Blood Pressure in Patients with Intermittent Claudication Increases Continuously During Walking

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Objectives. The purpose of this study was to compare the circulatory responses to walking in patients with peripheral atherosclerotic disease (PAD) and healthy controls.

Methods. The participants were eleven patients with diagnosed PAD, and a control group of six healthy age-matched adults. Blood pressure, heart rate (HR), and acral skin perfusion were recorded continuously before, during and after a walking exercise on a treadmill.

Results. The patients walked to maximum claudication distance (MCD) on a treadmill, median walking distance 103 (34–223) metres [median (range)], at 3.3 (1.0–4.5) km/h. There was a steep increase in HR and mean arterial pressure (MAP) while the patients were walking. At claudication the median rise in MAP was 46.6 (10.3–61.3) mmHg, systolic blood pressure (SP) increased by 84.9 (31.4–124.9) mmHg, and diastolic blood pressure (DP) by 21.7 (–0.1–31.7) mmHg. HR increased by 34.9 (12.9–48.1) beats/min. The control group walked for 5 minutes at 3.2 (3.0–3.3) km/h. In the control group the blood pressure initially increased moderately but stabilised thereafter. Median rise in MAP during walking was 8.5 (5.6–14.6) mmHg, SP increased by 30.9 (6.6–41.5) mmHg, and DP was reduced by 1.4 (–5.4–1.5) mmHg. HR increased by 27.1 (18.8–34.9) beats/min. We found no significant differences in acral skin perfusion during walking exercise between the patients and control group.

Conclusions. In patients with PAD, blood pressure increased continuously and significantly when walking to MCD (dynamic exercise). The level of increase in blood pressure was similar to that caused in response to isometric exercise.

Keywords: Intermittent claudication; Peripheral vascular disease; Exercise; Blood pressure.

Introduction

The cardiovascular response to isometric exercise has been studied extensively since first described by Lindhard in 1920. There is a gradual increase in systolic (SP), diastolic- (DP) as well as mean arterial pressure (MAP) until exhaustion occurs. The absolute increase in MAP is related to the strength of the contraction, and probably also to the size of muscle mass involved. The current view is that the blood pressure set point is continuously regulated upwards as long as the isometric exercise persists. The mechanism leading to the continuous up-regulation of blood pressure during isometric exercise is still not completely elucidated, but it is clear that signals arising from the working, and progressively more hypoxic, muscle play a major role.

Several studies have confirmed the considerable flexibility of cardiovascular control mechanisms in maintaining an appropriate arterial pressure. Haskell et al. found that heart transplant patients had the same pressor response as healthy controls, despite their denervated hearts. It also has been shown that precise blood pressure regulation is maintained during changes in central venous pressure.

The blood pressure response to dynamic exercise in healthy subjects is different from the one observed during isometric exercise. During dynamic exercise SP is usually moderately increased, DP falls or is unchanged, resulting in minor changes in MAP, as indicated in Fig. 1.

Today, patients with intermittent claudication (IC) are advised by physicians to keep walking until they are forced to stop because of pain. This type of exercise often results in symptom relief over time. The patients are informed that, in contrast to angina, it is
not dangerous to keep walking when one has pain in the leg. However, the accompanying cardiovascular responses are largely unknown.

The systemic cardiovascular response to exercise depends on whether the muscle contractions are mainly isometric or dynamic during the performance of an external workload. In another study we have shown that patients with PAD have an identical pressor response to isometric exercise as healthy subjects.18

Hypoxia in the working muscle is the main stimulus to blood pressure increases during isometric exercise.19–21 During walking, PAD patients experience pain in the legs induced by insufficient blood supply and hypoxia in the working muscles. Therefore it is reasonable to assume that walking with pain, due to hypoxia, release a pressor response similar to that observed during isometric exercise.

The hypothesis in the present study was that patients with PAD exhibit a similar pressor response during dynamic exercise and isometric exercise.

**Methods**

**Subjects**

Five female and six male patients participated [age 60.5 (56–84) years, [median (range)], height 168 (154–183) cm, weight 72 (52–90) kg]. All subjects had symptoms of IC and an ankle-brachial-index (ABI) < 0.8 [0.5 (0.3–0.8)] at rest. All were active smokers or had recently stopped smoking. Subjects undergoing anti-hypertensive medical treatment and patients with heart disease or orthostatic hypotension were not included in the study.

Six healthy subjects participated as a control, two females and four males [age 60.5 (58–65) years, height 178 (158–188) cm, weight 79 (58–89) kg]. No control subjects used any medications, they had normal blood pressure (blood pressure <140/90 mmHg), and had an ABI ≥ 1.0. All were non-smokers, although two had previously smoked.

Before participating in the study, all subjects underwent a physical examination. They were instructed not to drink coffee or tea, and not to exercise or eat for at least 2 h before the start of the experiment. Written informed consent was obtained from all participants, and the study was approved by the regional ethics committee.

**Measurements**

Recordings started with the patient standing motionless for 1 minute before starting to walk on a treadmill. The patient was instructed to indicate when pain occurred (Intermittent Claudication Distance (ICD)), and when pain forced them to stop (Maximum Claudication Distance (MCD)). At MCD, the patient immediately sat down on a chair without further movement. Recordings continued for three minutes while the patient was sitting. Treadmill speed varied between 1.0 and 4.5 km/h [3.3 (1.0–4.5) km/h], which corresponded to a slow to moderate walking speed. Each subject was tested four times on the treadmill, with 5 minutes rest between consecutive runs.

In the control group, the participants were asked to stand motionless for one minute on the treadmill, followed by walking for five minutes. After walking, the subjects immediately sat down for two minutes. Treadmill speed was set at 3.2 (3.0–3.3) km/h, and treadmill elevation was 4°. The controls also were tested four times.

Instantaneous HR measurements were obtained from the duration of each R-R interval of an ECG signal. A bandage strapped around the chest fixed...
the ECG probes and efficiently reduced signal noise. Laser doppler (Periflux PF 4000, Perimed AB, Sweden) was used to measure acral skin blood perfusion (ASBP) in the pulp of the left second finger. The laser doppler probes were attached to the skin with double-sided adhesive tape. The sampling frequency was 2 Hz. Finger arterial pressure was continuously acquired by a photoplethysmographic pressure recording device (Finometer, FMS Finapres Measurement Systems, Arnhem, Netherlands). The patient’s left arm was held on the chest by a ‘collar and cuff’ sling, and care was taken to ensure that the finger was at heart level. The instantaneous pressure output was transferred online to the recording computer where beat-to-beat MAP was calculated by numerical integration. The Finometer device has been shown to satisfy the validation criteria of the Association for the Advancement of Medical Instrumentation (AAMI), and it has therefore been recommended for measurements in the clinical set-up and for research purposes.22,23 Before starting, systolic blood pressure was measured with Finapres and was compared and calibrated with blood pressure measured in the brachial artery using doppler ultrasound. For ethical reasons we did not use invasive methods.

**Data analysis**

For data storage and analysis we used Regist3 software (developed by M. Eriksen, Norway). HR was acquired beat to beat from the ECG R waves. MAP was calculated for every heartbeat. For analyses the recorded variables were converted into a 2-Hz sampled signal by interpolation. Throughout the recording period, there was considerable beat-to-beat variation in the recorded variables. This variation has been reported by others and is partly due to the influence of respiration. Variations in the recorded variables not related to the pressor response were partly eliminated by calculating the average response from four identical runs for every test subject. This was done using the coherent averaging technique.27 Walking time, speed, and maximum claudication distance, varied for each test subject and between different subjects. To be able to compare the results, we therefore normalized our findings to a relative time axis. T = 0 represented time when subjects started walking. T = 100 represented the time when the patients had to stop walking due to claudication pain (MCD). Finally, the individual average curves from all subjects in each group were pooled and used to calculate the mean value in each set of synchronous samples for each 2-Hz time step. All calculations were performed in Microsoft Excel 2000.

**Statistical analysis**

The results are presented as medians (range). Mann-Whitney U test was used to test for significant differences between the patients and controls, and Bonferroni correction to correct for multiple comparisons. Differences were considered significant at p < 0.05. The statistical analyses were performed using the statistical program SPSS 12.0.

**Results**

**PAD patient group**

Median walking distance on the treadmill was 103 (34–223) metres, with median speed of 3.3 (1.0–4.5) km/h. The patients walked for a median of 134 (65–212) seconds. During the one-minute rest period prior to walking, the median blood pressure was 144.0/74.7 (104.1–167.4/46.2–104.3) mmHg [Systolic blood pressure/diastolic blood pressure] and MAP 99.8 (65.6–123.5) mmHg. Resting heart rate was 89.3 (74.9–105.6) beats/min. Laser doppler acral skin blood perfusion was 1400 (251–3182) arbitrary units. Immediately after they started to walk, blood pressure increased steeply for a few seconds, amounting to a 13.8 mmHg rise in MAP (Fig. 2). This

![Fig. 2. Scatter-plot of systolic (light grey) and diascolic (dark grey) blood pressure for all patients against a relative time axis in arbitrary units (AU). T = 0 represents the time when subjects started walking. T = 100 represents the time when the patients had to stop walking due to claudication pain (MCD). Finally, the individual average curves from all subjects in each group were pooled and used to calculate the mean value in each set of synchronous samples for each 2-Hz time step. All calculations were performed in Microsoft Excel 2000.](image)
corresponds to the “startle response”, change activated by psychic stimuli. After the startle response there was a relatively steep increase in HR and MAP while the patient was walking. When the MCD was reached, the median rise in MAP was 46.6 (10.3–61.3) mmHg, systolic blood pressure increased by 84.9 (31.4–124.9) mmHg, and diastolic blood pressure by 21.7 (2.1–31.7) mmHg. We also recorded some values of SP exceeding 300 mmHg. HR increased by 34.9 (12.9–48.1) beats/min. We found no significant change in ASBP when claudication started compared to being at rest. After the patients stopped walking, there was an immediate steep drop in blood pressure towards pre-exercise level. There was also a drop in HR, but the decrease was more gradual, levelling at pre-exercising level after approximately 3 minutes of rest.

The patients were instructed to indicate when they experienced pain during walking (ICD), and when they needed to stop walking due to pain (MCD). When the patients reported pain, and in the period when the patient was walking with pain, we found no significant deviation from the steady increase in HR and BP recorded before.

**Control group**

In the one-minute rest period prior to walking, we found a median blood pressure of 119.7/75.7 (95.1–143.5/50.2–84.2) mmHg, and a MAP 91.7 (66.6–105.9) mmHg. Resting heart rate was 77.7 (60.7–91.3) beats/min. Acral skin blood perfusion was 1851 (82–2680) AU. A startle response followed initiation of walking. Following this response there was an increase in HR and MAP, stabilising at a steady state level while the test subject was walking. The median rise in MAP during walking was 8.5 (5.6–14.6) mmHg, SP increased by 30.9 (6.6–41.5) mmHg, and DP was reduced, −1.4 (−5.4–1.5) mmHg. HR increased by 27.1 (18.0–34.9) beats/min. We found no significant change in ASBP during walking compared to rest. After walking, blood pressure and HR quickly dropped to pre-exercise level.

**Discussion**

The most important finding of this study was that patients with PAD have a significant and continuing increase in blood pressure when walking to MCD. The increase clearly exceeded that expected in a normal population and that observed in the control subjects (Fig. 3). Baccelli et al. have previously demonstrated an increase in blood pressure in PAD patients during walking, and found that the magnitude of the blood pressure rise was related to the severity of disease, as well as walking speed and duration. In this study we found that the level of increase in blood pressure was similar to the increase observed during isometric exercise. SP increased dramatically for some patients, with values exceeding 300 mmHg. The changes observed in HR were in accordance with those expected of subjects of this age group.

We found no changes in acral skin blood perfusion in response to claudication. Normally there is increased cutaneous blood flow during physical activity, when body temperature rises and perspiration starts. This usually occurs after 5 minutes of dynamic exercise. However, in the present study, no test subjects exceeded 5 minutes of walking.

Pain stimulus is known to induce a rise in HR and blood pressure. In our study we did not find any relative changes in the measured cardiovascular parameters when pain was encountered during walking. Neither transient changes nor deviation in the slope

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**Fig. 3.** Average systolic and diastolic blood pressures during treadmill walking, in 11 patients with intermittent claudication (right panel), as compared to 6 healthy controls (left panel). The controls all had a walking period of five minutes. The patients had shorter and different maximum claudication time. The time axis is therefore expressed in relative values, where T = 0 represents the time when subjects started walking and T = 100 represents the time when the patients had to stop walking due to claudication pain, as in Fig. 2.
of the recorded rise in HR and blood pressure were observed. This is an important observation in the context of the ongoing discussion regarding the optimal exercise training approach, whether patients should walk until they experience pain (ICD) or until they have to stop (MCD). In this study blood pressure was markedly higher at MCD compared to ICD. The potential benefit of walking to MCD compared to ICD must be weighed against the increased cardiovascular risk due to a higher systemic blood pressure. The present study does not have data to evaluate this. Both changes in pain perception during physical activity and adaptation to the intermittently pain exposed calves in PAD patients could contribute to the absence of the expected cardiovascular response to exercise.

The systemic cardiovascular response to exercise depends on whether the muscle contractions are mainly isometric or dynamic during the performance of an external workload. With the start of dynamic muscle contractions, there is a prompt increase in HR and stroke volume. The increase in heart rate is sustained by decreased vagal tone and greater sympathetic activity. Cardiac output is increased during dynamic exercise, made possible by elevated heart rate, increased stroke volume, and a greater venous return. Venous return is augmented by the increased activity of the muscle- and thoracic pumps, by mobilization of blood from the viscera, by higher pressure transmitted through the dilated arterioles to the veins, and by venoconstriction mediated by noradrenaline. The blood mobilized from the splanchnic area and other reservoirs may increase the amount of blood in the arterial circulation by as much as 30% during strenuous exercise. There is a net fall in total peripheral resistance due to vasodilatation in exercising muscles. Consequently, during dynamic exercise SP rises only moderately, whereas DP usually remains unchanged or falls slightly. Increase in SP depends upon the workload performed; and the increase at moderate dynamic exercise usually ranges from 50 to 70 mmHg, similar to our findings. In comparison, blood pressure changes during heavy-resistance exercise have shown extremely high values, up to 480/350 mmHg.

There is an association between exercise blood pressure and potential risk of stroke, cardiovascular events and mortality. Athletes who have severe hypertension should be restricted from high static sports until hypertension is controlled with medication and lifestyle modification. Physicians also recommend patients with cardiovascular disease, including aortic aneurysm, to avoid activity resulting in marked rise in blood pressure, e.g. heavy lifting. According to our findings, PAD patients experience a marked increase in blood pressure when walking to claudication. In patients with PAD, the changes in the vascular wall together with an elevated exercise blood pressure heighten the risk of cardiovascular events. We therefore recommend that these findings be taken into consideration when treating and formulating guidelines for patients with PAD, especially when they have other cardiovascular co-morbidities.

Elevated blood pressure during exercise, and the potential increased risk of cardiovascular events, is recognized in patients suffering from cardiovascular disease. Due to the beneficial effects of physical activity, exercise is still highly recommended for the prevention and treatment of cardiovascular disease. In patients with PAD supervised exercise programmes have resulted in functional improvements, as well as improved health-related quality of life. We still advise our patients to keep walking, but further studies are needed to assess the cardiovascular consequences versus potential benefits of walking to either to MCD or ICD.

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References


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