The Cardiovascular Effects of Upper-Limb Aerobic Exercise in Hypertensive Patients

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**Background:** Aerobic exercise is broadly recommended as a helpful adjunct to obtain blood pressure control in hypertension. Several hypertensive patients, however, are limited by musculoskeletal complaints or vascular occlusive disease from lower-limb exercise such as jogging or cycling. In the present randomized-controlled study, we evaluate whether an aerobic arm-cycling program provides a measurable cardiovascular benefit.

**Methods:** Twenty-four probands were randomly assigned to sedentary activity or a heart rate controlled 12 week exercise program, consisting of arm-cycling at target lactate concentrations of 2.0 ± 0.5 mmol/l. Endothelial function was assessed by flow-mediated dilation of the brachial artery. Augmentation index and large/small artery compliance ($C_1$ and $C_2$) were measured by computerized pulse-wave analysis of the radial artery.

**Results:** The exercise program led to a significant reduction in systolic (134.0 ± 20.0 to 127.0 ± 16.4 mmHg; $P = 0.03$) and diastolic blood pressure (73.0 ± 21.6 to 67.1 ± 8.2 mmHg; $P = 0.02$) accompanied by a significant improvement in $C_2$ (3.5 ± 1.6 to 4.8 ± 2.0 ml/mmHg T 100; $P = 0.004$). Flow-mediated dilation, augmentation index, and $C_1$ were not significantly affected ($P > 0.05$). Physical performance as derived from lactate and heart rate curves of lower-limb stress tests was unchanged, whereas maximal workload in an upper-limb ergometry significantly increased ($P = 0.005$). Blood pressure and vascular parameters remained unchanged in the control group.

**Conclusion:** Regular arm aerobic exercise leads to a marked reduction in systolic and diastolic blood pressures and an improvement in small artery compliance. Arm-cycling is a reasonable option for hypertensive patients who want to support blood pressure control by sports despite having coxarthrosis, gonarthrosis, or intermittent claudication.


Keywords: arm, arterial compliance, endothelial function, exercise, hypertension.

Abbreviations: AI, Augmentation index; BP, Blood pressure; C, Large artery compliance; C*, Small artery compliance; FMD, Flow-mediated dilation

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Introduction

Aerobic physical exercise is broadly recommended by current European and American hypertension guidelines [1–3]. It is preferably used in mild hypertension or as a useful adjunct to drug treatment. Hypertensive patients are encouraged to ‘engage in aerobic exercise on a regular basis, such as walking, jogging or swimming for 30–45 min, three to four times a week’ [1]. Although cardiovascular training can induce approximately 3–4 mmHg reduction in systolic and diastolic blood pressure (BP) reductions in normotensive individuals, the reduction in BP is even more pronounced in hypertensive patients [4]. Shear stress — as induced by physical exercise — is a potent stimulus on endothelial cells for an increase in nitric oxide production, leading to improved endothelial function and reduced vascular resistance [5].

With regard to the problem of advanced arteriosclerotic wall changes, comorbidities and limited physical fitness scepticism were expressed whether elderly hypertensive patients still achieve relevant changes in BP and vasomotor function. Recently, however, we have shown that aerobic exercise leads to a significant reduction in BP and an improvement in arterial vasodilatory capacity in elderly hypertensive patients as well [6]. The extent of the reduction in BP is independent of pulse pressure as a footprint of vascular ageing [6]. Thus, even old hypertensive patients with isolated systolic hypertension show a benefit from exercise with a marked reduction in 24-h ambulatory and office BP. In the course of life, however, musculoskeletal complaints and peripheral vascular occlusive disease may increasingly prevent elderly people from lower-limb exercises such as walking, jogging, or cycling. Coxarthrosis, gonarthrosis, and intermittent claudication constitute the most frequent physical reasons that rule out lower-limb exercise on a regular basis in older people. The upper limb is significantly less affected by both arthrosis and vascular occlusive disease. Owing to lower muscle mass, the workload achievable by upper-limb exercise is lower than that by lower-limb exercise. Therefore, it remains elusive whether aerobic arm exercise is able to evoke measurable effects on BP and arterial function.

The present work examines the cardiovascular effects of a 12-week upper-limb aerobic exercise training. It sheds light on the exercise-induced changes in BP and vasomotor function.

Methods

Study population

Patients were recruited from the hypertension outpatient clinic of our university hospital and by press announcement. Inclusion criteria were systolic BP of at least 140 mmHg and/or current antihypertensive treatment. Prior to the exercise program, cardiac function was examined by ECG at rest and under exertion. Exclusion criteria were continuous engagement in physical exercise training for more than 60 min a week in the past 12 weeks prior to inclusion in the study, known aortic insufficiency or stenosis higher than stage 1, hypertrophic obstructive cardiomyopathy (HOCM), congestive heart failure (higher than NYHA II), uncontrolled cardiac arrhythmia with hemodynamic relevance, systolic office BP of 180 mmHg or higher, signs of acute ischemia in exercise ECG, and change of antihypertensive medication in the past 6 weeks prior to inclusion or during follow-up period. Further indication of hypertension-associated target-organ damage was not regarded as exclusion criteria. According to these criteria, 24 patients (13 women, 11 men) were enrolled to the study. Patients’ characteristics including concomitant diseases are presented in Table 1. The preexisting antihypertensive medication remained unchanged throughout the study. Written informed consent was obtained from all participants prior to inclusion in the study. The study was approved by the local ethics committee at the Charité Berlin.

Protocol

Table 1 Patients’ characteristics (number of antihypertensive drugs presented as median and range, age and BMI presented as mean W ± SD)

<table>
<thead>
<tr>
<th>Concomitant diseases</th>
<th>Training (n=12)</th>
<th>Control (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>1 (8.3%)</td>
<td>1 (8.3%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>6 (50.0%)</td>
<td>4 (33.3%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>1 (8.3%)</td>
<td>2 (16.6%)</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>1 (8.3%)</td>
<td>1 (8.3%)</td>
</tr>
</tbody>
</table>

Upper-limb and lower-limb ergometries, office BP measurements, assessment of endothelial function, and measurement of augmentation index were performed before and after the observation period. Assessment of physical performance was carried out by a lower-limb bike stress test, as maximal workload in an arm-cycling stress test is too low to reflect maximal physical performance. The test was started with 25 W and increased in 25-W intervals every 3 min until exhaustion. Heart rate and arterial BP were assessed during each workload, lactate concentration in capillary blood was determined at the end of each workload, and lactate thresholds were determined according to Kindermann et al. [7]. A second stress test was carried out at baseline and follow-up with the arm-cycling device in order to determine training...
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intensity and measure maximal upper-limb workload. The test was started with a resistance of 12.5 W and a cycling frequency of 80–90 cycles/min. The workload was increased by 12.5 W every 3 min until exhaustion. Lactate concentration, arterial BP, and heart rate were evaluated at the beginning and the end of each workload.

The training program consisted of upper-limb cycling with an arm-cycling device (MOTOMed viva2; Reck- Technik, Betzenweiler, Germany). Sessions were designed according to an interval-training pattern and were carried out three times every week for 12 weeks. If patients missed a training session, the program was prolonged until they absolved 36 workouts. The initial duration of training sessions was 30 min. During the first week, training consisted of 15 workloads of 1 min; between workloads patients rested for 1 min. Exercise duration was gradually increased to 10 x 2 min per day in the second week, 8 x 3 min in the third and fourth, 3 x 6 min in the fifth and sixth, 2 x 12 min in the seventh and eighth, 2 x 15 min in the ninth and 10th, and 30 min without interruption in the 11th and 12th week. Training intensity corresponded to the workload necessary to reach a lactate concentration of 2.0 ± 0.5 mmol/l in capillary blood while maintaining a cycling rate of between 80 and 90 cycles/min. Heart rate during training was controlled by a heart rate monitor (Polar Sport Tester; Polar Electro OY, Kempele, Finland); BP was measured every 10 min with the probe still cycling; and lactate concentration was controlled every third training day. As lactate concentration sank below 1.5 mmol/l or increased beyond 2.5 mmol/l, resistance was modified until target levels were reached. During training sessions, patients were continuously supervised by study personnel. Patients in the control group did not participate in the exercise program.

Assessment of small and large artery compliance by pulse-wave analysis

All measurements were conducted in a quiet clinical research laboratory at a constant ambient temperature of 20–22°C as published previously [8, 9]. In pretests, reproducibility of results was assessed by calculation of reliability scores from nine measurements (three measurements per day on three consecutive days) in 10 patients. Shrout – Fleiss reliability scores were 0.97 (C1) and 0.98 (C2), indicating a high degree of reproducibility. All measurements were performed by the same person. Patients were resting in a supine position for 10 min. Systolic BP, diastolic BP, and heart rate were measured oscillographically. Arterial elasticity was assessed using computerized radial artery pulse wave analysis by means of the CR-2000 instrument (Hypertension Diagnostics, Eagan, Minnesota, USA). Radial artery waveforms were recorded for 30 s with an arterial tonometer sensor. Data was digitized at 200 samples/s. The beginning of systole, peak systole, onset of diastole, and end diastole for all pulse waves in a 30-s period were determined. After averaging the pulse waves of the analysis period, an algorithm developed by Cohn et al. [10] (Hypertension Diagnostics) was applied to define a third-order equation approximating the waveform and diastolic decay. According to a modified Windkessel model, pulse contour analysis of the diastolic pressure decay allows an estimation of ‘oscillatory’ small artery and ‘capacitive’ large artery elasticity (C1 and C2) [10]. The model uses an estimated cardiac output, which is a multivariate function of ejection time, heart rate, body surface area, and age and can be determined from the arterial pressure waveform, as validated by previous invasive and noninvasive studies [10]. Three measurements were performed and the mean value was used for statistical evaluation.

Assessment of endothelial function by flow-mediated dilation

Endothelial function was assessed in the brachial artery as published previously [6, 8, 9, 11, 12]. By means of high-resolution ultrasound, diameter changes in response to reactive hyperemia [flow-mediated dilation (FMD)] were measured, according to standard protocols [13]. Accuracy and reproducibility of the method had been documented previously. Flow-mediated vasodilation in response to reactive hyperemia (FMD) represents endothelium-dependent vasoreactivity. We had to refrain from assessing vasodilation in response to glyceroltrinitrate as a measure of endothelium-independent vasodilation, as application of glyceroltrinitrate was not covered by ethical approval.

The brachial artery was examined by two-dimensional ultrasound images, with a 10-MHz linear array transducer and a standard 128XP/10c-system (Acuson, Mountain View, California, USA). Artery diameters were measured by a computerized edge detection program (Cardiovascular Imagin Software; Information-Integrity, Boston, Massachusetts, USA); the images were acquired ECG-triggered at end-diastole. A resting scan was recorded for 2 min. A pneumatic tourniquet, placed distal to the elbow of the subject’s arm, was then inflated to a pressure of 300 mmHg for 3 min. The release immediately induces increased blood flow in the subject’s forearm for a few seconds, which represents the stimulus for endothelium-dependent vasodilation. The same experienced person performed all of the scans. The computer-assisted calculation of vessel diameters was conducted in a blinded fashion as published previously [9]. FMD represents the percentage of diameter increase caused by shear stress compared with baseline.

Assessment of arterial elasticity by augmentation index

The augmentation index is a well established measure of arterial elasticity. Augmentation index, systolic BP, diastolic BP, and heart rate were measured by the HEM-9000AI device (Omron Healthcare, Bannockburn, Illinois, USA) as published...
previously [11]. Augmentation index was assessed by computerized radial artery pulse-wave analysis. The HEM-9000AI device makes use of a multisensor array technology to detect pulse waves by applanation tonometry. The augmentation index was calculated as the difference between the first and second systolic peaks of the pulse wave. As augmentation index depends on heart rate, the device offers a software tool that adjusts augmentation index to a heart rate of 75 beats/min (augmentation index75). Three measurements were performed and mean values for BP and augmentation index were used for statistical evaluation.

**Statistical analysis**

Results are presented as mean ± SD. Pretest reliability of small and large artery measurements was estimated by calculation of Shrout – Fleiss scores. The correlation of the decrease in systolic/diastolic BP and the increase of C2 was tested by linear regression analysis. Comparison of systolic BP, diastolic BP, heart rate, FMD, C1, C2, augmentation index, augmentation index75, and maximal arm workload at baseline was performed using the Mann – Whitney U-test. Changes in parameters within each group were compared using the Wilcoxon test for paired samples. P-value less than 0.05 was regarded to be statistically significant.

**Sample size estimation**

Based on our previous studies on sports in hypertension [6, 14], we expected the intervention to result in a decrease of at least 9 mmHg in systolic BP in the training group with no changes in the control group. This difference was considered to be clinically relevant. A sample size of 12 in each group has 80% power to detect a difference in means of 9 mmHg assuming that the common standard deviation is 10 mmHg, a baseline systolic ABP of 135 mmHg and a two-sided P less than 0.05.

**Results**

At baseline, exercise and control groups showed no significant differences in age (P = 0.51), BMI (P = 0.29), systolic BP (P = 0.44), diastolic BP (P = 0.27), heart rate (P = 0.54), large artery compliance (P = 0.80), small artery compliance (P = 0.51), endothelium-dependent vasodilation (P = 0.25), augmentation index (P = 0.84), augmentation index75 (P = 0.84), and maximal arm workload level (P = 0.98). All the patients in exercise and control group completed the study. The training was well tolerated by all the patients in the exercise group. At the follow-up examination, all the patients of both exercise and control group stated that there was no change of drug prescription and drug intake compliance in the course of the study.

In the lower-limb ergometry, there were no significant changes in heart rate and lactate from baseline to follow-up at each workload in both exercise and control group (Fig. 1). Thus, physical performance remained unchanged in the lower-limb exercise test. In the upper-limb ergometry, maximal workload was higher after the training period (Table 2). This change was highly significant. In the control group, maximal workload was even significantly lower at follow-up compared with baseline (Table 2).

**Fig. 1**

Heart rate and lactate curves from lower-limb cycling stress tests at baseline and follow-up in exercise and control groups. Data are presented as mean ± SD.
Table 2 presents systolic and diastolic BP data, heart rate, augmentation index, small and large artery compliance, endothelium-dependent vasodilation, and maximal workload level in the upper-limb ergometry in training and control group before and after the observation period. Systolic and diastolic BPs were significantly reduced in the exercise group, whereas they remained unchanged in the control group (Fig. 2). There were no significant changes in heart rate at rest, augmentation index, adjusted augmentation index (augmentation index\(_{75}\)), and large artery compliance in both exercise and control group (Table 2). Small artery compliance, however, improved highly significantly in the exercise group, whereas a slight increase in small artery compliance in the control group failed to be significant. The amount of decrease in systolic and diastolic BPs did not correlate with the increase in C2 in the exercise group in an linear regression analysis (R\(^2\) 0.03 and 0.02, respectively). Endothelium-dependent vasodilation only slightly improved in the exercise group, changes largely failed to be significant. There was no change in endothelium-dependent vasodilation in the control group (Table 2).

### Table 2 Systolic and diastolic blood pressures, vascular function and maximal workload in upper-limb ergometry in exercise and control groups

<table>
<thead>
<tr>
<th></th>
<th>Exercise group [n=12]</th>
<th>Control group [n=12]</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>134.0 ± 20.0</td>
<td>127.0 ± 16.4</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>73.0 ± 21.6</td>
<td>77.1 ± 8.2</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>66.7 ± 9.1</td>
<td>65.5 ± 8.8</td>
</tr>
<tr>
<td>Augmentation index (%)</td>
<td>86.6 ± 9.2</td>
<td>84.5 ± 14.5</td>
</tr>
<tr>
<td>Augmentation index(_{75}) (%)</td>
<td>81.1 ± 7.2</td>
<td>80.4 ± 12.5</td>
</tr>
<tr>
<td>Large artery compliance (ml/mmHg x 10)</td>
<td>15.5 ± 6.6</td>
<td>13.8 ± 3.5</td>
</tr>
<tr>
<td>Small artery compliance (ml/mmHg x 100)</td>
<td>3.5 ± 1.6</td>
<td>4.8 ± 2.0</td>
</tr>
<tr>
<td>Endothelium-dependent vasodilation (%)</td>
<td>3.5 ± 1.7</td>
<td>3.8 ± 1.4</td>
</tr>
<tr>
<td>Maximal workload in upper-limb ergometry (workload level)</td>
<td>7.8 ± 2.8</td>
<td>9.4 ± 3.2</td>
</tr>
</tbody>
</table>

In the ergometry, a cycle frequency of 80 cycles/min at workload ‘1’ corresponds to 12.5 W, a workload of ‘2’ to 25 W, and so on. Δ denotes the change in parameter in the observation period, data presented as mean ± SD, P<0.05 was regarded significant.

**Fig.1**

Systolic and diastolic blood pressures (BPs) at baseline and follow-up in exercise and control groups. *P<0.05 was regarded significant.
Discussion

This is the first randomized controlled trial on the cardiovascular effects of aerobic upper-limb nonisometric exercise in hypertensive. We show that upper-limb endurance exercise on a regular basis leads to a significant reduction in systolic and diastolic BPs in elderly hypertensive patients. The extent of the BP reduction (7 mmHg systolic, 6 mmHg diastolic) is of clinical relevance.

Musculoskeletal complaints and vascular occlusive disease frequently prevent elderly people from engaging in sports. Coxarthrosis, gonarthrosis, and intermittent claudication constitute the most frequent problems. In order to establish a representative study population, we examined elderly hypertensive patients with a mean age of 66 years in the exercise group and 68 years in the control group.

There is a broad variety of mechanisms that have been proposed to mediate the exercise-induced reduction in BP. Most of these mechanisms lead to the common final pathways of increased arterial compliance and/or an improvement in endothelial function [5]. The increase in cardiac output and peripheral blood flow during physical activity results in an induction of arterial shear stress, which is a crucial prerequisite for the reduction in BP. The muscle mass of the upper limb, however, is lower than that of the lower limb. Hence, the workload achievable by upper-limb exercise is considerably lower than that achievable by lower-limb exercise. Our results indicate that the increased cardiac output during upper-limb endurance training is indeed a sufficient stimulus for a significant reduction in systolic and diastolic BPs. The findings on the changes of vascular properties reveal a significant increase in the small oscillatory artery compliance. Further markers of arterial stiffness such as large artery compliance and augmentation index were not affected by the exercise program. In contrast to our previous works on the vascular effects of exercise in the elderly, there was only a slight trend, but no significant improvement in endothelial function [6, 14]. The reasons for the lack of improvement in endothelial function remain speculative. On the one hand, the size of the study population might have been too small to reach statistical significance. On the other hand, it is possible that the workload of arm exercise was too low to lead to a relevant induction of nitric oxide production. In the latter case, the underlying mechanism may differ from the vascular changes after lower-limb exercise. Interestingly, physical performance in lower-limb ergometry did not improve as evidenced by both lactate and heart rate curves, whereas maximal workload in the upper-limb ergometry significantly improved after the training program. Although the maximal workload in the upper-limb ergometry may be regarded as a marker of increasing muscular mass, the lower-limb ergometry rather provides a measure of cardiovascular performance, as the muscle mass of the legs is proposed to remain constant.

The present findings show that regular upper extremity aerobic endurance training leads to a marked reduction in systolic and diastolic BPs accompanied by an improvement in oscillatory artery compliance. Arm-cycling may be regarded as a reasonable alternative for hypertensive patients who want to support BP control by sports, despite having coxarthrosis, gonarthrosis, or vascular occlusive disease.
Acknowledgements

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There are no conflicts of interest.

References