Clustering of coronary risk factors with increasing blood pressure at rest and during exercise
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Background The metabolic cardiovascular syndrome is the label given to the clustering of unfavourable levels of a number of coronary risk factors in subjects with high resting blood pressures. We found recently that exercise blood pressure had a strong independent prognostic value.

Objective To search for possible similar associations between exercise blood pressure levels and coronary risk factors by studying conventional and recently acknowledged coronary risk factors.

Methods The study population comprised 1999 healthy men aged 40–59 years. Age-adjusted coronary risk factor levels and their relation to resting and exercise blood pressures were studied. Resting blood pressure was measured after subjects had rested supine for 5 min. The exercise blood pressure used was the systolic blood pressure measured with the subject sitting on a bicycle ergometer at the end of a work load of 600 kpm/min (100 W) for 6 min.

Results Besides corroborating the relation between the metabolic syndrome and resting blood pressure levels, we observed similar or even stronger associations between levels of various coronary risk factors and exercise blood pressure. We found rather strong, direct associations between exercise blood pressure and total cholesterol level, fasting triglyceride level and body mass index whereas inverse relations were found for glucose tolerance, physical fitness, pulmonary functioning and the ability to increase heart rate during exercise. Virtually all these associations had a level of statistical significance of $P<0.001$.

Conclusions High exercise blood pressure levels are strongly associated with unfavourable levels of a number of important coronary risk factors. A similar metabolic syndrome to that observed in subjects with high resting blood pressures therefore appears to be present in subjects with high exercise blood pressure responses. These associations may considerably amplify the independent risk of high blood pressure responses to moderate exercise. J Hypertens 16:19–22 © 1998 Rapid Science Ltd.
from performing a symptom-limited bicycle exercise test, advanced pulmonary liver, renal and other chronic diseases or disorders were excluded. Further details about the selection procedures and exclusion criteria have been presented elsewhere [4,7,8]. Of 2341 eligible men, 2014 (86%) apparently healthy Caucasian men participated in the baseline study, of whom 15 were later excluded (see below).

Protocol

Their informed consent to participate in our study was obtained from all subjects. They were examined between 0730 and 1000 h after they had abainted from eating for at least 12 h and from smoking for at least 8 h. The baseline examination programme is summarized in Table 1. Forced expiratory volume in 1 s was measured with a spirometer. Cholesterol and triglyceride levels were determined by standardized methods [9]. As a measure of glucose tolerance, the rate of disappearance of glucose after intravenous injection of 50 ml 50% glucose (K value expressed in percentage per min) was used [10].

The blood pressure measurements were performed after familiarization of subjects with the laboratory, using a mercury sphygmomanometer for subjects both at rest and during exercise. Blood pressure at rest was taken after subjects had lain supine for 5 min in a quiet room with an ambient temperature in the range 20–25 °C; it was measured three times, always by the same physician. Korotkoff phase V was used to establish diastolic blood pressure. There was a systematic fall in blood pressure on going from the first to the second recording and then on average a small rise in blood pressure (< 1 mmHg) on going from the second to the third recording. We therefore decided to use the second reading (the most baseline recording).

Resting heart rate was measured for exactly 1 min with a stopwatch prior to measuring the blood pressure. Maximal heart rates were taken from the exercise electrocardiograms, excluding ectopic rhythms for some few subjects.

All subjects performed symptom-limited exercise on an electrically braked bicycle [11]. The initial work load of this test was 600 kpm/min (=100 W, 5880 J/min) and lasted for 6 min. Systolic blood pressure was measured every second minute. The peak systolic blood pressure under this work load, for almost all subjects the third recording, was used for further scrutiny. Increments in work load were thereafter made in steps of 300 kpm/min (=50 W) every 6 min. All subjects were encouraged to continue exercising until exhaustion; however, we adhered to common safeguards for terminating the test [4,11]. Also the maximum systolic blood pressure was recorded for further scrutiny but was not related to clinical outcome measures [2,3]. A final measurement was always performed just prior to termination of the test. The total work performed (working capacity) was the sum of the work done on each of the loads [4]. Maximal work load tolerated was defined as the highest work load tolerated for ≈ 1 min. Physical fitness was defined as working capacity divided by body weight.

This method for exercise testing has a high reproducibility, as previously reported [2–4]. The decision to use 600 kpm/min as the starting load was based on a presurvey pilot study with 80 middle-aged volunteers, all of whom were easily able to exercise under this load for 6 min. However, in the main study 15 men proved unable to exercise for 6 min under the initial load. The 1999 men for whom data were included were all able to continue under the 900 kpm/min load; 600 kpm/min proved on average to represent approximately 55% of the mean maximal work load tolerated for ≈ 1 min.

Statistical analysis

The statistical significance of the relation between a variable (e.g. physical fitness) and blood pressure, adjusted for age, was calculated by using multivariate linear regression analysis. This method was also used to calculate age-adjusted means in the various blood pressure intervals. The correlation between two continuous variables was assessed by Spearman’s correlation method.

Results

Serum cholesterol level (r = 0.14, r = 0.16), serum triglyceride level (r = 0.19, r = 0.17) and body mass index (r = 0.19, r = 0.10) increased, whereas glucose tolerance (r = –0.25, r = –0.18), physical fitness (r = –0.24, r = –0.40) and response of heart rate to exercise (r = –0.22, r = –0.20) decreased with higher blood pressure at rest (Table 2) and during exercise (Table 3), respectively. These six relationships were statistically highly significant and fairly comparable for blood pressure at rest and during exercise (P < 0.001 for all) except for P = 0.011 for the relationship between serum cholesterol level and blood pressure at rest and P = 0.014 for the relationship between glucose tolerance and exercise blood pressure.

A high exercise blood pressure was associated with lower pulmonary functioning (r = –0.20, P < 0.001). The association between resting blood pressure and pulmonary functioning was not statistically significant (r = –0.06, P = 0.14). The fractions of subjects who were smokers decreased with higher levels of blood pressure at rest.

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**Table 1 Baseline examination programme**

<table>
<thead>
<tr>
<th>Comprehensive case history</th>
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<tr>
<td>Physical examination</td>
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<td>Measurements of blood pressure and heart rate in subjects at rest</td>
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<td>Routine blood tests including determinations of serum cholesterol and triglyceride levels</td>
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<td>Intravenous glucose-tolerance test</td>
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<td>Assessment of pulmonary function</td>
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<td>Electrocardiography</td>
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<td>Electrocardiographically monitored symptom-limited bicycle exercise test</td>
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(P = 0.008) but was not significantly related to levels of exercise blood pressure (P = 0.47). Blood pressure at rest increased with increasing exercise blood pressure (r = 0.61, P < 0.001). The accumulation of risk factors was not strengthened by combining certain levels of blood pressure at rest and during exercise (data not shown).

**Discussion**

Besides corroborating the relation of the cardiovascular metabolic syndrome to resting blood pressure levels, we have observed similar or even stronger associations between levels of various coronary risk factors and exercise blood pressure. We found direct associations between exercise blood pressure and total cholesterol level, fasting triglyceride level, body mass index and glucose pressure at rest, whereas inverse relations were found for glucose tolerance, physical fitness, pulmonary functioning and the ability to increase heart rate during exercise. Combining resting and exercise blood pressure levels did not alter or strengthen these associations.

Whereas it is well known that, at a certain high level of resting blood pressure, there is also an accumulation of other risk factors that may multiply the individual risk [1], our finding that this also applies to exercise blood pressure is novel. In fact, serum cholesterol level, serum triglyceride level, body mass index and glucose tolerance, the constituents of the metabolic cardiovascular syndrome, all relate to exercise blood pressure in an identical way to that of blood pressure at rest. Furthermore, our finding that more recently acknowledged rather strong risk factors such as physical fitness [4], pulmonary functioning [5] and the maximal response of heart rate to exercise [6] relate to blood pressure, both at rest and during exercise, in a similar manner is also novel.

Maximal work capacity, as defined in the present study, has been shown to be highly correlated to maximal oxygen uptake [12], indicating that our measure of physical fitness is closely related to this most accepted measure of physical fitness. Systolic blood pressure increases during exercise as a function of work load. Since maximal working capacity varies among individuals, choosing 600 kpm/min to measure blood pressure means that individuals necessarily will be working at different percentages of their maximal capacity. Low fitness should therefore result in a relatively greater response of blood pressure to this load compared with the response of fitter subjects. In fact, measuring systolic blood pressure at 600 kpm/min could thus be an indirect way of assessing...
fitness without performing a maximal exercise test. This is borne out by the strong association between physical fitness and systolic blood pressure during exercise at 600 kpm/min. We could even see that a large seasonal variation in exercise systolic blood pressure is dependent on the seasonal variation in physical fitness [13].

Thus a high exercise blood pressure under the 600 kpm/min load could represent low physical fitness, although the two variables both carry independent prognostic information [2–4]; hence other parameters that are linked to physical fitness may be correlated to other coronary risk factors, too. However, the existence of a correlation does not necessarily mean that a causal relationship is operating.

Both difference in heart rate and maximal exercise-induced heart rate were strong, graded and independent long-term predictors of cardiovascular mortality among the present healthy middle-aged men [6]. However, a low difference in heart rate between maximal exercise and resting conditions was a better predictor than was a low maximal exercise-induced heart rate for recognizing individuals who had a particularly high risk of dying prematurely from cardiovascular diseases [6].

We found recently that smoking is a rather strong predictor for the 7-year rise in exercise blood pressure in the present cohort of men [14]. A possible explanation is offered by the well-known atherogenic effect of smoking and thereby stiffening of the arterial system [15]. Interestingly, as recently reviewed by Omvik [16] and corroborated in the present cross-sectional analysis, there is a lower percentage of smokers with higher blood pressure at rest. A possible explanation for this apparently paradoxical finding is selection bias. Conceivably, hypertensive middle-aged smokers more rarely could be characterized as ‘apparently healthy’ at the outset of the study, so it can be speculated that the combination of hypertension and smoking might lead to early cardiovascular disease at the time when they were supposed to be recruited to the study.

We cannot easily explain why a high exercise blood pressure is inversely related to pulmonary functioning, although this might also be related to the smoking habits. Thus spirometric results from the same cohort suggest that smoking exerts a negative effect on pulmonary functioning [5].

Previously we have shown that the peak systolic blood pressure after 6 min of 600 kpm/min bicycle exercise is an independent risk factor for the total cardiovascular mortality [2] and mortality caused by myocardial infarction [3] among our 1999 apparently healthy men during a mean follow-up of 16 years. By applying the Cox regression model to correct for possible influences, we demonstrated that those results [2,3] could not be explained in terms of differences in any other variable measured in the present study. Consequently, we suggested that exercise at this level unmasks a more severe form of hypertension. The present observed accumulation of cardiovascular and coronary risk found in the present survey can be added to the independent risk of high exercise blood pressure (i.e. our present data reveal an increase in the cardiovascular and coronary risk that is associated with increasing exercise blood pressure).

In summary, we find that high exercise blood pressure levels are rather strongly associated with unfavourable levels of a number of important coronary risk factors. A cardiovascular metabolic syndrome similar to that observed in subjects with high resting blood pressure therefore appears to be present in subjects with a high exercise blood pressure. This finding might considerably amplify the independent risk of high blood pressure responses to moderate exercise.

References