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Long-term ultra-marathon running and arterial compliance

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ABSTRACT

Recent reports that habitual marathon runners demonstrate higher levels of stiffness and cardiovascular risk factors have been of great interest to the medical and scientific community. Ultra-marathon running, that is any distance >42.2 km, is increasing in popularity; however, little is known regarding the physiological effects of the sport's unique training and racing practices on vascular health.

Objectives: To characterize and compare the arterial compliance of male long-term (>5 years) ultra-marathoners with recreationally active controls, and examine the associations of training related practices with systemic arterial compliance.

Design: We employed a case-control comparison design using long-term habitual ultra-marathon runners ($n = 18$) and an age matched cohort of normative recreationally active males.

Methods: Arterial compliance was measured at rest using radial applanation tonometry (CR-2000, HDI) for diastolic pulse contour analysis. Compliance was compared with normative data, participant characteristics, and associated exercise parameters.

Results: In representative ultra-endurance runners, large artery compliance of long-term participants was reduced compared with physically active age-matched controls ($p = 0.03$) and is related to select training variables. Specifically, in a representative subset for whom we obtained detailed training data, decreased compliance was related to longer typical running distance per training session ($r = -0.72$, $p = 0.03$); however, more broad definitions of frequency, intensity, and duration revealed no association for the runners as a whole.

Conclusions: Given the known associations of arterial stiffness with future cardiovascular events, ultra-endurance runners may be at an increased risk of a cardiovascular event compared with their normally active counterparts.

1. Introduction

The beneficial effects of regular moderate intensity physical activity participation for the promotion of cardiovascular health and prevention of cardiovascular disease is well established.[1] However, recent findings counter-intuitively suggest an elevated cardiovascular risk amongst runners participating in prolonged endurance exercise events, particularly the marathon.[2–5] Our research group, and others, have examined the rapidly growing sport of ultra-marathon (distances >42.2 km) and have shown evidence that both cardiac[6] and select components of vascular function[7] may be negatively influenced by participation in these events. As the scientific community's understanding of the vascular response to exercise expands, empirically supported theories have been proposed suggesting the existence of the "athletes artery", which similar to the "athletes' heart" undergoes an adaptive physiological response to prolonged strenuous exercise.[8] Related theories offer mechanistic explanations for cardiac arrhythmogenic remodelling and increased cardiovascular risk in these types of endurance athletes,[9] although this area of research remains controversial. It has been shown that arterial stiffness is a strong predictor of future cardiovascular events and all-cause mortality.[10] At present, the long-term effect of routine participation in ultra-marathon trail running on arterial compliance has yet to be established.

Research examining prolonged running has typically focused on elite performers, perhaps because the marathon and ultra-marathon distance were traditionally only attempted by this calibre of athlete. However, as ultra-marathon continues to grow[11] and a greater number of sub-elite and older athletes[12] undertake

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these extreme exercise routines; it is probable that the associated physiological stressors and consequent outcomes of participation may manifest differently. Although certain similarities between marathon and ultra-marathon running are apparent, the specific training and racing parameters surrounding ultra-marathon participation are poorly described in the literature, especially compared with the wealth of data that exists concerning the shorter marathon distance.

The purpose of this manuscript was two-fold. Firstly, we compared the arterial compliance of sub-elite, long-term ultra-endurance runners with representative normative data for healthy recreationally active males. Second, we sought to characterize the training and racing-related practices of ultra-endurance runners so as to examine the relationships of these exercise parameters with arterial compliance. In light of previous reports in marathon runners, we hypothesized that the arterial compliance of habitual ultra-marathon runners would be lower than regularly active controls. Further, we expected that decreases in compliance would be most pronounced in those runners who undertook the largest amounts of high intensity and prolonged duration training.

2. Methods

Using 18 long-term ultra-marathon runners, arterial compliance was measured non-invasively at rest via applanation tonometry (HDI/PulseWave CR-2000, Hypertension Diagnostics, Eagan, Minnesota) with arterial pulsewave contour analysis.[13] Inclusion criteria for this phase of the study required multiple consecutive years of ultra-endurance running participation (>5 years), male, aged <65 years, and no symptoms or diagnosis of a chronic condition, which was verified by a certified exercise physiologist following completion of the PAR-Q+ screening questionnaire.[14] All participants were still actively engaged in ultra-marathon competition, and measures were obtained during the resting phase preceding and upcoming race for each runner. Participants provided written informed consent in accordance with guidelines of the Clinical Research Ethics Review Board at the University of British Columbia who approved this study. To examine the effects of a chronic ultra-endurance training stimulus on arterial compliance, participants reported training practices such as training frequency, perceived intensity, weekly mileage, years of experience and prior race participation.

Prior to tonometric data acquisition, participants were instructed to avoid intense exercise (24 h pre-test), caffeine ingestion or a heavy meal the morning of testing. No participants smoked. Participants were placed in the supine position and instructed to lie quietly for 10 min prior to data collection. Noise reducing ear protection was provided. After stabilizing the wrist in slight hyperextension and maximizing signal strength, radial artery tonometry measurements were taken using the right wrist with an automated sphygmomanometer affixed to the upper left arm for calibration. Measurements were collected in duplicate with the mean value used for analysis. The HDI/PulseWave CR-2000 uses a modified 2 element Windkessel model with a transfer function that allows for the calculation of central large artery (C_1) and oscillatory small artery (C_2) compliance. This method of dividing total systemic resistance into individual components using mathematical modelling has been shown to yield reliable and repeatable measures in healthy subjects.[15] Owing to the standardized automation, accurate and reliable measures have a low reliance on operator technical skill (particularly in comparison with hand-held tonometric systems used for pulse wave velocity), allowing valid comparison to previously published data. Thus, measures of arterial compliance in ultra-endurance athletes collected in the current investigation were compared with published age and gender matched data of healthy recreationally active controls[16] who participated in ≥30 min of exercise ≥3 days/wk. For comparison, physical activity (kcal/day) was calculated for ultra-endurance runners using training frequency, intensity, duration and bodyweight according to the methodology employed by Pohjantahti-Maaroos et al. with the control population.[16]

Table 1
Descriptive participant characteristics (mean ± SD) of experimental and control group.

	Ultra-marathon runners (n = 18)	Active controls (n = 35)[19]
Age (years)	49.3 ± 6.6	49.4 ± 7.5
BMI (kg/m^2)	23.7 ± 1.8	23.8 ± 2
Physical activity (kcal/day)	1006 ± 257	507 ± 300[a]
Resting heart rate (bpm)	52 ± 6	52 ± 9
Hypertensive (n/%)	0/0	1/2.9
SBP (mmHg)	127.2 ± 8.3	127.2 ± 9.2
DBP (mmHg)	74 + 6.8	73.9 ± 6.7

[a] $p < 0.001$.

Arterial compliance measures were compared with age matched normative data for healthy recreationally active controls using Student's t-tests. Multiple linear regression and Pearson correlation were employed to analyze associations of arterial compliance with training variables. All analyses were performed using SPSS software (version 20.0; IBM, Armonk, NY). Significance for all tests was set a priori at $p < 0.05$. Results are reported as mean ± SD.

3. Results

Participants had an average of 10 ± 5 years of ultra-endurance training and racing experience. Excluding one outlier, who had participated in >150 ultra-marathons over the past 20 years, the average number of ultra-marathons completed was 24 ± 17 races (37 ± 47 races with outlier inclusion). Participants reported a mean training frequency of 5 sessions per week with an estimated distance of 88 ± 27 km. A typical run was self-reported to be at a training intensity of 13.2 ± 1.2 (range 12–15) using the Borg 6–20 scale.[17] Descriptive data for ultra-marathon runners and controls are presented in Table 1, demonstrating little variation with the exception of the physical activity stimulus per week, which is approximately two-fold in the ultra-marathon group.

Comparison of large artery compliance revealed habitual ultra-marathon runners to have lower compliance compared with normally active controls ($p = 0.03$, Fig. 1). Small artery compliance of ultra-marathon participants was not different from controls. There was a significant relationship between years of ultra-marathon participation and small artery compliance ($r = -0.57$, $p = 0.02$); however, after controlling for age, these variables were not correlated significantly. Multiple linear regression confirmed that no other training related exercise variables (frequency, intensity, weekly distance, number of previous races) were predictive of either large or small artery compliance. However, in a follow up analysis using a subset of runners ($n = 9$) who reported more detailed training data than was available for the entire study group, we found decreased compliance to be related to longer typical running distance per training session ($r = -0.72$, $p = 0.03$). Considering anthropometric and descriptive cardiovascular variables (height, weight, age, resting heart rate, blood pressure) large artery compliance was inversely related to resting systolic blood pressure (Fig. 2) and small artery compliance to weight ($r = 0.49$, $p = 0.01$) and age ($r = -0.44$, $p = 0.02$).

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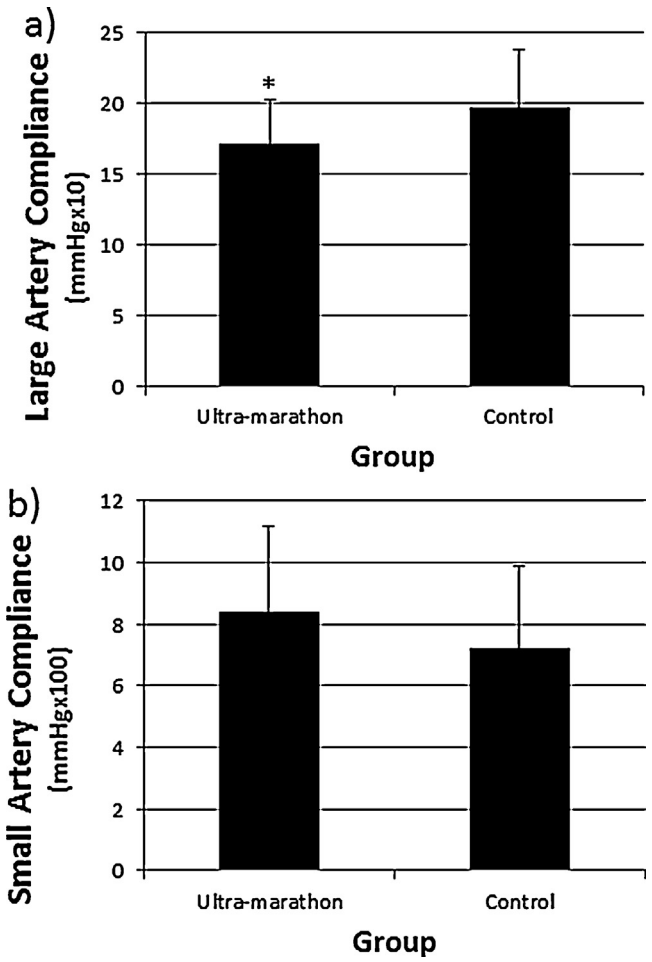

Fig. 1. Comparison of large (a) and small (b) arterial compliance at rest between long-term male ultra-marathon trail runners and age matched recreationally active controls. $^{*}p < 0.05$.

4. Discussion

The major novel finding of this investigation was that long-term male ultra-endurance runners had lower large artery compliance compared with age matched recreationally active controls. This finding is important as it supports prior work examining arterial stiffness in competitive marathoners.[4] These findings highlight that an inverted-U shape dose–response curve may exist for the exercise-related benefits in arterial structure and function. Recently, a compelling relationship between induced systemic inflammation and reduced large artery compliance has been established using experimental human models[18] and new research has demonstrated that eccentric exercise training leads to inflammation and arterial stiffening.[19] Given the intrinsic eccentric component of running, especially on downhill[20] segments of a course, ultra-marathon running has potential for high levels of inflammation from high volume exposure. This effect may also be exaggerated in the current population of ultra-marathon runners, who specifically engage in off-road trail running, most commonly in mountainous terrain wherein prolonged downhill running is common. Such high levels of inflammation following ultra-marathon racing have been repeatedly demonstrated,[21] yet it is still unclear if this type of systemic inflammation happens recurrently following training bouts and if the race-related increases in inflammatory markers ultimately lead to altered baseline compliance.

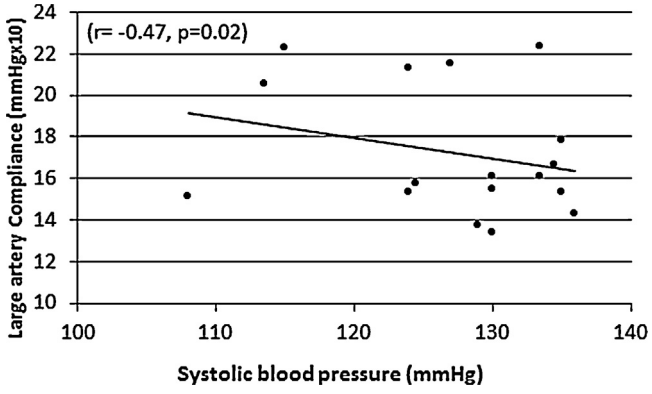

Fig. 2. The relationship between large artery compliance and systolic blood pressure in a group of male ultra-marathon trail runners.

In contrast to our results, Knez et al.,[22] have previously reported no significant differences in arterial stiffness between ultra-endurance athletes and controls using the augmentation index method. These discordant results may be explained by a number of factors. Firstly, in contrast to our homogenous population, "ultra-endurance athletes" represented a rather heterogeneous population, comprised of those with substantially lower years of training experience (avg. 6.2 ± 5.5 years) and including triathletes of both genders. As triathlon training includes substantial non-weight bearing swim and bike training it is likely that the body is not stressed to the same extent. Training patterns are also very different, such that run training is typically done in a single workout whereas triathlon training is often split into smaller bouts by exercise discipline. Secondly, in a recent investigation using concurrent measures, Vlachopoulos et al. reported increased pulse wave velocity, yet no changes in augmentation index following a marathon.[4] In light of literature suggesting augmentation index may be an inadequate measure of arterial compliance and coronary artery disease risk,[23] the null findings of Knez et al. may indeed be purely methodological. In the current investigation, we used the method of diastolic pulse contour analysis from radial pulse applanation tonometry to examine both large and small artery compliance. Large artery measures categorize the stiffness of large capacitive vessels such as the aorta; whereas the small artery is concerned more with microvascular circulation. Compliance estimates using this method strongly agree with invasively determined direct measures[24] and are also related to MRI derived measures of aortic distensibility and endothelial function.[25,26] However, it should be noted that despite the agreement of this measure with more invasive measures and the benefit of a low reliance on operator skill, this technique also has important limitations that cannot be ignored. As arterial stiffness is an independent predictor of cardiovascular risk,[10] the current findings suggest that compared to their recreationally active counter-parts, ultra-marathon runners could be at an elevated risk for future cardiovascular events. However, this interpretation is drawn only from large artery compliance, and we showed no relationship of small artery compliance with running after controlling for age. It should be noted that in a longitudinal follow-up study of cardiovascular events using the same tonometric pulsewave analysis technology, only small artery compliance was shown to remain a significant predictor of recorded events after controlling for age.[27] However, small artery measures have been criticized for being somewhat ambiguous as they may be largely influenced by factors including systemic vascular resistance[28] and these measures may be further subject to introduced variation in calculated variables such as cardiac output.[29] Importantly, the majority of investigations demonstrating increased cardiovascular risk with stiffer arteries have employed pulsewave velocity measures in the

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(large) descending aorta; thus large artery findings from the current investigation have relevance, and follow-up investigation using the gold standard pulsewave velocity[30] of the aorta in this group of athletes is warranted.

Interestingly, in a sub-group for whom more detailed training data was available, we found decreased compliance to be related to longer typical running distance in training, which corroborates the finding of Vlachopoulos et al. showing a relationship to minutes of exercise per day.[4] Although this data warrants reporting, we choose to abstain from making conclusive statements or overstating the results owing to the relatively small size of the sub-sample.

While indicating a starting point for further health-research into the effects of prolonged exercise on human vasculature, a limitation of the present data is that no cause and effect relationship can be established given the cross-sectional nature of this analysis and an inability to control for other possible influences between or within groups. It is possible that the observed ultra-endurance running and vascular stiffness relationship within this group is driven by other facets of an ultra-endurance runner's lifestyle. To speculate, this could include factors such as: group self-selection (i.e. those who are driven to run extreme distances), the repeated use of high glycemic carbohydrates during and following training, or potential negative lifestyle alterations stemming from the common misconception that dedicated runners are immune to cardiovascular disease. On the contrary, it is also possible that increased vascular risks are offset by other beneficial cardiovascular adaptations as a result of ultra-marathon running and are thus of little consequence to health; one such example being the report of an improvement in sub-endocardial perfusion capacity despite longer ejection durations amongst these athletes.[22] Further investigation involving parallel measurement techniques, longitudinal designs, comprehensive lifestyle profiles, and comparison to both inactive and active controls with large samples are necessary before the real magnitude and aetiology of this risk can be confirmed and comprehensively interpreted. At present, it is premature to recommend that athletes should avoid ultra-marathons altogether, or decrease average training distance or volume based on the association of running distance with large artery stiffness to preserve vascular health, especially in light of the many direct and indirect benefits of most aerobic exercise.

5. Conclusion

The major finding of this investigation was that long-term male ultra-endurance runners had lower large artery compliance when compared with age matched normative controls that were only recreationally active. Given the known associations of arterial stiffness with future cardiovascular events, ultra-endurance runners may be at an increased risk of a cardiovascular event compared with their normally-active counterparts, but further investigation is required to explain the possible mechanisms and implications of this finding.

Practical implications

- Long-term involvement in ultra-marathon may be associated with cardiovascular risk.
- Long-term ultra-marathon participation may affect the resting compliance of human vasculature in a similar manner as marathon participation, despite different training and racing exercise exposures (intensity and duration).
- Further evidence that an inverted U dose–response for exercise may exist.

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