Temporal Response of Arterial Stiffness to Ultra-Marathon

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Abstract

The purpose of this investigation was to characterize the arterial stiffness of male ultra-marathon runners (n=9) using pulse wave velocity (cfPWV) and radial tonometry over the course of an ultra-marathon and during recovery. Measures were collected at rest, immediately following 45 km/75 km of running, then following 60 and 90 min of recovery. No statistical difference was found between baseline cfPWV and normative values. The cfPWV of ultra-endurance runners decreased at 45 km (3.4 ± 1.6 m/s, p = 0.006), followed by an increase (1.6 ± 1.8 m/s, p = 0.04) toward baseline levels at the 75 km mark. Radial tonometry measures also indicated small artery stiffness was transiently increased after 75 km. The amount of training time (r = 0.82, p = 0.007) and the duration of a typical training session (r = 0.73, p = 0.03) were correlated strongly with persisting decrements in large artery compliance at 60 min of recovery. The finding that arterial stiffness decreased at the 45 km distance and then reverted back toward baseline levels with prolonged running, may indicate a role of exercise duration or accumulated stress for affecting vascular compliance. At present, it is premature to suggest that athletes should alter training or racing practices to protect vascular health.

Introduction

Participation rates in endurance and ultra-endurance running events have increased dramatically in recent years [14], leading to unprecedented numbers of athletes training for and racing at distances up to and exceeding the typical marathon. The demographic composition of participants is also changing from the young, elite athlete to incorporate greater numbers of older and sub-elite competitors [15]. Arterial stiffness is known to be associated with an increased risk of cardiovascular and all-cause mortality [29]. It is well established that habitual participation in regular aerobic physical activity is associated with lower levels of arterial stiffness at rest and an attenuation of the progressive stiffening of arteries with age [27]. Research has also demonstrated a chronically increased resting arterial stiffness in some competitive endurance athletes [30] when compared with recreationally active controls; yet this area remains controversial, results are mixed [23] and underlying mechanisms of this effect are unclear. Our laboratory has presented evidence that participation in an ultra-marathon itself may lead to an acute increase in systemic arterial stiffness [4] and it is possible that this may relate to more enduring arterial changes. At present, the time-course of vascular changes during a race and into recovery has not been examined, but a more in-depth understanding is crucial for interpreting the consequences of these effects. The primary purpose of the present investigation was to evaluate the temporal changes in arterial stiffness of a group of ultra-marathon runners during and following participation in a 75 km trail-running race. We hypothesized that arterial stiffness would be increased as a result of competitive ultra-marathon participation, but that these changes would resolve quickly during recovery.

Methods

Experienced male ultra-marathon runners (n=9) were recruited from local running clubs and through online ultra-running forums. Inclusion criteria required male ultra-runners, aged <65 years, with no signs, symptoms or diagnosis of a chronic
condition, which was verified using the PAR-Q+ screening questionnaire [32]. All participants provided written informed consent in accordance with guidelines of the Clinical Research Ethics Review Board at the University of British Columbia that approved this study. This study also meets the ethical standards of this journal [10]. To examine the effects of a chronic ultra-endurance training stimulus on changes in arterial stiffness, we used a case control design and required all participants to report training practices such as running frequency and weekly mileage. Resting arterial stiffness was measured at baseline using both carotid-femoral pulse wave velocity (cfPWV) and radial applanation tonometry (AT) (CR-2000, Hypertension Diagnostics, Eagan, Minnesota), 3 days prior to competition. Participants were instructed to refrain from strenuous exercise, smoking, and caffeine for ≥24 h prior to laboratory measures.

Maximal aerobic power (VO₂max) was measured in the laboratory following baseline vascular measures using a graded exercise test on a mechanically driven treadmill with gas analysis. Breath-by-breath expired gas and ventilatory parameters were acquired and averaged every 15 s using a calibrated metabolic cart (Ergocard; Medisoc, Dinant, Belgium). Rating of perceived exertion (RPE) and heart rate (S610i; Polar Electro, Oy, Finland) were recorded within the last 15 s of each stage. The staged test began with a 3 min warm-up using 5 mph-0% grade after which the first 2 min stage was introduced using 6 mph-0% grade. Each successive 2 min stage increased 1 mph and 2% grade until test termination. Termination criteria included: a failure of oxygen consumption to increase at least 150 mL·min⁻¹ with an increase in workload or participant volitional fatigue with a RPE greater than 17 on the Borg 6–20 scale. The test took an average of 11 ± 1 min to complete.

We employed a repeated measures experimental design to examine the temporal effects of prolonged running participation on human vasculature. Vascular stiffness measures were repeated on each runner throughout participation in an ultra-marathon trail running foot race after 45 km (mid-race approximate marathon distance), following the completion of 75 km, 60 min post-finish, and 90 min post-finish. At each measurement, AT and cfPWV measures were recorded simultaneously following a 10 min period of supine rest.

**Pulse wave velocity**

Pulse waves were collected at the carotid and femoral artery for analysis of cfPWV using infrared photoelectric sensors and recorded on LabChart software (Version 5.5.6. ADInstruments, Colorado Springs, CO) via signal processing through an ADI Powerlab. A single investigator screened all recordings and selected a minimum of 30 consecutive cardiac cycles, which were averaged to calculate the pulse transit time from foot-to-foot of consecutive waves. The foot of the wave was auto-detected using a specifically designed software macro to recognize and mark the last point before the upstroke. The distance between measurement points on the carotid and femoral arteries was measured as the shortest distance (to the nearest 0.5 cm) above the body using a standard anthropometric tape. For comparison of baseline measures with published norms, cfPWV measures were corrected using a scaling factor of 0.8 according to the method outlined by Sugawara et al. [26], and as was employed for the publication of large scale normative cfPWV data used for comparison [21].

**Applanation tonometry**

Applanation tonometry measures were collected using the radial artery of the right wrist with an automated sphygmomanometer affixed to the upper left arm for brachial pressure calibration. Prior to collection, the participant’s wrist was stabilized and the signal strength maximized according to manufacturer instructions [11]. The CR-2000 uses a modified 2 element Windkessel model which allows both large artery (C₁) and small artery (C₂) compliance estimations to characterize the capacitive vessels such as the aorta and small oscillatory vessels associated with microvascular circulation, respectively. Combined with anthropometric participant data for the calculation of body size, pulse contour data is used to auto-calculate additional cardiovascular indices including heart rate, blood pressure, pulse pressure, cardiac output, and systemic vascular resistance. The theoretical basis for the method of systemic arterial compliance using the area under the diastolic pulse wave has been described in detail [20] and strong agreement between measures has been reported for invasively determined direct measures [6] as well as intima media thickness [20] and MRI derived measures of aortic distensibility and endothelial function [25, 33]. As opposed to cfPWV, which specifically considers the descending aortic segment, it is postulated that C₁ and C₂ measures offer a more inclusive estimation of the stiffness of the systemic large and small arteries respectively.

The ultra-marathon race was specifically scheduled for the purposes of this investigation, and took place on the forested trails surrounding the campus of the University of British Columbia. Participants were encouraged toward realistic competitive performance through use of a representative race format as opposed to prolonged individual treadmill running. This format also permitted race tactics, pacing, and hydration/fuelling to occur as they naturally would in ultra-marathon trail running races. The course was typical of an ultra-marathon trail running course, with various undulations in terrain, winding turns, natural and man-made obstacles (i.e., boardwalks), and one major climb each lap (140 m vertical). Participants were directed to complete 5 laps of a 15.1 km course, with each lap starting and finishing at the laboratory. On race day, the weather was clear and sunny with a barometric pressure of 749.3 mmHg, 35% humidity at race start (7 am) and temperatures varying from 20.1–26.8 °C throughout the day. Aid stations with food and drink were placed approximately every 3 km throughout the course, allowing collection of subjective (RPE) and objective (heart rate, from coded wrist watch) physiological data 5 times per lap. Following the third lap (45 km), or at a distance approximating the standard marathon (42.2 km), participants had a mandatory break during which vascular measures were repeated.

**Statistical analysis**

Baseline arterial stiffness was compared with an age-weighted population mean value using a one sample t-test. Temporal changes in cfPWV, applanation tonometry, and related cardiovascular measures were examined using repeated measures ANOVA with simple and repeated contrasts to compare individual stages to baseline and between consecutive stages, respectively. To control for the potential influence of changes in blood pressure, cfPWV measures were examined with and without a correction for mean arterial pressure (cfPWV/MAP), which was calculated using the blood pressure measured simultaneous to cfPWV with the integrated sphygmomanometer of the applanation tonometer. Relationships between participant characteristics,
including training practices, and changes in arterial stiffness from baseline were examined using Pearson correlation. Analyses were performed using SPSS software (version 20.0; SPSS, Inc., Chicago, IL). Significance was set a priori at p<0.05 and results are reported as mean±SD.

Results

Descriptive participant characteristics of the competitive ultramarathon group are presented in Table 1. All athletes completed the full ultra-marathon distance, with the exception of 2 participants who withdrew prior to the final lap (60 of the 75 km). Follow-up measures were completed on both athletes who stopped after lap 4, as they had still completed an “ultra-marathon” distance (i.e., ≥50 km), albeit shorter than the intended 75 km race distance. A comparison of the results including and excluding the 2 drop-outs revealed no significant effect on vascular measures at exercise cessation or on recovery; thus data for these subjects was included in the final analysis. The time between exercise cessation and vascular measures; thus data for these subjects was included in the final analysis.

Pulse wave velocity
Comparison of baseline cfPWV measures with published normative data [21] from a large population study (n=1,455) revealed that 78% of our participants had resting cfPWV values above the normative mean, and 44% had values above the 90th percentile. A one sample t-test against the estimated age-weighted normative mean was not statistically significant. CfPWV was decreased at both the 45 km (p=0.001) and 75 km (p=0.04) distances, Fig. 1. CfPWV was at the lowest recorded value at the 45 km distance, but significantly increased (p=0.04) back toward baseline levels following completion of the full 75 km. With a greater variability about the means, cfPWV was no longer statistically different from baseline at 60 and 90 min of recovery (p=0.07 and 0.05 respectively). By the time of each measurement, blood pressure revealed no major departures from rest, thus resulting in no substantial differences between raw cfPWV and cfPWV adjusted for MAP. No noteworthy relationships between training practices or physiological racing variables and changes in cfPWV existed.

Applanation tonometry
Radial AT measures of compliance (the inverse of stiffness) revealed little significant group mean variation in for either C1 or C2 with the exception of a decrease in C2 following completion of 75 km (p=0.03), Fig. 2. Few relationships existed between typical training practices and changes in arterial compliance from baseline; however, reductions in C1 compliance (increases in stiffness) at 1-h post-race were strongly associated with both the typical weekly training time (r=0.82, p=0.007) and the duration of a training session (r=0.73, p=0.03). Furthermore, individual reductions in the athletes’ C2 compliance at 45 km were related to VO2max (r=0.83, p=0.006) and training intensity (RPE) (r=0.86, p=0.003). There were no significant associations between in-race physiological data and alterations in arterial compliance.

Associated cardiac estimates from the applanation tonometer cardiovascular profile unit are presented in Table 2. Heart rate showed an expected increase from baseline during the race, which later decreased during recovery but was still elevated above resting levels. Estimated cardiac output was similarly increased the 45 km and 75 km marks, but returned to baseline levels during recovery. Systemic vascular resistance decreased immediately post exercise, followed by a return to baseline levels in recovery.

Discussion

The major novel finding of the present investigation was that the cfPWV of ultra-marathon runners decreased after running the distance of a marathon (45 km), but this decrease in arterial stiffness below baseline levels began to revert by the completion of 75 km. The magnitude of this returning arterial tone that occurred between 45 km and 75 km was substantial (1.6 m/s) and of a magnitude that would be considered to be of clinical importance at rest.

Table 1  Descriptive participant statistics of male ultra-endurance runners (n=9) participating in a 75 km ultra-marathon trail running race.

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Mean ± SD</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>43.1 ± 13.4</td>
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<tr>
<td>Height (cm)</td>
<td>175.3 ± 5.7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.8 ± 5.2</td>
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<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>124.4 ± 7.7</td>
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<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>73.8 ± 4.6</td>
</tr>
<tr>
<td>Average training distance per run (km)</td>
<td>23.6 ± 5.9</td>
</tr>
<tr>
<td>Average training time per run (min)</td>
<td>146.9 ± 58.5</td>
</tr>
<tr>
<td>Average training frequency (per wk)</td>
<td>3.8 ± 0.9</td>
</tr>
<tr>
<td>Average training intensity (RPE 6–20)</td>
<td>13.2 ± 1.2</td>
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<tr>
<td>Weekly exercise (min/wk)</td>
<td>532.4 ± 130.7</td>
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<tr>
<td>Ultra-marathon experience (years)</td>
<td>8.7 ± 6.6</td>
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<tr>
<td>VO2max (mL . kg⁻¹ . min⁻¹)</td>
<td>49.4 ± 6.3</td>
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Table 2 Cardiovascular indices of male ultra-marathon runners calculated using radial applanation tonometry, before, during, and after participation in an ultra-endurance marathon race.

<table>
<thead>
<tr>
<th></th>
<th>Baseline (resting)</th>
<th>Marathon (45 km)</th>
<th>Ultra-Finish (75 km)</th>
<th>60 min post-race</th>
<th>90 min post-race</th>
</tr>
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<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>124.4 ± 7.3</td>
<td>121.8 ± 8.3</td>
<td>119.9 ± 7.9</td>
<td>116.6 ± 10.3</td>
<td>119.8 ± 11.5</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>73.8 ± 4.3</td>
<td>68.8 ± 6.1</td>
<td>68.4 ± 6.1</td>
<td>69.7 ± 8.2</td>
<td>70.0 ± 6.1</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>91.6 ± 6.5</td>
<td>88.8 ± 6.4</td>
<td>89.7 ± 5.6</td>
<td>89.2 ± 7.1</td>
<td>89.5 ± 7.1</td>
</tr>
<tr>
<td>pulse pressure (mmHg)</td>
<td>50.7 ± 5.5</td>
<td>53 ± 6.2</td>
<td>51.5 ± 6.5</td>
<td>46.9 ± 7.2</td>
<td>49.9 ± 9.9</td>
</tr>
<tr>
<td>rate (beat/min)</td>
<td>52 ± 5</td>
<td>78 ± 8*a</td>
<td>76 ± 9*a</td>
<td>71 ± 8*a</td>
<td>71 ± 8*a</td>
</tr>
<tr>
<td>cardiac output (L/min)</td>
<td>4.9 ± 0.5</td>
<td>5.4 ± 0.5*b</td>
<td>5.7 ± 0.7*b</td>
<td>5.2 ± 0.6*</td>
<td>5.1 ± 0.6</td>
</tr>
<tr>
<td>systemic vascular resistance (dyne·sec·cm⁻²)</td>
<td>1476 ± 202</td>
<td>1305 ± 189*b</td>
<td>1237 ± 265*b</td>
<td>1320 ± 213</td>
<td>1349 ± 267</td>
</tr>
</tbody>
</table>

Pulse wave velocity
Baseline values
Compared with normative population data, we noted that ultra-runners tended to have cfPWV values that were consistently (7/9) above their expected age group values, with just under half of these runners falling above the 90th percentile for their age group. This purely observational finding corroborates previous research concerning marathon runners, in which a higher cfPWV was found compared with recreationally active controls and was attributed to the high intensity of habitual marathon training and racing [30]. Altersations in baseline arterial stiffness of runners may also result from training adaptations, which could benefit performance, but have effects that endure beyond exercise and become pathophysiological during rest. In particular, it has been suggested that an augmented stroke volume resulting from training induced hypervolemia and bradycardia may contribute to increases in vascular load and an eventual fatigue and fragmenation of vascular elastin fibres [12, 30]. This resting vascular load may be further amplified by alterations in central pulse pressure and the arrival of reflected pressure waves during a prolonged systolic period [12]. Related adaptations in cardiac elastance and training/racing induced inflammation may also play a causative role for the habitual runner [31]. Notably, we did not reveal statistical significance between our overall group mean and normative data using a one-sample t test; however, we cautiously interpret this finding as our sample was relatively small and this statistical method required comparison with a normative mean created by averaging the means across age groups. Consideration of each runner’s PWV value within his own age-category may be of greater validity considering the known effect of age on cfPWV. The observation that the majority of runners were in the high end of their age category for cfPWV is noteworthy given the departure from the expected values, which makes this finding of potential clinical (if not statistical) significance. Elevated central PWV is a strong predictor of future cardiovascular events and all-cause mortality, such that an increase in PWV by 1 m/s is associated with a 15% increase in risk [29]. Thus, ultra-marathoners in the present study whose values closely approximated this magnitude of increase from age-matched norms (1 ± 1.7 m/s above the mean or 0.7 ± 1.7 m/s above the median) would be expected to have a 12–15% increase in cardiovascular risk. However, given the depth and breadth of evidence that endurance exercise is associated with a decreased risk of cardiovascular morbidity and mortality [9, 19, 28], the long-term implications for this particular group are unclear and deserving of further investigation.

PWV following prolonged exercise
Vlachopoulos et al. [30] examined changes in cfPWV following a marathon race and reported no change in cfPWV whereas we showed a reduction in arterial stiffness at the 45km mark, which approximated this same distance. Given previous research demonstrating that particularly high intensity exercise results in notable arterial stiffening [24], it is probable that the observed
affects at a race distance approximating the marathon are intensity dependent. During a discrete competitive 42.2 km marathon, the typical intensity is extremely vigorous; however, in the current investigation as part of a longer ultra-marathon race, the intensity of the first 45 km was lower, owing to necessary pacing strategies of the competitors. Davies and Thompson [7] have shown that accomplished runners who can maintain 82±3% of \( V_\text{O2 max} \) during a marathon were capable of sustaining only 67±6% of \( V_\text{O2 max} \) during an ultra-marathon of ~85 km. In line with this observation, we note that our athletes raced at 68% \( V_\text{O2 max} \), and this form of moderate intensity physical activity has repeatedly been shown to be associated with decreases in arterial stiffness post-exercise and at rest with moderate duration bouts [13, 17, 22]. The discrepancy between increased baseline arterial stiffness and acutely decreased arterial stiffness following moderate intensity exercise may, amongst other causes, be related to the increase in heart rate associated with the exercise itself [12]. During and immediately after exercise an elevated HR would serve to avoid the simultaneous arrival of the systolic and reflected pressure waves in opposition to the effect that a bradycardic training adaptation has for augmenting systolic pressure waves at rest. In the absence of extreme intensity or distance it is also likely that there is an adequate bioavailability of vasoactive substances (which are mediated by factors such as shear stress and inflammation) to sustain appropriate vasodilation and reductions in peripheral vascular resistance [8, 31], which would serve to reduce the propagation of pressure waves. Given evidence that repeated bouts of high intensity exercise increase arterial stiffness in a stepwise manner [24] and past evidence of systemic arterial stiffening with more prolonged exercise exposures [4], we propose that particularly long duration exercise may have the same eventual effect in the absence of high intensity. This is supported to some extent by our finding that cfPWV did not remain at a state of decreased stiffness (demonstrated at the 45 km mark) despite an unchanged exercise intensity. Given evidence of arterial stiffening following a more prolonged race [4], it seems possible that arterial stiffness may have continued past baseline values had the ultra-marathon been of a greater duration. Compelling experimental evidence shows that induced systemic inflammation directly contributes to arterial stiffening [31], and it is well documented that ultra-marathon is associated with increased inflammatory response [16], potentially offering another mechanistic explanation to sub-acute and more chronic stiffening. We postulate that the high-volume exposures of exercise and the associated inflammatory response may thus have residual baseline effects, explaining the above average cfPWV at baseline. In support of this theory, inflammatory responses following an off-road running race have been shown to be strongly correlated with baseline levels, such that runners who revealed the greatest increases in inflammation post-race were also the individuals with the highest levels at rest [1].

**Applanation tonometry**

**AT following prolonged exercise**

In contrast to previous findings regarding the effects of ultra-marathon racing by our group [4], we observed only an increase in \( C_2 \) (small arteries), but not \( C_1 \) stiffness (large arteries) in the current investigation. The increase in \( C_2 \) is most likely attributable to changes in the peripheral vasculature at the local working muscles and supports previous findings of differential body segment effects of exercise [8, 23]; however, the lack of an effect on \( C_1 \) differs from previous ultra-marathon findings [4]. The major difference between investigations was the volume of exercise exposure, which suggests the possible existence of a dose-response (or a threshold) effect. In our original investigation, participants ran through mountainous terrain for distances of 120–195 km, which required between 20–40 consecutive hours to complete [4]; whereas in the present investigation, the ultra-marathon was on less physically challenging terrain, averaged about 50% of the distance, and only required 11±3 h (range 8.5–13.8 h). Given evidence that inflammatory responses and associated arterial stiffening can occur one or more days post exposure [1, 3], it is possible that these responses would have presented in participants of the longer distance race, but not in the shorter ultra-marathon (or marathon distance) used in the present investigation. Systemic arterial compliance changes may also have occurred past the 90 min post-race recovery measure, but this cannot be confirmed. Despite this null finding, this data offers preliminary insight into the conditions likely associated with changes in arterial function and the role of exercise duration. Future investigations should include measures of inflammation and a longer post-race follow-up period.

Lastly, we observed strong relationships between training variables and outcomes such that participants who trained less (both in terms of session time and total weekly exercise), had greater \( C_1 \) stiffness at the 1-h mark of recovery, and participants who trained at a lower exercise intensity (RPE) had greater amounts of \( C_2 \) stiffening at the 45 km mark. This could be interpreted to suggest that lower training volumes left some competitors less prepared to deal with the vascular stress imposed by this type of exercise, which was reflected in a relative large artery stiffening at 1 h of recovery. Similarly, those who trained with less intensity may have revealed greater stiffening of the peripheral vasculature (\( C_2 \)) owing to local metabolite changes and exhaustion of endothelial function mediators [8], which did not occur to the same extent in more fit participants who were adapted to higher training stresses. This is supported by the fact that \( V_\text{O2 max} \) was also strongly associated with changes in \( C_2 \) stiffness at the 45 km point, such that the more fit participants revealed smaller changes from baseline, but remains speculative. Although group mean data did not vary from baseline at these time points, these associations explain the relationships that exist within the individual variability. It is thus possible that fitness was a further contributory factor to the inter-individual variability, which is consistent with inflammatory exercise responses [2, 5], and specific investigation into the impact of fitness on vascular response during ultra-endurance exercise is needed.

In the present investigation differences were found between measures of aortic stiffness (cfPWV) and arterial compliance (AT), which are the theoretical inverse of one another. However, it is important to note that despite their similarities (i.e., the descending aorta is indeed a large capacitance artery) these measures differ substantially and both offer strengths and limitations which have been reviewed previously [18]. One major difference is that stiffness is determined by wave velocity as measured across a discrete distance, whereas compliance is estimated across regions of the body from a single point on the distal radial artery using a transfer function. Aside from differing methods of computation, these measures also detect the properties of different segments of the body; wherein cfPWV is specific to the properties of the descending aorta alone and \( C_1 \) offers a more inclusive estimation of all capacitance vessels throughout...
the body, not just central vasculature. As such, both measures offer unique evidence and are best interpreted in relation to like measures.

Practical applications
The finding that arterial stiffness decreased at the 45km distance and then reverted back toward baseline levels with prolonged running, may indicate a role of exercise duration for affecting vascular compliance, even in the absence of extreme intensity, which is known to lead to acute stiffening. At present, it is premature to suggest that athletes alter training or racing practices to protect vascular health, as the magnitude, duration and implications of possible changes are still unclear.

Conclusion
Tracking the arterial stiffness of ultra-marathon runners throughout prolonged exercise revealed a change toward more distensible arteries following 45km of moderate intensity running. Although the intensity remained consistent, this effect was not maintained following an additional 30km of running.

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