Systolic Blood Pressure Response to Exercise Stress Test and Risk of Stroke

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Background and Purpose—Systolic blood pressure (SBP) during exercise has been found to predict a future diagnosis of hypertension, coronary heart disease, and cardiovascular disease death. No studies have been conducted to show a relationship between SBP during exercise test and stroke. The aim of the present study was to study the associations between SBP rise, percent maximum SBP at 2 minutes after exercise, and the risk of stroke in a population-based sample of men with no prior coronary heart disease.

Methods—SBP was measured every 2 minutes during and after the exercise test. The subjects were a population-based sample of 1026 men without clinical coronary heart disease, antihypertensive medication, or prior stroke at baseline. During an average follow-up of 10.4 years, there were 46 cases of stroke (38 ischemic strokes).

Results—Men with SBP rise >19.7 mm Hg per minute of exercise duration had a 2.3-fold increased risk of any stroke and a 2.3-fold increased risk of ischemic stroke compared with men whose SBP rise was <16.1 mm Hg/min. Similarly, percent maximum SBP at 2 minutes after exercise (SBP at 2 minutes’ recovery divided by maximum SBP) was associated (highest tertile) with a 4.6-fold increased risk of any stroke and a 5.2-fold increased risk of ischemic stroke.

Conclusions—SBP rise during exercise and percent maximum SBP at 2 minutes after exercise were directly and independently associated with the risk of all stroke and ischemic stroke. Exercise SBP testing may be recommended as an additional tool in the prediction of future stroke. (Stroke. 2001;32:2036-2041.)

Key Words: blood pressure ■ exercise test ■ hypertension ■ risk factors ■ stroke prevention

Elevated resting systolic blood pressure (SBP) is a common risk factor for stroke. Incidence of stroke increases proportionally to blood pressure. SBP during exercise has been found to predict hypertension, coronary heart disease, and cardiovascular disease death. No studies have been conducted to show a relationship between SBP during exercise test and stroke. The aim of the present study was to study the associations between SBP rise, percent maximum SBP at 2 minutes after exercise, and the risk of stroke in a population-based sample of men from eastern Finland.

Subjects and Methods

Subjects
Subjects were participants in the Kuopio Ischemic Heart Disease Risk Factor Study, which was designed to investigate risk factors for CVD, atherosclerosis, and related outcomes in a population-based sample of men in eastern Finland. Of the 3433 men aged 42, 48, 54, or 60 years who resided in the town of Kuopio or its surrounding rural communities, 198 were excluded because of death, serious disease (eg, cancer), or migration away from area. Baseline examinations were conducted on 2682 men (82.9%) between March 1984 and December 1989.

Men who had prior stroke (n=69) or coronary heart disease (n=677) were excluded. Prevalent coronary heart disease was defined as either a history of myocardial infarction or angina pectoris, angina pectoris on effort based on the London School of Hygiene Cardiovascular Questionnaire, or use of nitroglycerin for chest pain once a week or more frequently. Men who used antihypertensive medication (n=268) or who had abnormal SBP response (n=31) also were excluded. We excluded men with any kind of antihypertensive medication use to avoid a confounding effect of...
these medications on the results. Abnormal SBP response was defined as SBP decrease or no increase in 3 consecutive measurements during exercise compared with the starting value. Men with a decrease or no increase in SBP during exercise were excluded because these subjects have previously been found to have a poor prognosis, most likely owing to preexisting CVD. Complete data were available for 1026 men.

Exercise Stress Test
A maximum symptom-limited exercise-tolerance test was performed with an electrically braked bicycle ergometer. For 348 men (33.9%) examined before June 1986, the testing protocol comprised a 3-minute warm-up at 50 W followed by a step-by-step increase in workload by 20 W/min. The remaining 678 men (66.1%) were tested with a linear increase in the workload at 20 W/min. The SBP rise did not differ markedly between the 2 protocols. An electrocardiography (ECG) recording was printed every 30 seconds during exercise. The Mason-Likar lead system was used, including leads V₁, V₅, and aVF. An ECG recording was printed every 30 seconds based on averages of 6-second intervals during exercise and at least 7 minutes of recovery while subjects sat on the bicycle. Exercise ECGs were coded manually by a cardiologist. The criteria for myocardial ischemia during the exercise test were ischemic ECG changes, defined as upsloping, horizontal, or downsloping ST-segment depression ≥1.0 mm at 80 ms after the J point.

The most common reasons that subjects stopped the exercise test were leg fatigue (522 men), exhaustion (216 men), breathlessness (111 men), and pain in the leg muscles, leg joints, or back (42 men). The test was discontinued because of cardiorespiratory symptoms or abnormalities in 132 men. These included arrhythmias (47 men), a marked elevation in systolic or diastolic blood pressure (26 men), abnormalities in 132 men. These included arrhythmias (47 men), a marked elevation in systolic or diastolic blood pressure (26 men), chest pain (5 men), or ECG changes (5 men). For a total of 3 men, the exercise test was not performed because of severe CVD or other disease. After the exercise test, each participant remained seated on the bicycle for 8 minutes. The same protocol was followed by all participants.

Assessment of Blood Pressure
Resting blood pressures for each subject were obtained by the same experienced nurse using a random-zero sphygmomanometer after the subject had rested in the seated position for 5 and 10 minutes. The mean of these 2 values was used as resting blood pressure. Blood pressure during exercise was measured and recorded both manually and automatically when the subject was sitting on the bicycle. Blood pressure during exercise was measured every 2 minutes both manually and automatically during exercise until the test was stopped and every 2 minutes after exercise. In the present study, we used only manually measured blood pressure values. The highest SBP achieved during the exercise test was defined as the maximum exercise SBP. The SBP rise was defined as an average rise of SBP per minute of exercise test time. Blood pressure was also measured during recovery after exercise at regular intervals of 2, 4, 6, and 8 minutes with subjects seated on the bicycle. Percent maximum SBP at 2 minutes after exercise was calculated as SBP at 2 minutes recovery divided by maximum SBP.

Assessment of Covariates
The collection of blood specimens and measurement of serum lipids have been described elsewhere. Assessment of smoking and alcohol consumption was performed as described previously. Body mass index was computed as the ratio of weight (kg) to the square of height (m²).

Ascertainment of Strokes
Incident strokes between 1985 and 1992 were ascertained through the FINMONICA stroke registry. Information on incident strokes between 1993 and 1997 was obtained by computerized linkage to the national hospital discharge registry. Diagnostic information was collected from hospitals and classified by 1 neurologist (J.S.) with diagnostic criteria identical to the FINMONICA criteria. The average follow-up time to the first stroke was 10.4 years. There were 46 strokes of any type and 38 ischemic strokes. Each definite stroke was classified as either an ischemic stroke (International Classification of Diseases [ICD]-9 codes 433 to 434, ICD-10 code I63) or a hemorrhagic stroke (ICD-9 codes 430 to 431, ICD-10 codes I60 to I61).

Statistical Analysis
The associations of SBP during exercise and recovery with the risk of stroke were analyzed with SPSS Cox proportional hazards' models. Covariates were entered as uncategorized into Cox models. Covariates were selected by entering common stroke risk factors (age, smoking, serum LDL cholesterol, diabetes, body mass index, and alcohol consumption) in forced Cox models. When the predictive values of resting and exercise SBP were compared, additional multivariate analyses were performed. In these analyses, resting and exercise SBP were entered simultaneously in a forced Cox model with other presented covariates. Relative hazards adjusted for risk factors were estimated as antilogarithms of coefficients from multivariate models. Their CIs were estimated under the assumption of asymptotic normality of the estimates. All tests for statistical significance were 2-sided. Statistical analyses were performed with SPSS 9.0 software for Windows.

Results
Baseline Characteristics
Mean resting SBP in the entire study population was 129 mm Hg (range 91 to 207 mm Hg; Table 1). Resting SBP correlated positively with SBP immediately before the exercise test while subjects were seated on the bicycle (r=0.70, P<0.001), SBP at 2 (r=0.64, P<0.001) and 4 minutes of exercise (r=0.61, P<0.001), SBP rise per minute of exercise duration (r=0.30, P<0.001), maximum SBP (r=0.42, P<0.001), and SBP at 2 minutes after exercise (r=0.53, P<0.001). The rise in SBP appeared to plateau after 10 minutes of exercise (Figure). The distributions of other known risk factors for stroke are presented in Table 1. The characteristics of SBP measurements during exercise test at baseline according to quartiles of SBP at rest are shown in Table 2.

Resting SBP and Risk of Stroke
A resting (casual) SBP increase of 1 SD was associated with a 1.4-fold increased risk of any stroke and a 1.4-fold
increased risk of ischemic stroke (Table 3). An SBP increase immediately before the exercise test while subjects were seated on the bicycle was associated with a 1.4-fold increased risk of any stroke and a 1.4-fold increased risk of ischemic stroke (Table 3).

### SBP at Moderate Workloads and Risk of Stroke
A 1-SD increment of SBP at 2 and 4 minutes from the start of the exercise test was associated with an increased risk of stroke (Table 3). If resting SBP was added into the forced models, the relationship of SBP at 2 and 4 minutes and resting SBP was not significant. Maximum SBP was not associated with the risk of stroke.

### SBP Rise During Exercise Test and Risk of Stroke
The SBP rise per minute of exercise duration was associated with the risk of stroke (Table 3). A 1-SD increment of SBP rise per minute (18.8 mm Hg) was associated with a 2.3-fold increased risk of any stroke and a 2.3-fold increased risk of ischemic stroke. After further adjustment for resting SBP, SBP rise per minute of exercise duration was associated almost statistically significantly with the risk of any stroke (relative risk [RR]=2.06, 95% CI 0.99 to 4.49, \( P=0.051 \)). Men with an SBP rise >19.7 mm Hg per minute of exercise duration had a 2.3-fold increased risk of any stroke and a 2.3-fold increased risk of ischemic stroke compared with men whose SBP rise was <16.1 mm Hg/min (Table 4). Additionally, exercise duration was related to the risk of stroke after adjustment for other known risk factors, excluding maximum oxygen uptake, as shown in Table 4. Maximum oxygen uptake correlated strongly with exercise duration (\( r=0.71, \ P<0.001 \)).

### Percent Maximum SBP at 2 Minutes After Exercise and Risk of Stroke
SBP after exercise was related to an increased risk of stroke. The RR was 1.6 for any stroke and 1.7 for ischemic stroke at 2 minutes of recovery for an increment of 1 SD (Table 3). After further adjustment for resting SBP, the respective RRs were 1.47 (95% CI 1.01 to 2.15, \( P=0.04 \)) for any stroke and 1.58 (95% CI 1.03 to 2.43, \( P=0.03 \)) for ischemic stroke. Percent maximum SBP at 2 minutes after exercise was related to an increased risk of stroke (Table 4). A high ratio of SBP at 2 minutes after exercise and maximum exercise (highest tertile) was associated with a 4.6-fold increased risk of any stroke and a 5.1-fold increased risk of ischemic stroke.

### Exercise SBP in 2 Protocols
A 1-SD increment of SBP at 2 (RR=1.91, 95% CI 1.32 to 2.78, \( P<0.001 \)) and 4 (RR=2.12, 95% CI 1.42 to 3.16, \( P<0.001 \)) minutes from the start of the exercise test was associated with increased risk of any stroke. Similarly, SBP rise per minute of exercise duration (RR=5.09, 95% CI 1.13 to 23.0, \( P=0.03 \)), SBP at 2 minutes after exercise (RR=2.07, 95% CI 1.31 to 3.24, \( P=0.002 \)), and SBP increase immediately before the exercise test while seated on the bicycle (RR=1.60, 95% CI 1.10 to 2.33, \( P=0.02 \)) predicted the risk of stroke. These associations were not statistically significant with the first protocol used, mainly because of the small number of end points in this group of 348 men.

### Percent Maximum SBP at 2 Minutes After Exercise and Risk of Stroke
Percent maximum SBP at 2 minutes after exercise was related to an increased risk of stroke. The RR was 1.6 for any stroke and 1.7 for ischemic stroke at 2 minutes of recovery for an increment of 1 SD (Table 3). After further adjustment for resting SBP, the respective RRs were 1.47 (95% CI 1.01 to 2.15, \( P=0.04 \)) for any stroke and 1.58 (95% CI 1.03 to 2.43, \( P=0.03 \)) for ischemic stroke.

### Table 2. Characteristics of SBP During Exercise Test in 1026 Men With No History of Stroke, Coronary Heart Disease, and Antihypertensive Medication at Baseline According to Quartiles of SBP at Rest

<table>
<thead>
<tr>
<th>Characteristics of SBP During Exercise Test</th>
<th>Mean (SD)</th>
<th>Q1 (SD)</th>
<th>Q2 (SD)</th>
<th>Q3 (SD)</th>
<th>Q4 (SD)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting SBP on bike</td>
<td>148.2 (21.2)</td>
<td>131.4 (14.2)</td>
<td>141.1 (14.5)</td>
<td>151.3 (15.0)</td>
<td>168.7 (20.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP at 2 min of exercise</td>
<td>164.8 (24.0)</td>
<td>147.9 (16.5)</td>
<td>157.1 (17.7)</td>
<td>167.8 (19.4)</td>
<td>186.2 (23.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP at 4 min of exercise</td>
<td>175.1 (24.5)</td>
<td>158.0 (17.4)</td>
<td>167.5 (19.7)</td>
<td>179.8 (19.0)</td>
<td>194.9 (24.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximal SBP during exercise</td>
<td>210.3 (26.0)</td>
<td>196.7 (22.3)</td>
<td>205.4 (24.7)</td>
<td>214.5 (21.6)</td>
<td>224.4 (26.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP rise per min of exercise duration</td>
<td>18.8 (4.7)</td>
<td>17.4 (3.9)</td>
<td>18.0 (5.2)</td>
<td>19.0 (3.9)</td>
<td>20.9 (4.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP 2 min after exercise</td>
<td>188.5 (27.7)</td>
<td>171.3 (26.3)</td>
<td>181.6 (21.7)</td>
<td>193.2 (22.4)</td>
<td>207.8 (26.4)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Q1 indicates quartile 1, <118.5 mm Hg; Q2, 118.5–126.5 mm Hg; Q3, 126.6–138.5 mm Hg; and Q4, >138.5 mm Hg.
Discussion

A high SBP rise per minute of exercise and percent maximum SBP at 2 minutes after exercise were independently associated with an increased risk of stroke in a population-based sample of men from eastern Finland. Furthermore, high SBP at 2 and 4 minutes from the start of the exercise test was related to increased risk of any stroke. SBP rise per minute of exercise and SBP at 2 minutes after exercise were 2 important predictors for the risk of stroke after resting SBP was taken into account. On the basis of our findings, SBP during exercise appears to add to the prognostic value of SBP at rest. SBP rise during exercise provides information about the hemodynamic response to increasing physical stress that is not available from SBP at rest. Dynamic exercise produces a large increase in SBP without much change in diastolic blood pressure. In a previous study, the highest CVD mortality rate was observed in men with both elevated resting and exercise blood pressure. Fagard et al reported that SBP at moderate and peak workloads was directly associated with the risk of cardiovascular events in hypertensive men. All these studies were based on cardiovascular events, but there were no studies concerning SBP during progressive exercise testing and the risk of stroke. We determined that both SBP at

<p>| TABLE 3. SBP At Rest and During and After Exercise as Risk Factors for Stroke |
|---------------------------------------------|-----------------|-----------------|-----------------|
| Risk Factor (SD)                          | Any Stroke (n=46) | Ischemic Stroke (n=38) |
|---------------------------------------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Relative Risk</th>
<th>Relative Risk</th>
<th>Relative Risk</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting SBP before test (16.8 mm Hg)</td>
<td>1.42 (1.09–1.86)</td>
<td>1.41 (1.05–1.89)</td>
<td>0.02</td>
</tr>
<tr>
<td>Resting SBP on bike* (21.6 mm Hg)</td>
<td>1.38 (1.07–1.77)</td>
<td>1.39 (1.05–1.83)</td>
<td>0.02</td>
</tr>
<tr>
<td>Maximal SBP during exercise (26.8 mm Hg)</td>
<td>1.11 (0.81–1.52)</td>
<td>1.14 (0.81–1.61)</td>
<td>0.44</td>
</tr>
<tr>
<td>Relative risks are expressed per 1-SD linear sustained increase in each variable of SBP and are adjusted for age, examination years, alcohol consumption, cigarette smoking, serum LDL cholesterol, diabetes, and body mass index.</td>
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</table>

| TABLE 4. SBP Response According to Tertiles of Percent Maximum SBP at 2 Minutes After Exercise and SBP Rise per Minute of Exercise Time and Risk of Stroke |
|---------------------------------------------|-----------------|-----------------|-----------------|
| Risk Factor (95% CI)                        | Any Stroke (n=46) | Ischemic Stroke (n=38) |
|---------------------------------------------|-----------------|-----------------|-----------------|
| Percent maximum SBP at 2 minutes after exercise* (ratio) | Relative Risk | Relative Risk |
| 1st tertile (<0.85)                         | 1.00 (Reference) | 1.00 (Reference) | 6               |
| 2nd tertile (0.85–0.95)                     | 2.29 (0.86–6.14) | 2.46 (0.84–7.18) | 0.10            |
| 3rd tertile (>0.95)                         | 4.61 (1.72–12.35) | 5.12 (1.74–15.03) | 0.003           |
| P=0.001 for linear trend                    |                | P=0.002 for linear trend |
| SBP rise per minute of exercise time†      | Relative Risk | No. of Cases | Relative Risk | No. of Cases |
| 1st tertile (<16.1 mm Hg/min)               | 1.00 (Reference) | 10             | 1.00 (Reference) | 7             |
| 2nd tertile (16.1–19.7 mm Hg/min)           | 1.30 (0.56–3.01) | 0.54           | 1.39 (0.51–3.71) | 0.51           |
| 3rd tertile (>19.7 mm Hg/min)               | 2.26 (1.03–4.94) | 0.04           | 2.29 (1.13–6.87) | 0.03           |
| P=0.03 for linear trend                    |                |                | P=0.02 for linear trend |
| Exercise duration‡                         | Relative Risk | No. of Cases | Relative Risk | No. of Cases |
| 1st tertile (<10.5 min)                     | 1.00 (Reference) | 9              | 1.00 (Reference) | 6              |
| 2nd tertile (10.5–12.5 min)                 | 1.35 (0.57–3.20) | 0.50           | 1.65 (0.60–4.53) | 0.33           |
| 3rd tertile (>12.5/min)                     | 2.58 (1.14–5.82) | 0.02           | 3.30 (1.26–8.60) | 0.01           |
| P=0.02 for linear trend                    |                |                | P=0.009 for linear trend |

Adjusted for age, examination years, maximal oxygen uptake, alcohol consumption, cigarette smoking, serum LDL cholesterol, diabetes, and body mass index.  
*Percent maximum SBP at 2 minutes after exercise was defined as the ratio of SBP at 2 minutes’ rest and maximal SBP during exercise.  
†SBP rise was defined as average rise of SBP per minute of exercise test time.  
‡Adjusted for age, examination years, alcohol consumption, cigarette smoking, serum LDL cholesterol, diabetes, and body mass index.
Figure 2: The relationship between SBP rise and exercise capacity. The SBP rise is plotted against the exercise capacity of the subjects. The line represents the best fit for the data. The y-intercept is the expected SBP rise for a subject with an exercise capacity of 0. The x-intercept is the expected exercise capacity for a subject with an SBP rise of 0. The area under the curve represents the total SBP rise for all exercise capacities.

In conclusion, hypertension accelerates the atherosclerotic process in carotid and vertebral arteries, which usually starts in the larger extracerebral arteries, particularly in the carotid bifurcation. This process, with time, spreads distally to the smaller intracerebral arteries, leading to increased vascular resistance and hypertension during exercise and hence the increased risk of cardiovascular events. This mechanism may be the same for the development of stroke in men with high SBP during exercise. It is possible that the steep rise in exercise blood pressure produces poor arterial compliance. This causes a higher SBP rise in subjects with underlying arteriosclerotic disease or structural vascular changes and vice versa. With increasing age, blood vessels become less elastic, and peripheral vascular resistance also increases in older normotensive individuals, which may be one reason for the steep rise in SBP at physical stress compared with elevation of SBP at rest.

A possible limitation of the present study is that SBP recordings may be inaccurate at peak exercise. However, it is easier to measure SBP during a bicycle ergometer test than during a treadmill test because the arms are not at rest when subjects are walking on a treadmill. Another potential limitation is the use of indirect arm-cuff sphygmomanometry for the SBP measurements, although exercise stress testing and noninvasive SBP measurements reflect real-life practice. A feature concerning the study design was that we used 2 different protocols, and it appeared that exercise blood pressure was related strongly to the risk of stroke while a linear increase of 20 W/min was used without a warm-up period. Because of the small number of end points among those men who performed the exercise test with 3 minutes of warm-up at 50 W/min, we cannot objectively interpret the results in this group. On the other hand, our primary aim was to investigate the increase of SBP rise during standardized exercise testing and to predict the risk of stroke while using common protocols. Additionally, there is large individual variation in exercise capacity that may result in different SBP responses to exercise. This could be one of the reasons that maximum SBP during exercise did not have a predictive value. In fit persons, high SBP during exercise with long exercise duration may reflect their extensive cardiac output. Thus, SBP at a fixed workload depends on physical fitness and represents different levels within spans of the SBP rise in different individuals. Therefore, we adjusted for maximum oxygen uptake to minimize the confounding problems introduced by differences in exercise capacity between fit and unfit subjects.

Given our results, we can generalize our findings among subjects with no history of stroke or coronary heart disease and no use of medication for hypertension. Exercise SBP response may provide an additional tool to identify subjects at high risk for future stroke, and measures such as antihypertensive medication and physical exercise may be recommended as primary preventive measures to these high-exercise SBP responders. Furthermore, at the same time, it may be used as a screening tool to identify high-risk individuals for exercise hypertension and stroke among patients undergoing exercise stress testing in clinical practice. However, more clinical trials are needed before exercise SBP can be broadly recommended as an additional predictor for stroke.
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25. Kurl et al Exercise SBP Response and Stroke Risk 2041
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Stroke. 2001;32:2036-2041
doi: 10.1161/hs0901.095395

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