Systemic Arterial Compliance Following Ultra-Marathon

Authors   **J. F. Burr**[1], **S. S. D. Bredin**[2], **A. Phillips**[3], **H. Foulds**[3], **A. Cote**[1], **S. Charlesworth**[1], **A. C. Ivey**[3], **T. C. Drury**[3], **R. Fougere**[1], **D. E. R. Warburton**[3]

Affiliations   [1] University of British Columbia, Cardiovascular Physiology and Rehabilitation Laboratory, Physical Activity and Chronic Disease Prevention Unit, Vancouver, Canada
[2] University of British Columbia, Cognitive and Functional Learning Laboratory, Vancouver, Canada
[3] University of British Columbia, Experimental Medicine, Vancouver, Canada

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Correspondence
Dr. Jamie F. Burr
University of British Columbia
Cardiovascular Physiology and
Rehabilitation Laboratory
Physical Activity and Chronic
Disease Prevention Unit
Rm 205
Unit II Osborne Centre
V6T 1Z3 Vancouver
Canada
Tel.: +1/604/822 1337
Fax: +1/604/822 9222
j.burr@physicalactivityline.com

Abstract
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There is a growing interest in training for and competing in race distances that exceed the marathon; however, little is known regarding the vascular effects of participation in such prolonged events, which last multiple consecutive hours. There exists some evidence that cardiovascular function may be impaired following extreme prolonged exercise, but at present, only cardiac function has been specifically examined following exposure to this nature of exercise. The primary purpose of this study was to characterize the acute effects of participation in an ultra-marathon on resting systemic arterial compliance. Arterial compliance and various resting cardiovascular indices were collected at rest from 26 healthy ultra-marathon competitors using applanation tonometry (HDI CR-2000) before and after participation in a mountain trail running foot race ranging from 120–195 km which required between 20–40 continuous hours (31.2 ± 6.8 h) to complete. There was no significant change in small artery compliance from baseline to post race follow-up (8.5 ± 3.4–7.7 ± 8.2 mL/mmHg^{x100}, $p=0.65$), but large artery compliance decreased from 16.1 ± 4.4 to 13.5 ± 3.8 mL/mmHg^{x10} ($p=0.003$). Participation in extreme endurance exercise of prolonged duration was associated with acute reductions in large artery compliance, but the time course of this effect remains to be elucidated.

Introduction
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The popularity of prolonged duration ultra endurance races, such as Ironman-distance triathlon and ultra-marathon races (any event >42.2 km), has increased dramatically in recent years [16]. At present, relatively little is known regarding the cardiovascular effects of participation in ultra endurance exercise, but our laboratory and others have demonstrated a transient change in cardiac dynamics indicative of cardiac fatigue as a result of participation [25]. In particular, it has been shown that left ventricular systolic and diastolic function are impaired following ultra endurance running, but factors such as myocardial damage or strong vagal reactivation do not appear to be responsible for these reductions [36]. Decrements in cardiac function, such as a reduced ejection fraction and stroke volume, are understood to be influenced by the interaction of ventricular and arterial characteristics [39]. Specifically, it has been shown that the coupling between arterial and ventricular elastic properties is inversely related to cardiac ejection frac-

tion and that this is an important determinant of cardiac performance [29]. Sub-optimal coupling between the ventricle and the vasculature has been implicated in reductions of cardiac performance during maximal exercise [29]. Although work has been done to investigate the effects of prolonged endurance exercise on cardiac function, arterial function (the other primary component of this system) has yet to be characterized under similar conditions.

Arterial Compliance
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In general, arterial stiffness at rest is recognized as a cardiovascular risk factor [19,23] due to the increased workload placed on the myocardium. However, habitual aerobic exercise, has been shown to promote the maintenance of a compliant arterial system [5,8], which is associated with a reduced risk for cardiovascular disease and ischemic events owing to an improvement of coronary artery perfusion [13], and a lowering of both pulse pressure and wall stress [3]. In con-

Table 1 Descriptive statistics and training background of ultra-marathon mountain trail running race study participants by race distance and gender categories.

Race Distance	Gender	Age (yr)	Height (cm)	Body Mass (Kg)	Rest HR (bpm)	SBP (mmHg)	DBP (mmHg)	Training days/week	Training km/week	Years of participation
195 km	female (n=2)	38.5±7.8	162.9±11.8	60.1±5.2	61±9	120±8	67±6	5.5±2.1	74±37	6.5±2.1
	male (n=9)	42.1±6.1	176±6.8	72.9±5.6	52±9	127±9	70±7	5.3±1.2	92±22	5.7±2.9
120 km	female (n=7)	44.9±11.3	161.7±3	59.6±4	60±9	121±13	71±7	4.4±1.3	64±11	2.6±1.3
	male (n=8)	48.1±6	176.7±7.5	79.4±12.3	60±6	131±5	76±6	4.9±0.7	84±31	4.6±2.3

yr=year, cm=centimetre, kg=kilogram, bpm=beats per minute, SBP=systolic blood pressure, DBP=diastolic blood pressure

trast to the widely accepted beneficial effects of aerobic exercise on arterial compliance, some evidence suggests that habitual high volume resistance training may lead to unfavourable effects on arterial compliance [26], although this literature remains controversial. Acute, short duration bouts of both aerobic and resistance exercise result in a transient increase of arterial compliance [7,15,30]; however, this effect appears to be intensity and frequency dependent considering evidence that supra-maximal (sprint) exercise cumulatively diminishes central arterial compliance in a stepwise manner with successive bouts [34]. In a 4-week training program of previously sedentary individuals performing moderate intensity aerobic exercise, it has been demonstrated that significant changes in arterial compliance can occur in as little as 1 week [5]. As such, it is very possible that even acute (individual) exercise sessions such as an ultra-marathon could have meaningful effects on vascular function.

Presently some evidence exists of an association between the number of marathons or ultra-marathons completed and myocardial fibrosis in life-long athletes, which would function to decrease ventricular compliance [43]. Without an understanding of vascular function under similar conditions, it is difficult to interpret how the interactions of ventricular-vascular coupling may occur. Recent investigations comparing regular marathon runners to matched controls have demonstrated a higher baseline aortic stiffness [18,41] and a higher than expected atherosclerotic disease prevalence in this habitually active population [27,35], which may exert some influence on cardiovascular coupling and performance. Interestingly, however, these same investigators did not observe acute changes in arterial compliance following a marathon distance race [41]. Typically, marathon racing would be expected to be performed at a higher intensity (%VO$_2$) than ultra marathon racing, as a result of the duration and length of each race. As such, prediction of the effects of prolonged duration, lower intensity exercise is complicated and poorly understood.

The purpose of this study was, thus, to determine the acute effects of participation in an ultra-marathon on resting systemic arterial compliance before and after ultra marathon participation. We hypothesized that prolonged exercise would lead to increased arterial compliance, with similar magnitude changes to those findings reported following a short duration acute bout of moderate intensity exercise.

Methods
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26 competitors (45±8.2 years, range 28–56 years, 9 female) participating in a mountain trail running ultra-marathon volunteered for this study. Participants had previous ultra marathon experience ranging from 2–110 races (mean 19±23, median 21.2), with prior participation in 3±3 races in the same calendar year. The event took place mid-summer through mountainous terrain in British Columbia, Canada with a peak height of 2 300 m and low of 600 m including 4 major ascents. The temperature ranged from 30° Celsius (86° Fahrenheit) during daytime hours to 6° Celsius (42.8° Fahrenheit) during the evening. Inclusion criteria for participants required a pre-race health screening, and successful completion of the ultra-endurance distance allowing capture by the investigators. 5 participants on whom baseline information was collected were excluded from follow-up as a result of not completing the race at the finish line due to premature withdrawal resulting from fatigue (n=3), hyponatremia (n=1) or injury (n=1).

2 simultaneous ultra marathon races with a common finish line were used. 11 participants (9 m, 2 f) completed a 195 km distance and 15 individuals (8 m, 7 f) covered a distance of 120 km. Descriptive participant statistics are provided in ⊙ **Table 1**. All participants were required to complete the Physical Activity Readiness Questionnaire for safe exercise participation and 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. The authors have read and understood IJSM's ethical standards document and this study meets the ethical standards of the journal [11].

Arterial compliance was measured non-invasively via applanation tonometry (HDI CR-2000, Hypertension Diagnostics, Eagan, Minnesota) for diastolic pulse contour analysis. The theoretical basis for the method of systemic arterial compliance using the area under the diastolic pulse wave has been described in detail [21] and significant associations have been reported with intima media thickness [21] and the beta-index with regional aortic stiffness [5]. This method of vascular assessment using waveform shape analysis may be superior for measuring systemic arterial compliance, as opposed to segmental pulse wave velocity [20], and is based on a modified 2 element Windkessel model that allows for the calculation of large central (capacitive) artery and small (oscillatory) artery compliance. According to Beltran et al., who coined the terms "large capacitive" and "small oscillatory" compliance, and who were involved with the design of the HDI applanation tonometer, "the capacitive component assesses the arterial storage capacity, which is a function predominantly of the larger conduit arteries. The oscillatory or reflective component is related to the cushioning effect of compliance, at the arterial reflective sites that are thought to reside primarily in small arteries and arterioles, and at branching sites of small arteries" [2]. The calculations of small and large arterial compliance are accomplished by the software of the applanation tonometry unit using a paradigm described in detail by McVeigh et al., which divides total systemic resistance into individual components using mathematical modeling [24]. This technique has been validated with invasive and non-invasive testing [6,33,44], has been applied to exercise studies investigating

acute short duration exercise [30], and has been shown to be of clinical and physiological relevance [33].

Prior to data acquisition, participants were instructed to lie quietly in the supine position for 5–10 min. Noise reducing ear protection was provided. After stabilizing the wrist and maximizing signal strength, radial artery tonometry measurements were collected using the right wrist with an automated sphygmomanometer affixed to the upper left arm. 30 s measurements were taken in duplicate with the average used for analysis. The HDI CR-2000 allows for estimation of related cardiovascular indices including pulse pressure, cardiac ejection time, stroke volume, and cardiac output based on calculations using radial artery waveforms, oscillometric pulse readings, body surface area, and age [12].

All baseline measures were performed at least 1 day prior to competition. Height was measured using a wall mounted stadiometer with the participants standing barefoot, feet together and against the baseboard. Body mass was measured with a minimum of clothing to the nearest kilogram using a digital scale, re-calibrated before each measurement (Tanita TBF-300WA, Arlington Heights, Illinois). Blood pressure and heart rate (HR) were collected simultaneously with tonometric measures. Immediately following the race, participants were met at the finish line, and post-race weight was recorded. The participant was then shuttled in a research vehicle a short distance (approximately 800 m) to a quiet temperature controlled room for reassessment of arterial compliance and related cardiovascular measures, which were completed within approximately 20–60 min post finish.

Statistical analysis

Change scores (delta) were calculated from baseline to post-race measures for each variable, and analysis of variance (ANOVA) was used to determine whether race distance (195 k vs. 120 km), or gender significantly influenced outcomes. We lacked sufficient representation to further divide by discrete age groups. Since no differences existed by race distance or gender, comparisons of variables between baseline and post-race measures were performed using paired samples t-tests, with participants of both race distances considered together as "ultra-marathoners". Associations between training volume (self reported training frequency and km per week), racing experience (total number of races and races in the current season), years of participation, race time (pace), and age with baseline and pre-post change scores were examined using Pearson correlation. All analyses were performed using SPSS software (version 16.0; SPSS, Inc., Chicago, IL). Significance for all tests was set at p < 0.05 a priori. Results are reported as mean ± SD.

Results

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Participants required between 19.9–41.9 h to complete an ultra marathon distance race. Specifically, participants required 25.8 ± 3.5 h and 37.4 ± 4.3 h to complete the 120 and 195 km distances, respectively. There was no significant difference in the average pace maintained by participants in the longer (5.3 ± 0.7 km/h) or shorter race (4.7 ± 0.7 km/h), nor was there any difference in pace according to age or gender. There was an expected association between participant age and baseline large artery compliance (r = −0.43, p = 0.03) as well as between training volume (km/wk) and both large (r = 0.57, p = 0.001) and small

Table 2 Comparison of pre-race (baseline) and post-race (follow-up) cardiovascular characteristics of participants competing in an ultra-marathon mountain trail running race lasting longer than 25 h.
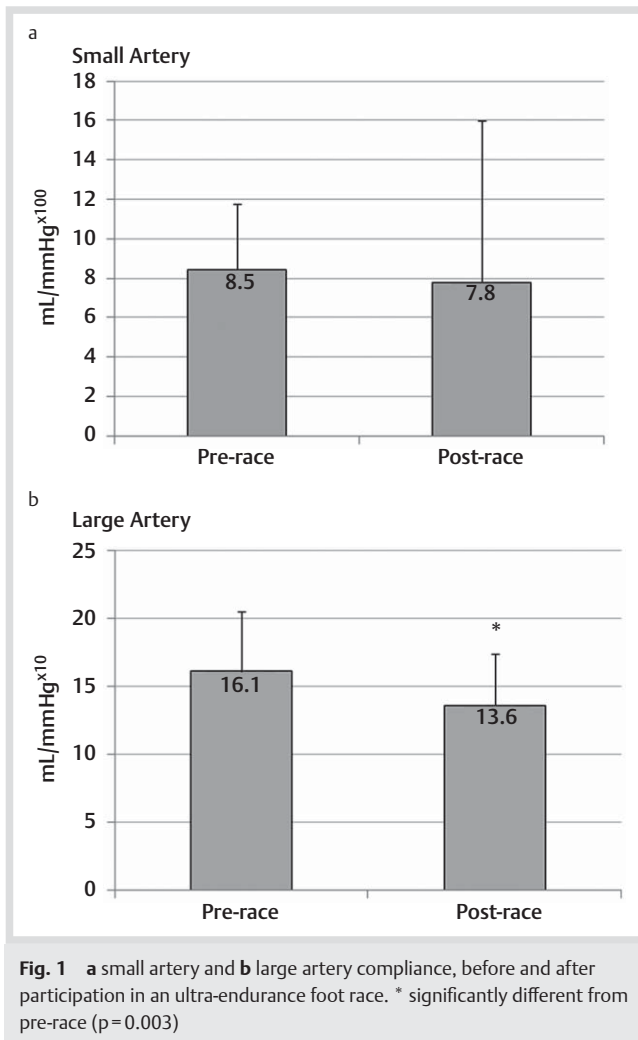
s	Pre-race	Post-race	*p* value
body mass (kg)	70.6 ± 11.6	69.1 ± 11.4	0.02
SBP (mmHg)	126 ± 10	118 ± 9	0.001
DBP (mmHg)	72 ± 7	66 ± 7	<0.001
HR (bpm)	57 ± 10	73 ± 12	<0.001
SVR (dyne·sec·cm^{-5})	1436 ± 154.1	1300.7 ± 128.3	0.001
pulse pressure (mmHg)	54.4 ± 6.1	52.7 ± 5.3	0.1
cardiac output (L/min)	5.1 ± 0.6	5.5 ± 0.5	0.001
ejection time (msec)	3.3 ± 17.8	3.1 ± 27.1	0.002
stroke volume (ml/beat)	91 ± 13	75 ± 14	<0.001

kg = kilogram, SBP = systolic blood pressure, DBP = diastolic blood pressure, SVR = systemic vascular resistance

(r = 0.41, p = 0.04) artery compliance at baseline. Reductions in both large and small arterial compliance, from baseline to post-race, were strongly associated with baseline values (large r = 0.6, p = 0.001, small r = 0.8, p = < 0.001), but relationships between participant age and changes in arterial compliance from baseline were not significant. Similarly, racing experience, years of ultra-endurance participation, and weekly training frequency had no relationship to the degree of arterial compliance at baseline or the changes observed following the race. All cardiovascular data, pre and post-race, are presented in ◉ **Table 2**. From pre-race baseline, body weight decreased an average of 1.5 ± 3.1 kg and significant decreases were evident in post-race systolic blood pressure (8 ± 10 mmHg) and diastolic blood pressure (6 ± 7 mmHg). Pulse pressure did not change from baseline, whereas systemic vascular resistance decreased 135.2 ± 181.2 dyne·sec·cm^{-5}. Estimated cardiac output increased statistically, though not meaningfully (0.3 ± 0.5 L/min) given the typical accuracy of this direct measure. Ejection time was reduced (20.1 ± 29.1 msec), while there was a decrease in stroke volume (16 ± 12 mL/beat) and increase in HR (16 ± 11 bpm). Small artery compliance did not significantly change as a result of participation in the ultra endurance running race (◉ **Fig. 1a**); whereas large artery compliance decreased by 2.6 ± 4.1 mL/mmHg^{x10} (◉ **Fig. 1b**). Analysis of the delta scores revealed no effect of race distance or gender on arterial compliance (large or small) or any other cardiovascular variable.

Discussion

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We evaluated the effects of participation in a mountain trail running ultra-marathon race on acute arterial compliance. This is the first study to examine the effects of extreme prolonged aerobic exercise on vascular function. In agreement with previously published literature, at baseline we found that older participants had less compliant arteries compared to younger participants and that participants who reported a greater aerobic exercise training stimulus (km/wk) demonstrated greater baseline compliance [5,31]. The major novel finding of the current investigation is that large artery compliance decreased following participation in ultra endurance exercise. Furthermore, this effect occurred to the greatest extent in those participants who had the highest levels of baseline large artery compliance, as can be seen in ◉ **Fig. 2**. The changes in arterial compliance observed in the present study, are of a magnitude that has been

a

Small Artery

b

Large Artery

Fig. 1 **a** small artery and **b** large artery compliance, before and after participation in an ultra-endurance foot race. * significantly different from pre-race (p = 0.003)

Fig. 2 Individual participant large artery compliance before and after ultra marathon race participation.

shown previously to exist between health and disease. For example, differences of 3.1 ml/mmHg^{x10} for large artery compliance and 1.9 ml/mmHg^{x100} for oscillatory compliance have been reported between healthy controls and patients with essential hypertension [45], a known cardiovascular risk factor. Using comparable systemic arterial compliance measures, other groups have reported alterations in arterial compliance ranging from 17–22% [22,30], which are similar in magnitude to the changes observed in the current investigation (16%).

Akin to our results for large and small artery compliance respectively, other investigators have shown that central arterial compliance decreases after acute high intensity exhaustive exercise, while peripheral compliance is increased [32]. This differential effect between small and large arterial compliance may be related to metabolite-induced vasodilation in the exercising limbs, which is less likely to affect the large central arteries [32]. However, aortic pulse wave velocity measures employed during exercise have demonstrated that aortic compliance is reduced in comparison to baseline resting levels [37]. Given a prolonged exhaustive exercise stimulus, such as an ultramarathon, it is possible that this effect may be sustained post exercise as opposed to returning to baseline levels following exercise cessation.

In contrast to our results, albeit indirectly, other investigators using the same arterial compliance measurement techniques have demonstrated that a single bout of moderate intensity
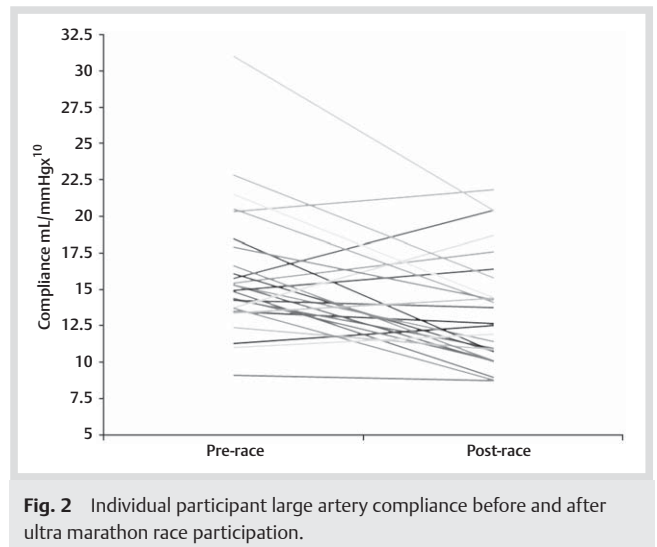
cycle ergometer exercise increased small, but not large, arterial compliance [15,30]. It is likely that the self-selected exercise intensity of participants in our study was similar to the moderate intensity prescription used in the existing literature (considering the relatively slow average pace and prolonged race duration); however, substantial differences exist in the exercise stimulus (i.e. 30 min vs. 30 h). As such, the disparity in our findings seems most likely to be explained by differences in exercise duration. Possible explanations for the observed decreases in large artery compliance include impaired endothelial function [42] and altered sympathetic adrenergic vasoconstrictor tone [9] as a direct result of exhaustive exercise. Clear associations between inflammation and aortic stiffness have been reported [46], and strong relationships exist between ultra-marathon running, oxidative stress [38] and inflammation [14]. Rather convincingly, experimentally induced acute systemic inflammation has been demonstrated to cause arterial stiffness and this could be related to the unfavourable effect of inflammation on nitric oxide bioavailability [40] and endothelial function [4]. High level exercise-induced oxidative stress has also been associated with alterations in endothelial function, and has even been suspected to enhance the development of atherosclerosis [17]. This relationship, along with the findings of the current investigation, may help to explain the recent links between marathon participation, coronary atherosclerosis [18,27], and increased aortic stiffness [41]. These factors may also play a causative role in the observed increase of myocardial fibrosis in life-long veteran endurance athletes [43]. It has been postulated that the repeated exposure of exercise-related oxidative stress makes trained athletes better able to tolerate inflammation and free radical activity [1]; however, the present exercise stimulus may exceed this tolerable level.

As of yet, we are unable to mechanistically dissect the underlying causes of decreased arterial compliance, as this investigation is the first to objectively characterize the vascular response to prolonged exercise. Interestingly, we observed a baseline effect such that those who reported greater training mileage revealed an increased compliance at rest; however, the greatest decreases in compliance occurred in those with the highest values pre-race. The consequences of these changes on arterial compliance on both short term risk and longer term health are unclear. It seems possible that the lower intensity and duration training

that frequently accompanies preparation for an ultra-marathon has beneficial effects on health by maintaining a compliant arterial system, while the actual race (at least transiently) increases arterial stiffness and the potential risk for an ischemic event. It is also possible that the ultra marathon exercise stimulus itself, which acutely manifests as post-race stiffness, chronically leads to the beneficial adaptations observed at rest. However, this is purely speculative at present, and the time course of acute changes in arterial compliance following exercise of varying intensity and duration remains poorly understood.

Traditional cardiovascular variables revealed expected results after a prolonged endurance exercise stimulus [36]. Following a period of quiet recovery, systolic and diastolic blood pressure revealed a post exercise hypotensive response, as would typically be expected following prolonged exercise [28]. The observed post-race reduction in stroke volume may be influenced in part by the reduction in body weight (indicating a loss of plasma volume), but may also be related to impaired cardiac efficiency (or fatigue), which occurs after prolonged exercise [36]. This is known to affect cardiac ejection fractions as a result of reduced systolic and diastolic peak strain rates [10]. The decreased cardiac efficiency and reduced stroke volume may also be influenced directly by the diminished arterial compliance, which is known to increase the work of the heart [3] through venticular vascular coupling.

This study has a number of limitations. Firstly, the non-invasive measurement of systemic arterial compliance can only be calculated using indirect models of circulation, which introduce a possibility of estimation error. For example, the calibration of tonometry measures against brachial blood pressure could potentially influence post-exercise measures. However, given the methodological challenges of field based research immediately following race completion (wherein more invasive measures are not feasible), the use of the current systemic stiffness model is justified considering the specific limitations of alternative non-invasive measures examining regional and local stiffness [20]. Secondly, alterations in HR are known to effect measures of arterial compliance calculated using applanation tonometry (augmentation index); however, the expected effect would be in the direction of improved arterial compliance [42]. As such, we are confident that the relatively modest increase in post-exercise HR is not responsible for our finding of decreased capacitive arterial compliance. A methodological limitation of our study was the somewhat varied time between exercise cessation and the initiation of post-race measures, which occurred due to unanticipated race-related/human factors. Longer delays (or more rest) would be expected to decrease the effects of exercise on arterial compliance. In light of this, it is possible that the observed effects of prolonged exercise on arterial compliance (in both large or small arteries) could be underestimated in some of the subjects who were tested after a longer delay. Our follow-up examination of change scores from pre to post-race revealed no significant differential effect of race distance or gender on arterial compliance. This may suggest that there is a threshold beyond which the well known effects of acute exercise on arterial compliance are reversed, and that both race distances (or durations) exceeded this point and affected both genders similarly. It is also possible, however, that some comparisons and interactions (i.e. distance by gender) were underpowered for these comparisons given the small number of female participants who completed the longer race distance. Lastly, it should be noted that an association exists between arterial compliance

and the menstrual cycle and this effect, on which data was not collected from female participants, could affect gender responses.

Due to the heterogeneity of our sample, and the current paucity of data regarding the time course of the apparent reduction in arterial compliance following extreme prolonged exercise, it should be noted that this paper is primarily descriptive at this point in time. Future investigations should include well controlled serial measures of post-race compliance to determine the time-course changes of this effect. Studies would also benefit from a thorough examination of training practices, including objective quantification of training and racing frequency, intensity, and duration. Further assessment of aerobic fitness and nutritional intake would be beneficial to determine if the effects on arterial compliance are augmented or mitigated as a result of these factors. At present, there is also very little known about the acute dose-response relationship between the volume of acute physical activity and vascular effects, thus studies designed to specifically examine increasingly larger volumes of physical activity and the associated effect on arterial compliance are warranted .

Conclusion
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With the accumulating evidence that extremely high volume aerobic exercise may be associated with decreases in cardiovascular function and the growing number of persons undertaking training and racing at this distance, a better understanding of the effects of ultra endurance exercise health is needed. We have shown that participation in aerobic exercise for between 20–40 h as part of a mountain trail running ultra-marathon foot race led to acute decreases in large artery compliance. The evidence presented may help to explain potential links between existing findings regarding cardiac fatigue during following ultra endurance racing, and high volume aerobic exercise training with increased atherosclerosis and arterial stiffness in marathon runners [18,41]. These changes may be related to the oxidative and inflammatory effects reported to occur during ultra endurance running [17,40].

Conflict of Interest: The authors declare no conflict of interest.

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