Original research

Arterial stiffness results from eccentrically biased downhill running exercise

J.F. Burr*, M. Boulter, K. Beck

Applied Human Science, Human Performance and Health Research Laboratory, University of PEI, Canada

A R T I C L E   I N F O

Article history:
Received 18 January 2014
Received in revised form 18 February 2014
Accepted 1 March 2014
Available online 12 March 2014

Keywords:
Arterial compliance
Pulse wave velocity
Marathon
Endurance
Inflammation
DOMS

A B S T R A C T

Objectives: There is increasing evidence that select forms of exercise are associated with vascular changes that are in opposition to the well-accepted beneficial effects of moderate intensity aerobic exercise. To determine if alterations in arterial stiffness occur following eccentrically accentuated aerobic exercise, and if changes are associated with measures of muscle soreness.

Design: Repeated measures experimental cohort.

Methods: Twelve (n = 8, f = 4) moderately trained (VO2max = 52.2 ± 7.4ml.kg⁻¹.min⁻¹) participants performed a downhill run at ~12° grade using a speed that elicited 60% VO2max for 40 min. Cardiovascular and muscle soreness measures were collected at baseline and up to 72 h post-running.

Results: Muscle soreness peaked at 48 h (p < 0.001). Arterial stiffness similarly peaked at 48 h (p < 0.04) and remained significantly elevated above baseline through 72 h.

Conclusions: Eccentrically accentuated downhill running is associated with arterial stiffening in the absence of an extremely prolonged duration or fast pace. The timing of alterations coincides with the well-documented inflammatory response that occurs from the muscular insult of downhill running, but whether the observed changes are a result of either systemic or local inflammation is yet unclear. These findings may help to explain evidence of arterial stiffening in long-term runners and following prolonged duration races wherein cumulative eccentric loading is high.

© 2014 Sports Medicine Australia. Published by Elsevier Ltd. All rights reserved.

1. Introduction

The health benefits of participation in regular aerobic exercise are well established. Amongst the cardiovascular benefits of regular moderate intensity exercise is the reduction of arterial stiffness, which is associated with a reduced risk for cardiovascular disease and ischaemic events owing to decreased atherosclerosis, an improvement of coronary artery perfusion, and a lowering of both pulse pressure and wall stress. Given the clear relationship to future morbidity and mortality, arterial stiffness is now recognized as an important independent predictor of cardiovascular risk. Despite the known beneficial cardiovascular effects of habitual moderate intensity aerobic exercise, high-volume resistance training has been shown to elicit transient arterial stiffening and long-term participants manifest these changes persistently such that their resting levels substantially differ from controls who are only recreationally active; however, this area remains a controversial area and results are mixed. Counter intuitively, recent evidence examining the arterial properties and cardiovascular health of long distance runners has similarly demonstrated higher than expected baseline arterial stiffness compared to recreationally active controls and there is conflicting evidence as to whether or not participation in a long-distance race itself causes arterial stiffening. From our own published and unpublished observations, our laboratory has noted that substantial post-race arterial stiffening occurred only in races that were of prolonged duration (>24h baseline to follow-up) and which involved heightened physical stresses including a higher exercise intensity or substantial terrain challenges, such as the traversing of mountains. As such, we posit that the observed effect on arterial stiffening may be related to exercise induced muscle damage and inflammation, which typically requires 24–48 h to manifest and is enhanced by eccentric muscle contractions, which occur repeatedly during running – particularly while descending hills. This theory fits with existing evidence showing that long distance running causes high levels of oxidative stress and inflammation. In fact, recent strength training literature shows that eccentric training results in notable arterial stiffening from baseline and is associated with measures of muscle damage and inflammation whether using small or large muscle mass. Using experimentally induced
inflammation Vlahopoulos et al.\textsuperscript{15} have convincingly demonstrated a cause-and-effect relationship of systemic inflammation with arterial stiffening, however, some difference in the progress of the inflammatory cascade may occur depending on whether inflammation is systemically induced or stimulated by exercise.\textsuperscript{16}

Treadmill-based downhill running has long been established as a valid and reliable method to induce delayed onset muscle soreness and inflammation,\textsuperscript{17,18} particularly when the exposure exceeds an amount normally encountered by the participants. A downhill running exercise model allows investigation of the effects of the eccentric muscle contractions associated with running in the absence of extreme aerobic exercise intensity or duration. The purpose of the present investigation was thus to determine the role of eccentric muscle contractions during aerobically based exercise for affecting changes in arterial stiffness. Furthermore, we sought to investigate the temporal course of alterations from baseline to determine the time of onset, duration of the effect, and the association of changes in arterial stiffness with measures of muscle soreness. We hypothesized that even moderate intensity eccentrically biased running would result in significant muscle soreness, and associated arterial stiffening within twenty-four to forty-eight hours.

2. Methods

A mixed sex population of recreationally active subjects ($n = 13, m = 9, f = 4$) were recruited from the university community. Inclusion criteria indicated good general health, free from injury or pregnancy, not currently or previously engaging in eccentric exercise training, and no history of smoking, alcohol dependence, diagnosed heart disease, peripheral vascular disease, diabetes, cancer, pulmonary disease, orthopaedic conditions or use of medication. Participants were 25 ± 6 years of age, had a mean systolic pressure of 115 ± 9, diastolic pressure of 75 ± 5, were 175 ± 8 cm tall, and weighed 74.6 ± 16 kg. VO$_{2}$max was 52.2 ± 7.4 ml kg$^{-1}$ m$^{-1}$ (male 55.6, female 45.4). All participants provided written informed consent and this study was approved by the institutional Research Ethics Board for investigations involving human participants.

Participants visited the laboratory for baseline testing either 3 or 4 days prior to the downhill running test. All baseline testing commenced on either Thursday or Friday morning, with experimental procedures taking place the following week. During the study period, participants were requested to abstain from exercise, and NSAID use was prohibited. Baseline measures including blood pressure, carotid-femoral pulse wave velocity (PWV), radial artery augmentation index (Alx), and both subjective and objective muscle pain were recorded at each time point. Participants were given a period of no less than 2 full days recovery following the VO$_{2}$max test, prior to the commencement of the downhill running intervention. Fig. 1 graphically illustrates the procedural timing of all measurements. With the exception of the 6 h follow-up, all measures were taken at the same time each morning to control for diurnal variation. Participants were instructed to eat a light breakfast 2 h prior to arrival, and to standardize their morning meal from baseline through the last day of follow-up.

Following the assessment of baseline muscle pain and the cardiovascular measures described to follow, aerobic fitness testing was performed using a mechanically driven treadmill with analysis of expired gases. The fitness test commenced at a fast walking speed (4 mph) and progressed 0.45 ms$^{-1}$ (1 mph) and 2% grade until the participant reached his or her maximal safe running speed, after which only the incline was progressed. Breath-by-breath metabolic measurements were performed using a Cosmed Quark CPET system (Cosmed, Rome, Italy) and were averaged over 30 s for analysis. Metabolic testing required an average of 11.7 ± 1.2 min. The test was terminated when participants reached volitional fatigue (RPE = 19 or 20) and had an RER greater than 1.15. Attainment of a true VO$_{2}$max was verified by a plateau in oxygen consumption (increase < 150 ml min$^{-1}$) with an increase in workload. All participants reached a true max according to these criteria.

Blood pressure was measured using a standard sphygmomanometer at the brachial artery of the left arm while the participant was seated with his or her arm supported on a table at the level of the heart. Prior to the measurement of blood pressure, participants sat quietly for a period of 10 min to ensure accurate resting values. All measurements were taken in a quiet temperature and humidity controlled laboratory.

Subjective muscle pain was recorded using a 10 cm visual analogue scale wherein the participant marked the line corresponding to their rating of leg pain in daily life since the last assessment. Participants were instructed to make a mark on the line with the far left indicating “no discomfort at all” and the far right being “the most extreme muscular pain you have experienced”. This scale was quantified by measuring the distance to the nearest 0.1 cm from the left edge of the scale to the participant’s mark. These methods have been previously used and validated.\textsuperscript{19} Objective leg pain was quantified using a push-pressure strain gauge dynamometer (Fabrication Enterprises, White Plains, NY) with a cylindrical 1 cm$^{2}$ flat contact head applied to the mid muscle belly (measured from the superior patella to the anterior inferior iliac crest) of the vastus lateralis, immediately anterior to the iliotibial band. Participants were instructed to look away from the dynamometer and verbally indicate when the progressively applied pressure first became uncomfortable. Push-pressure muscle pain measures have been shown to be highly reproducible, and have been recommended for experimentally induced alterations in muscle pain sensitivity.\textsuperscript{20}

Carotid to femoral PWV was measured with participants in the supine position. Using an electrocardiogram, pressure waves were gated to systolic contraction and were collected consecutively from the carotid then femoral artery. Signal capture at each site was performed manually once a sufficient quality signal was obtained. Pulse wave arrival was determined using the intersecting tangent method to detect the foot of each wave. For velocity calculations, distance was measured with a standard anthropometric tape using a straight line above the body from the carotid to femoral sites, with an adjustment for the distance from the carotid site to the suprasternal notch. Pulse wave velocity of the descending aorta was our primary outcome variable to estimate arterial stiffness as PWV is recognized as the gold standard measure and is less affected by the physiological alterations known to occur in conjunction with a bout of exercise compared to other common estimation methods.\textsuperscript{25}

Resting Alx was calculated from pulse waves collected at the right radial artery using a high fidelity Millar strain gauge transducer (Millar instruments, Houston, TX). Participants sat quietly with the right forearm resting on a table and the wrist supported in slight hyperextension. Signal quality was controlled using the auto-capture feature of the SphygmoCor CPVH software (Atcor Medical, Sydney, Australia) and the operator index was recorded at 93 ± 5% for all captures. Alx measures standardized to a heart rate of 75 bpm were employed for analysis to reduce the tachycardic effect of the downhill run on post-run measures. Augmentation index is a measure of the reflected waves within the arterial tree extending down to the radial artery level, and although this can offer some insight into stiffness properties and the work of the myocardium, reflected waves can be affected by changes in other exercise related cardiovascular factors, such as cardiac time intervals. As such, Alx was included only as a secondary measure.

The downhill run was performed using the same treadmill as the VO$_{2}$max test set to a decline of −12° with a specifically constructed elevation device placed under the rear of the belt platform. Participants ran at a speed eliciting 60% VO$_{2}$max (pace range 1.9–3.2 m/s)
for 40 min while exercise intensity was monitored continuously with heart rate telemetry and periodic (approx. every 5 min) measures of expired gases. Participants were instructed against using the handrails of the treadmill while running so as not to affect the work required of the legs. All follow-up measures succeeding the run and at each follow-up visit were repeated using the methodology reported above.

Temporal changes in muscle soreness, arterial stiffness (AIx, PWV) and related cardiovascular indices were analyzed using repeated measures $1 \times 5$ (baseline, post-run, 24 h, 48 h, 72 h) ANOVA. To maintain adequate statistical power (>80%) no further division by age or gender was attempted. Both deviation and simple contrasts were used post hoc to compare to the immediately preceding measure and the baseline, respectively. Possible associations between arterial stiffness and muscle soreness were examined using Pearson correlation of both raw measures and change scores from baseline. Analyses were performed using SPSS (Version 20.0), with significance for all tests set a priori at $P \leq 0.05$. Results are reported as mean ± SD.

3. Results

One participant was unable to complete the full 40 min duration of the run due to leg fatigue and was excluded from follow-up measures. No other participants dropped-out nor did any adverse events occur during the intervention or follow-up. Included participants reported regular participation in active physical activity and demonstrated moderate to high levels of aerobic fitness (range 41.3–66.1 ml kg$^{-1}$ min$^{-1}$). Table 1 presents cardiovascular, arterial, and muscle soreness data at each measurement point. Baseline measures of PWV and AIx confirmed that participants had mean arterial stiffness measures that were comparable to expected age and sex matched norms. Both systolic and diastolic blood pressure were within a normal range at baseline and revealed no significant deviation at any measurement point. Mean heart rate remained elevated 15 min following the run (13 ± 12 bpm), but heart rate was not different from baseline at any other measurement. Muscle soreness varied throughout the trial for both the analogue and tolerable pressure measures ($P < 0.001$). Fig. 2a presents delayed tolerable pressure muscle soreness, with the analogue scale measurements imposed on a secondary axis. Graphical presentation of this data illustrates the similarity of the shape of these curves, and it is noted that the two measures had statistically consistent changes in the reported muscle soreness at successive time points.

Pulse wave velocity revealed a significant increase in arterial stiffness following the downhill running intervention ($p = 0.04$) which was first evident at 48 h post-run and remained elevated at the final measurement 72 h later (Fig. 2b). A significant relationship between the level of muscle soreness, or a change in muscle soreness, and changes in arterial stiffness was not evident at any time point; however, after removal of one significant non-responding outlier (circled in Fig. 2c) changes in PWV and changes in perceived muscle soreness were correlated $r = 0.65, p = 0.03$. No changes from baseline were observed in AIx at any time point.

4. Discussion

The major novel finding of the present investigation was that arterial stiffening, evidenced by an increase in carotid-femoral PWV, occurred approximately 48 h following a bout of downhill running. This is the first study to show this effect using an eccentrically biased aerobic exercise stimulus and we are unaware of other investigations which have considered the temporal effect of an aerobic exercise bout over a similar period of follow-up. Despite the modest duration and moderate aerobic intensity employed (compared to the typical intensity/duration of a typical running race), the work of downhill running represents a formidable muscular challenge, and this stimulus is well known to cause significant muscular insult. Our hypothesis that eccentrically biased downhill running would precede arterial stiffening was supported, which raises interesting questions about the potential long-term role of repeated or unaccustomed eccentric muscle loading for affecting arterial stiffness and health.

As expected, downhill running led to substantial increases in participant’s perception of muscle soreness, with a slight increase in pain immediately subsequent to the downhill run, followed by a more pronounced change at 24 h and peaking at 48 h of recovery. Changes in PWV similarly occurred between the 24 and 48 h measurements suggesting a possible relationship between these
Table 1
Cardiovascular indices, arterial stiffness measures, and muscle soreness associated with eccentrically biased aerobic exercise. Measures are reported at baseline, 15 min after a 40 min downhill run and six, twenty-four, forty-eight and seventy-two hours post-run.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Time point</th>
<th>Rest</th>
<th>Post-run</th>
<th>6 h</th>
<th>24 h</th>
<th>48 h</th>
<th>72 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td></td>
<td>61 ± 7</td>
<td>77 ± 8†</td>
<td>68 ± 12</td>
<td>63 ± 8</td>
<td>63 ± 8</td>
<td>63 ± 9</td>
</tr>
<tr>
<td>Brachial systolic pressure (mmHg)</td>
<td></td>
<td>118 ± 10</td>
<td>114 ± 9</td>
<td>117 ± 8</td>
<td>118 ± 8</td>
<td>116 ± 10</td>
<td>117 ± 10</td>
</tr>
<tr>
<td>Brachial diastolic pressure (mmHg)</td>
<td></td>
<td>76 ± 4</td>
<td>77 ± 3</td>
<td>77 ± 5</td>
<td>75 ± 4</td>
<td>74 ± 3</td>
<td>74 ± 4</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td></td>
<td>87.9 ± 4.8</td>
<td>88.3 ± 3.3</td>
<td>89.2 ± 3.5</td>
<td>88.1 ± 3.2</td>
<td>86.6 ± 3.9</td>
<td>86.4 ± 3.4</td>
</tr>
<tr>
<td>Soreness pressure (kg)</td>
<td></td>
<td>3.8 ± 0.6</td>
<td>3.3 ± 0.7a</td>
<td>3.3 ± 0.9a</td>
<td>2.8 ± 1.3b</td>
<td>2.6 ± 1.3b</td>
<td>2.9 ± 1.2b</td>
</tr>
<tr>
<td>Soreness analogue scale (cm)</td>
<td></td>
<td>0.5 ± 0.6</td>
<td>2.9 ± 2.7†</td>
<td>3.4 ± 2.3†</td>
<td>6.1 ± 2.3†b</td>
<td>7.2 ± 2.4†b</td>
<td>4.5 ± 2.3†b</td>
</tr>
<tr>
<td>Augmentation index (75 bpm)</td>
<td></td>
<td>−0.2 ± 3.2</td>
<td>−0.7 ± 2.6</td>
<td>−1.1 ± 3</td>
<td>−1.5 ± 2.9</td>
<td>−0.8 ± 3.2</td>
<td>−1.8 ± 3.1</td>
</tr>
<tr>
<td>Pulse wave velocity (m/s)</td>
<td></td>
<td>5.1 ± 0.6</td>
<td>5.3 ± 0.6</td>
<td>5.3 ± 0.6</td>
<td>5.4 ± 0.7</td>
<td>5.6 ± 0.9</td>
<td>5.5 ± 0.5</td>
</tr>
</tbody>
</table>

† Different from previous, p < 0.05.  
‡ Different from previous, p < 0.001.  
§ Different from baseline, p < 0.05.  
* Different from baseline, p < 0.001.

Fig. 2. (a, top left) Muscle soreness resulting from eccentrically biased downhill running. The primary axis (left-solid line) displays the pressure (kg) participants could withstand being pressed against the muscle belly of the vastus lateralis before notable discomfort. The secondary axis (right-dashed line) displays the participant’s subjective rating of discomfort using a 10 cm visual analogue scale. Variability data and p values are only presented for the primary axis for clarity, but both displayed similar patterns. (b, top right) Carotid to femoral pulse wave velocity (PWV) at baseline, 15 min following a 40 min downhill run, and after six, twenty-four, forty-eight and seventy-two hours of recovery. It can be seen that PWV was significantly increased at twenty-four hours post run and did not return to baseline levels by seventy-two hours. Error bars represent SD. (c, bottom) Scatterplot of changes in muscle soreness (analogue scale) and changes in PWV from baseline to 48 h peak. Non-significant relationship (r = 0.52, p = 0.08), when circled non-responder outlier data point is removed (r = 0.65, p = 0.03).

physiological processes; however, this association was only supported after removal of one apparent outlying response.

It has previously been shown that both inflammation and arterial stiffening independently occur in runners following high-intensity prolonged exercise, such as the marathon,\textsuperscript{9,22} and moderate-intensity extreme duration, such as the ultra-marathon.\textsuperscript{11,23} In the present investigation, using a downhill running exercise model that promotes muscular insult without great emphasis on the aerobic intensity or duration of exercise, changes in arterial stiffness occurred in line with the expected timing of a systemic inflammatory response. We did not specifically track plasma markers of oxidative stress and inflammation, however, this well-accepted association offers a potential mechanism for the observed response. An alternative hypothesis to a systemic alteration is that localized inflammation led to swelling in the legs and associated alterations in the transmural pressure and perfusion of resistance vessels. With a decreased peripheral flow, upstream flow could also be affected, thus decreasing shear stress and flow mediated dilatation in the proximal vascular tree. If such is the case, it would be likely that changes in vascular resistance would be associated with alterations in the arterial muscle tone of conductance vessels. Such a change in the lower extremities affecting upstream flow could also help to partially explain the differential effect of PWV collected using carotid-femoral arteries versus AIx, which estimates purely from the radial artery and would be less affected by localized changes in the legs. These physiological
pathways offer possible explanations for the observed effect, but remain speculative at present.

Irrespective of the underlying mechanistic causes of arterial stiffening, the finding that an increased emphasis on the eccentric component of running preceded delayed onset arterial stiffening is noteworthy and contributes to our understanding of the human vascular response to exercise. The magnitude of arterial stiffening in the present investigation was of modest clinical significance (0.5 m/s), but must be interpreted in context. An increase in PWV of 1 m/s has been demonstrated to increase the risk of a cardiovascular event by 15%. The observed increase of 0.5 m/s, although only half of this value, notably occurred after only a 40 min runs that was moderately taxing to the cardiovascular system, yet imposed high muscular stress. This exercise duration and intensity were selected because they offered a reasonable (but not overly intimidating) eccentric exercise challenge and approximated established protocols known to be effective for producing DOMS. Although the current work was undeniably challenging, it is very possible that the eccentric loading during a prolonged running event such as the marathon or ultra-marathon (lasting >2–40 h) could still be significantly higher, and post-race muscle soreness is a common symptom for participants.

Recent reports have demonstrated additional cardiac specific effects of running including a strong association between the number of marathons or ultra-marathons completed and myocardial fibrosis in long-term runners, which may also be related to arterial stiffening. With a better understanding of the interplay of the various facets of exercise (frequency, intensity, duration, type) it is possible that potential cardiovascular risk could thus be better controlled through appropriate training cycles, particularly in light of evidence showing that the negative effects of high volume resistance training on arterial stiffening can be negated through the use of moderate intensity aerobic exercise before (but not after) weightlifting. Consideration of the timing between workouts and the specific use (or avoidance) and timing of hill—workouts may also prove important, but at present there is insufficient evidence on which to base recommendations for athletes to alter their training practices.

There are some limitations to this study, which should be recognized and significant areas for future direction. It is important to note that the downhill running stimulus was intentionally unfamiliar to the participants, who were not specifically endurance athletes and did not regularly run downhill. As such, the novelty of the exercise stimulus itself may have contributed to the physiological response and thus the dose–response remains uncertain. At present, it is unknown if this effect would occur to a similar extent once participants were habituated to downhill running workouts, or if a period of adaptation would blunt this effect, but this is a worthy area of future investigation. It is also unknown if successive bout of moderate intensity exercise (downhill or otherwise) would diminish this effect, or add to it in a stepwise cumulative fashion, as has been shown for repeated bouts of sprint exercise.

At this preliminary stage of investigation we are unable to determine a precise mechanistic cause to explains why downhill running is associated with changes in arterial stiffness (i.e. local or systemic factors), and thus extrapolation and generalization of these findings must be done with caution. Furthermore, the specific persistence of this effect still remains somewhat unclear, as the 72 h measurement remained significantly above baseline following the increase at 48 h, despite indications that it was starting to decrease. In the present investigation, changes were only observed in measures of PWV but not augmentation index, which matches previously published data following marathon participation and may well be related to measurement methodology. In both of these investigations carotid-femoral PWV (i.e. the descending aorta) has been employed for central measures of arterial stiffness, but further insight into vascular changes might be gained by including measures of peripheral vasculature (i.e. femoral to dorsal pedis and carotid to radial) and endothelial function in future work.

5. Conclusion

When exposed to an eccentrically accentuated aerobic exercise stimulus for 40 min, moderately trained participants demonstrated significant increases in arterial stiffness following 48 h of rest. Although a similar temporal pattern of increases were observed in measures of muscle soreness, a direct relationship between arterial stiffening and delayed onset muscle soreness was not apparent. Given the temporal relationship of changes, the known effect of downhill running to elicit an inflammatory response, and the demonstrated relationship between inflammation and arterial stiffening it seems likely that inflammation (or inflammatory mediated alterations) plays a mechanistic role in the observed changes, whether systemically or locally.

It is essential to note that the present results should not be interpreted to suggest that aerobic exercise is necessarily bad for cardiovascular health. In fact, there is a considerable body of persuasive evidence that suggests otherwise. In the present study the exercise stimulus employed was considerably beyond that which would normally be encountered during health-related physical activity or without purposeful effort and design, and as such represents the more extreme end of the exercise spectrum. The authors suggest that the results of this study should be interpreted as more evidence of an inverted U shaped hypothesis of physical activity, with overextending exercise leading to cardiovascular responses that are in opposition to the generally accepted beneficial effects of the more moderate exercise that is recommended in most physical activity guidelines. Although the present data demonstrates acute changes in arterial compliance, which may possibly contribute to more long-term alterations in vascular stiffness, the full implications of this finding for health or performance remain to be elucidated, and it is possible that the observed effects are within the natural process of adaptation.

Practical implications

• Eccentrically biased aerobic exercise is associated with a delayed arterial stiffness similar to eccentric strength training
• Muscle soreness and arterial stiffening peak at approximately 48 h post-exercise
• It is premature to suggest that training practices be altered as health/performance implications are yet unclear

Acknowledgements

The authors have no financial support or competing interests to declare.

References

6. Kawano H, Tanimoto M, Yamamoto K et al. Resistance training in men is associated with increased arterial stiffness and blood pressure but does not adversely
affect endothelial function as measured by arterial reactivity to the cold pressor test. Exp Physiol 2008; 93(2):296–302.