolic BP (Rec-SBP, 3 minutes): Sex-specific, age-predicted systolic BP ≥95th percentile at the third minute of the recovery phase.
4. Elevated recovery diastolic BP (Rec-DBP, 3 minutes): Sex-specific, age-predicted diastolic BP ≥95th percentile at the third minute of the recovery phase.
5. New-onset hypertension: Systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg or use of antihypertensive medications on follow-up.3

Statistical Analyses
All statistical analyses were sex-specific. Group means and SDs were used to summarize baseline clinical variables. Multivariable regression analyses were performed to assess the strength and independence of association of BP response during exercise and recovery with new-onset hypertension. The principal outcome, new-onset hypertension, was coded as yes/no and was analyzed with logistic regression models. Each of the 4 BP responses (exercise and recovery, systolic and diastolic BP) was assessed separately by means of unadjusted, age-adjusted, and age plus clinical covariate–adjusted analyses. The clinical covariates were diabetes, body mass index, cigarette smoking, alcohol consumption, and baseline resting systolic and diastolic BP. In addition, the recovery BP responses were adjusted for the duration of exercise and peak systolic and diastolic BP during exercise. Results are summarized by ORs and 95% CIs, with OR expressed for a BP response ≥95th percentile value. An association was considered statistically significant at P<0.05.

A secondary analysis was performed in subjects with high-normal BP (SBP, 130 to 139 mm Hg and DBP, 85 to 89 mm Hg) to assess the additional, incremental value of exercise BP responses over and above baseline BP in predicting new-onset hypertension. Sex-specific age-predicted cutoff points for the 95th percentile value were derived from linear regression models. All analyses were done on a Sparcstation 2 (SUN Microsystems) using the Statistical Analysis System (SAS).17

Results
Subjects
Of 3867 subjects who attended the baseline examination and underwent treadmill testing, 1557 subjects were excluded from eligibility: 906 were excluded because of hypertension at the index examination, 206 did not attend the follow-up examination, 397 did not enter stage 2 of the exercise treadmill test, 23 had incomplete BP information, and 25 were excluded for age <20 or >69 years. Of the 1026 normotensive men and 1284 normotensive women eligible for this study, 228 men (22%) and 207 women (16%) were newly hypertensive at the 8-year follow-up visit.

The clinical and exercise characteristics of study participants (n=2310) are summarized in Tables 1 and 2, respectively. Approximately 80% of subjects achieved target heart rate. The mean resting, exercise, and recovery systolic and diastolic BPs were higher in men than in women. Sex-specific, age-predicted 95th percentile values for systolic and diastolic BP at the second stage of exercise are presented in Table 3. The distribution of BP responses during stage 2 of exercise and at 3 minutes of recovery are shown in Figures 1 and 2, respectively.

Progression to Hypertension
Observed (crude) probabilities of progression to hypertension as a function of the exercise and recovery BP responses are displayed in Figures 3 and 4, respectively. Exercise and recovery systolic and diastolic BP responses exhibited positive relations to the probability of developing hypertension.

Table 1. Baseline Clinical Characteristics of the Study Sample

<table>
<thead>
<tr>
<th></th>
<th>Men (n=1026)</th>
<th>Women (n=1284)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>42.2±9.6</td>
<td>41.9±9.3</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.3±3.4</td>
<td>23.8±4.1</td>
</tr>
<tr>
<td>Smoker, %</td>
<td>37</td>
<td>36</td>
</tr>
<tr>
<td>Alcohol, oz/wk</td>
<td>4.6±5.1</td>
<td>2.2±3.0</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>2.1</td>
<td>0.6</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>119±10</td>
<td>113±12</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>77±7</td>
<td>73±7</td>
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</tbody>
</table>

BP is mean of 2 physician measurements. Results are expressed as mean±SD or percentage.
Subjects in the highest decile of exercise and recovery BP responses had a 40% and 30% probability of developing hypertension, respectively.

Logistic regression analyses were used to examine the association of each BP response variable with new-onset hypertension. Unadjusted logistic regression analyses showed that an exaggerated exercise systolic and diastolic BP response during the second stage of exercise and an elevated recovery of systolic and diastolic BP at the third minute of recovery were associated with risk of hypertension both in men and women (Table 4). After age adjustment, the association with increased odds of developing hypertension persisted for exercise and recovery variables. An exaggerated diastolic BP response during stage 2 of exercise was observed to have the strongest association with new-onset hypertension in both men (OR, 7.46; 95% CI, 2.15, 8.07) and women (OR, 5.06; 95% CI, 2.93, 8.76).

After further adjustment for diabetes, smoking, body mass index, alcohol intake, and baseline systolic and diastolic BP, the exaggerated diastolic BP response during stage 2 of exercise was observed to have the strongest association with new-onset hypertension in both men (OR, 4.16; 95% CI, 2.15, 8.05) and women (OR, 2.17; 95% CI, 1.19, 3.96) (Table 4). An elevated systolic BP at the third minute of recovery (OR, 2.48; 95% CI, 1.33, 4.64) and elevated diastolic BP at the third minute of recovery (OR, 2.21; CI, 1.14, 4.25) were also predictors of new-onset hypertension in men. After exercise duration and peak exercise BP as potential confounders of recovery responses had been accounted for, an elevated systolic BP at the third minute of recovery remained predictive of hypertension in men (OR, 1.92; 95% CI, 1.00, 3.69), and there was a nonsignificant association with recovery diastolic BP response (OR, 1.66; 95% CI, 0.83, 3.32).
We observed that baseline resting systolic BP ($\chi^2$, 23.4 in men and 34.7 in women) and resting diastolic BP ($\chi^2$, 11.3 in men and 13.1 in women) had stronger associations with new-onset hypertension compared with exercise diastolic BP ($\chi^2$, 16.4 in men and 6.1 in women) and recovery systolic BP ($\chi^2$, 6.5 in men and 2.1 in women) responses. The additional contributions of exercise diastolic BP response (stage 2) and recovery systolic response (third minute) to the overall $\chi^2$ statistic (above that contributed by the baseline BP) were 9.7% ($P<0.0001$) and 4.4% ($P=0.004$) in men and 2.2% ($P=0.01$) and 0.86% ($P=0.12$) in women, respectively. In an additional analysis, pulse pressure during the second stage of exercise ($\chi^2$, 0.35 in men and 0.15 in women) and third minute of recovery ($\chi^2$, 0.36 in men and 0.08 in women) did not enter the model.

The additional value of exercise BP responses above resting BP is graphically presented in Figure 5. Among subjects with high-normal BP ($n=428$), a higher propensity to develop new-onset hypertension was observed in those with a higher quartile of exercise diastolic and systolic BP response.

**Discussion**

In normotensive men and women, an exaggerated diastolic BP response to exercise was associated with a 2- to 4-fold risk for new-onset hypertension. A diminished recovery systolic BP response was also predictive of hypertension in men. Although previous work has shown exercise-induced hypertension to be predictive of incident hypertension,4,6,10 this is the first prospective population-based study to examine the exercise BP response during treadmill testing as a predictor of new-onset hypertension.

### TABLE 4. Unadjusted, Age-Adjusted, and Fully Adjusted ORs for New-Onset Hypertension Associated With Exercise and Recovery BP Response ≥95th Percentile

<table>
<thead>
<tr>
<th>Variables</th>
<th>Unadjusted OR (95% CI) for HTN</th>
<th>Age-Adjusted OR (95% CI) for HTN</th>
<th>Fully Adjusted OR (95% CI) for HTN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men ($n=1026$)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ex-SBP (stage 2)</td>
<td>2.27 (1.28–4.03)</td>
<td>2.22 (1.23–3.99)</td>
<td>1.00 (0.53–1.89)</td>
</tr>
<tr>
<td>Ex-DBP (stage 2)</td>
<td>5.84 (3.23–10.56)</td>
<td>7.46 (2.15–8.07)</td>
<td>4.16 (2.15–8.05)</td>
</tr>
<tr>
<td>Rec-SBP (3 min)</td>
<td>3.77 (2.13–6.67)</td>
<td>4.14 (2.29–7.48)</td>
<td>2.48 (1.33–4.64)</td>
</tr>
<tr>
<td>Rec-DBP (3 min)</td>
<td>1.91 (1.07–3.42)</td>
<td>3.02 (1.64–5.54)</td>
<td>2.21 (1.14–4.25)</td>
</tr>
<tr>
<td>Women ($n=1284$)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ex-SBP (stage 2)</td>
<td>3.42 (2.03–5.78)</td>
<td>3.58 (2.07–6.18)</td>
<td>1.36 (0.73–2.50)</td>
</tr>
<tr>
<td>Ex-DBP (stage 2)</td>
<td>4.10 (2.45–6.86)</td>
<td>5.06 (2.93–8.76)</td>
<td>2.17 (1.19–3.96)</td>
</tr>
<tr>
<td>Rec-SBP (3 min)</td>
<td>4.10 (2.45–6.86)</td>
<td>3.79 (2.21–6.50)</td>
<td>1.61 (0.89–2.91)</td>
</tr>
<tr>
<td>Rec-DBP (3 min)</td>
<td>2.89 (1.70–4.98)</td>
<td>3.69 (2.11–6.47)</td>
<td>1.56 (0.83–2.92)</td>
</tr>
</tbody>
</table>

HTN indicates hypertension; Ex-SBP (stage 2), exaggerated systolic BP during second stage of exercise; Ex-DBP (stage 2), exaggerated diastolic BP during second stage of exercise; Rec-SBP (3 min), elevated systolic BP at the end of third minute of recovery; Rec-DBP (3 min), elevated diastolic BP at the end of third minute of recovery. Fully adjusted OR is the OR adjusted for age, diabetes, body mass index, smoking, alcohol intake, and baseline resting systolic and diastolic BP.
latent tendency toward hypertension.5 Several definitions of exaggerated BP response have been reported, including some based solely on systolic BP and others on systolic and diastolic BP together.4–10 Scant information is available regarding the examination of each separately. In this study, the exercise diastolic response was predictive of the development of hypertension and was the strongest exercise predictor of hypertension in both men and women. This finding is consistent with an earlier report describing diastolic BP changes with exercise in borderline hypertensives who subsequently went on to develop hypertension.10 The latter study, however, was restricted to men and did not adjust for confounding variables.10 This exercise-induced rise in diastolic BP in the prehypertensive stage is similar to that described in high-risk subjects (with high-normal BP and family history of hypertension)7 and borderline hypertensives10 and can be explained by increased resting peripheral vascular resistance in the early stages of hypertension20 and impaired capacity for exercise-induced vasodilatation.7,10,21,22

The strong relation observed between exaggerated systolic response and incident hypertension in univariate analysis (Table 4) was attenuated in multivariate analysis, suggesting that exercise systolic response was a weaker predictor of hypertension than the diastolic response. This finding is at odds with several other studies that have reported exercise systolic BP as a strong predictor of hypertension.5,6,10,23 Those studies included small numbers of female subjects, did not adjust for confounding variables, and used different cutoff points for exaggerated BP responses. The CARDIA study, which observed a weak association between exercise systolic BP response and hypertension, was restricted to younger subjects and did not separately examine the diastolic BP or recovery-phase responses.4 In our study, the exercise protocol was standard, and BP measurements from the second stage of exercise were used to limit the influence of exercise duration and physical conditioning. Also, the predicted cutoff points defining an exaggerated BP response were age- and sex-specific.

Recovery BP Response and Hypertension

In the age-adjusted models (Table 4), both systolic and diastolic BP at the third minute of recovery were associated with new-onset hypertension. After adjustment for potential confounders, including duration of exercise and peak BP responses, the recovery systolic BP continued to remain a predictor of hypertension in men. Our findings are consistent with earlier reports that examined the recovery response of BP in young men after submaximal exercise.5,24 Autonomic dysregulation has been described in the early stages of hypertension.26 Because the immediate postexercise period is associated with a withdrawal of sympathetic tone and a rebound increase in vagal tone,25 it is possible that abnormalities of autonomic control and vasoreactivity could extend into the early recovery phase of exercise. Consequently, a blunted decline in the peripheral vascular resistance could explain the elevated recovery systolic BP in men predisposed to hypertension.

Sex differences in exercise BP response and its association with hypertension could be related to physiological26 or hormonal27 differences in cardiovascular response to exercise. Age is another important determinant of BP response to exercise. Our results concur with a recent report28 suggesting that BP changes with dynamic exercise in normotensive individuals are accentuated with increasing age.

Resting and Exercise BP

We observed a stronger association between resting BP and risk for subsequent hypertension than with exercise BP. Although this finding is supported by some studies,4,19 several others have suggested that BP during exercise is a better predictor of hypertension than resting BP.5,10,29 This discrepancy probably arises from differences in methodology, characteristics of the study sample, and clinical covariates considered in the analyses. In this study, we have shown the additional value of exercise and recovery BP responses as predictors of hypertension after adjustment for baseline systolic and diastolic BP. In a subset analysis of subjects with high-normal resting BP (subjects at high risk of developing
hypothesis), we have shown the additional and incremental value of exercise systolic and diastolic BP responses above resting measurements. Subjects with high-normal resting BP who exhibit an exercise BP response in the top quartile are more likely to develop resting hypertension in the future.

**Strengths and Limitations**

Our study included a large population-based sample in which referral bias was inherently minimal. An important strength of this study is the well-characterized study sample. The relatively large number of subjects who developed hypertension allowed more precise estimation of the risk of hypertension and permitted adjustment for age and baseline BP.

Although the reproducibility of BP response during treadmill testing has not been studied at the Framingham Heart Study, earlier reports have indicated a good reproducibility for BP measured during and after exercise. A potential limitation of the study is that habitual physical activity was not taken into account. The effect of this, however, was diminished by the use of stage 2 BP measurements, which eliminated the effect of endurance and duration of exercise and standardized the exercise response. BP response is also more easily and accurately measured at this level of exercise, which in fact corresponds to the level of exercise and duration of exercise and standardized the exercise response. BP response is also more easily and accurately measured at this level of exercise, which in fact corresponds to levels of daily physical activities. Low-intensity workloads (equivalent to stage 2 Bruce protocol) require a minimum of subject cooperation and allow for more objective and reproducible results. The study sample was predominantly white, and it is possible that results from the present study may not be generalizable to other ethnic and racial groups. Although previous work has suggested an association between left ventricular mass and exercise BP response, inclusion of echocardiographic findings was beyond the scope of this project.

**Clinical Implications**

Given the health costs of hypertension and the importance of early detection of this disorder, exercise and recovery BP responses during standard treadmill testing may serve as risk markers for new-onset hypertension. Exercise treadmill testing may help identify individuals at risk for the development of hypertension in whom closer follow-up is warranted and in whom nonpharmacological strategies should be investigated for their ability to prevent hypertension.

**References**


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