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Eight months of marathon school training reduced blood pressure, systemic vascular resistance and extracellular water volume

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The effects of an eight-month marathon school training program on blood pressure (BP) and underlying hemodynamics were examined in 45 participants and 43 controls. Hemodynamics were recorded using whole-body impedance cardiography, radial tonometric pulse wave analysis, and third-finger BP measurements during passive head-up tilt. The mean ages were 40.9 and 42.2 years, and body mass indexes (BMI) 25.1 and 25.8 kg/m^2, respectively. Marathon training decreased mean weight (-1.6 kg), fat percentage (-2.7%), and BMI (-0.5 kg/m^2) and increased maximal oxygen uptake (+3.2 ml/kg/min) and insulin sensitivity (+0.013 units) ($p < 0.03$ for all). During head-up tilt, systolic BP and cardiac output decreased, while diastolic BP, heart rate, and systemic vascular resistance (SVR) increased, but training did not affect these posture-induced changes. Initial aortic and third finger systolic/diastolic BP were numerically but not significantly lower in the marathon vs. control group (by 3.4/2.3 and 5.5/4.5 mmHg, respectively, $p > 0.075$). Final BP values were significantly lower in the marathon group (by 7.2/4.5 and 10.9/10.2 mmHg, respectively, $p < 0.01$). Marathon training reduced SVR by 167 dyn×s/cm^5×m^2($p = 0.041$), and extracellular water volume by 0.34 L ($p = 0.045$). To conclude, aerobic exercise training appears to lower BP, a significant cardiovascular risk factor, by reducing SVR and decreasing extracellular water volume.

Keywords Blood pressure, Exercise, Hemodynamics, Head-up Tilt, Marathon

Cardiovascular disease is the leading cause of morbidity and all-cause mortality in most of the world, while a great proportion of the world's population is characterized by insufficient level of physical activity and poor cardiorespiratory fitness[1]. Elevated blood pressure (BP) is the most significant cardiovascular risk factor leading to the loss of active life years in the whole world[2,3]. Regular physical exercise has a wide range of direct and indirect physiological effects that are considered beneficial for cardiovascular health[1].

Generally, higher levels of regular physical activity, exercise training, and cardiorespiratory fitness are correlated with reduced risk of cardiovascular disease[1]. Both endurance and resistance training are considered to moderately lower BP in hypertensive and normotensive subjects[4]. Regular exercise is recommended as a non-pharmacological measure to lower BP in primary hypertension[5], and it is also considered to favorably influence insulin sensitivity and the lipoprotein profile in plasma[4,6,7]. Acute aerobic exercise is known to lower BP for several hours, but it is unclear to what extent recurrent short-term decreases in BP contribute to the long-term effects of exercise on BP[8]. In fifty hypertensive subjects, 8–12 weeks of treadmill exercise decreased systolic and diastolic daytime ambulatory BP by -6 and -3 mmHg, respectively, without influencing arterial compliance and cardiac output[9].

Although personalized exercise prescription is endorsed in the treatment of hypertension[4], all studies do not consistently indicate that physical exercise is beneficial. A randomized cross-over study found that acute resistance or aerobic exercise temporarily enhanced measures of wave reflection in 21 healthy adult males[10]. A cross-sectional study found higher muscle sympathetic nerve activity (MSNA) in 16 endurance athletes than in 15 untrained control subjects[11]. In 70–77 year-old male and female Norwegian subjects ($n = 1567$), five years of supervised exercise, either high-intensity interval training or moderate-intensity continuous training, had

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little effect on cardiovascular risk profiles without influences on cardiovascular events[12]. In some individuals regular and increased physical activity may even adversely affect BP, plasma lipids, and cardiovascular health[6,13]. A prospective study comprising more than 25,000 Korean individuals reported a direct association between physical activity and coronary artery calcium scores, and the 5year increase in coronary artery calcium score was higher in participants engaged in physical activity than in inactive subjects[14]. Altogether, the exact dose-response relationship between the extent and duration of exercise and the putative reduction in cardiovascular disease risk remains unclear[6].

Although our active life is predominantly spent in the upright position, most studies have focused on hemodynamic recordings performed in supine position[15–17]. In the upright posture, blood pools to the lower extremities, decreasing cardiac output. This activates the sympathetic nervous system, which increases heart rate and systemic vascular resistance (SVR) to maintain the level of BP[18,19,20]. The changes in BP during orthostatic challenge are not uniform, as either an increase or a decrease in BP may be observed[21]. In a 17-year-long follow-up of hypertensive subjects, exaggerated systolic BP response to standing independently predicted adverse cardiovascular events[22].

The aim of this prospective follow-up study was to examine whether 8 months of professionally instructed marathon-school training could lower BP and to investigate the potential underlying mechanisms using non-invasive recordings of cardiac output, SVR, large artery stiffness, and extracellular water volume. Since exercise can reduce sympathetic tone, increase parasympathetic tone, and decrease β-receptor sensitivity in the heart[1,23,24], we examined whether marathon training induced changes in functional cardiovascular regulation by assessing hemodynamic responses to passive head-up tilt.

Subjects and methods

Study participants

Voluntary participants of a professionally instructed marathon school (Varala Sports Institute, Tampere, Finland; www.varala.fi/en/) were invited to participate in hemodynamic recordings and laboratory testing at the beginning and at the end of the training protocol. The marathon school period was from the end of August till the end of May each year, and the time difference between the initial and final recordings was ~8 months. The 43 controls with corresponding sex distribution and age were recruited from our ongoing investigation on hemodynamics in primary and secondary hypertension currently comprising 1442 subjects, the enrolment of whom has been previously described[25]. The study protocols were approved by the ethics committee of the Tampere University Hospital (codes R06086M and R07110M) and registered in international databases (Eudra-CT 2006-002065-39, clinicaltrials.gov NCT01742702). The protocols comply with the Declaration of Helsinki. Signed informed consent was obtained from all participants.

Alcohol consumption was evaluated as standard drinks (~ 12 g of absolute alcohol) per week. Smoking history and cigarette consumption in estimated pack-years was recorded. Weight and fat percentage were monitored using InBody 770 (InBody Co., Ltd., Seoul, Korea). All participants were in sinus rhythm.

Evaluation of exercise performance and supervision during the marathon school

Evaluation of exercise performance was based on lactate measurements from fingertips during a heart rate monitored (Suunto T6, www.suunto.com) running exercise in the beginning and at the end of the marathon school. Lactate determination is widely recognized outcome measure in exercise testing for evaluating aerobic and anaerobic thresholds[26]. The participants ran for a minimum of three and maximum of seven km on a 300-meter-long inside track, during which lactate measurements were taken after each completed km. Running speed was progressively increased so that heart rate was steadily elevated by 5–10 beats/min after each km. The distance covered provided the information about the running speed. The final lap represented the maximal performance of each participant. Aerobic and anaerobic thresholds and maximal oxygen uptake were estimated using mathematical algorithms based on multivariate adaptive regression splines as described earlier[27]. This algorithm created a piece-wise linear model providing a stepping block into non-linearity after grasping the concept of linear regression[27].

Based on the evaluated physical performance of the participants, the exercise programs were individually designed and supervised by a professional instructor (MJ). The training aimed to improve (i) basic fitness and muscle strength, (ii) running technique and speed resistance, and (iii) finalize physical performance for a marathon run (www.tesku.fi/2019/12/maratonkoulu/). Twenty-four participants recorded and stored 63 (23) % [mean (standard deviation, SD)] of their training data with heart rate monitors. Before the last 3 months their mean weekly exercise time was 214 (88) min at heart rate 130 (8) beats/min representing 75 (4) % of their estimated maximal heart rate.

During the last 3 months of the marathon school, the instructor (MJ) escorted all subjects to a supervised 26-kilometer-long running exercise once per week in subgroups of corresponding physical performance.

Laboratory analyses

Blood samples were collected after approximately 12 h of fasting: at the beginning of the study from the control group, and both at the beginning and end of the study from the marathon group. Plasma C-reactive protein (CRP), potassium, sodium, creatinine, cystatin C, lipids, and glucose analyses were performed using Cobas Integra 700/800 (F. Hoffmann-LaRoche Ltd., Basel, Switzerland) or Cobas 6000, module c501 (Roche Diagnostics, Basel, Switzerland), and plasma insulin using electrochemiluminescence immunoassay (Cobas e411, Roche Diagnostics). Quantitative insulin sensitivity check index (QUICKI) was calculated by the use of fasting plasma insulin and glucose concentrations[28]. Blood counts were analyzed using ADVIA 120 or 2120 (Bayer Health Care, Tarrytown, NY, USA).

Hemodynamic recordings: blood pressure, pulse wave analysis, and impedance cardiography

Before the recordings the participants were instructed to withhold from caffeine, smoking, and heavy meals for ≥ 4 h, and avoid the use of alcohol for ≥ 24 h. To minimize the known acute effects of exercise on hemodynamics[29], the participants were instructed to avoid all strenuous exercise for 24 h before the recordings. Beat-to-beat hemodynamic data was recorded for 5 min in the supine position, followed by 5 min of passive head-up-tilt[18] according to a previously described protocol[25,30]. The mean values of each minute during the 10-minute recording were calculated. For pulse wave velocity (PWV) and ECW only the supine values (0–5 min) were used.

A tonometric sensor (Colin BP-508T, Colin Medical Instruments Corp., USA) was used to capture radial pulse wave form, calibrated four times during each 10-min recording by contralateral brachial BP measurements. Aortic BP and pulse wave reflections were derived using the SphygmoCor® software (PWMx device, AtCor Medical, Australia)[31]. Heart rate, stroke volume, cardiac output, ECW, ECW balance, and aortic-to-popliteal PWV were determined using whole-body impedance cardiography (CircMon®, JR Medical Ltd., Estonia), as previously described[25,32]. SVR was calculated from the tonometric BP and cardiac output by CircMon®[32]. Stroke volume, cardiac output, and SVR were related to body surface area and presented as indexes (SI, CI, and SVRI, respectively). The repeatability and reproducibility of this measurement protocol is good[18,30,33]. BP was also measured from the left 3rd finger using a continuous plethysmographic method (Finometer®, Finapres Medical Systems, the Netherlands).

Statistical analyses

Assuming a training-induced reduction of 6 (8) mmHg in systolic BP[34], the minimum required participant number was 40 subjects in both groups (alpha 0.05, Beta 0.80). The characteristics of the groups were compared using the independent samples t-test for normally distributed variables and the Mann-Whitney U-test for non-normally distributed variables. Levene's test was used to test the homogeneity of variances. Sex distributions were compared using the Chi-Square test. When the analyses required the use of covariates, univariate analyses were applied for between group comparisons. Percent change in plasma volume was evaluated using the formula by Strauss et al. [100 × (initial hemoglobin/final hemoglobin) × (final hematocrit × 0.01/initial hematocrit× 0.01) -100][35]. To examine the within group changes in marathon school participants, either t-dependent test for normally distributed variables or Wilcoxon signed rank test for non-normally distributed variables were applied.

The hemodynamic analyses comprised minutes 1–5 in supine posture and minutes 6–10 during head-up tilt. The generalized estimating equation (GEE) was applied to analyze the hemodynamic data. This method enabled the analysis of repeated measurements over a 10-minute period to examine the influence of the study group, changes in variables during the study, and the interaction between group and posture on the hemodynamic variable of interest, i.e. whether the change in this variable differed between groups in response to head-up tilt. Linear scale response was applied, and the autoregressive option was chosen for the correlation matrix, since successive measures of hemodynamics are autocorrelated. The results were presented as means, and SDs, standard errors of the mean (SE), or medians and 25th -75th percentiles. SPSS version 29.0 (IBM SPSS, Armonk, NY, USA) was used, and $P < 0.05$ was considered significant.

Results

Study participants, results of blood tests, physical performance

Four participants dropped out during the follow-up: two during the first month, one after 4 months, and one after 7 months (the last drop-out due to pregnancy). As participation in the training was not a part of the study protocol but was based on voluntary participation in the marathon school, these four subjects were excluded from the analyses. The final marathon school group comprised 15 men and 30 women aged 21 to 55 years, and the controls 17 men and 26 women aged 24 to 58 years (Table 1).

Altogether 15 (33%) marathon school participants and 20 (46%) controls used medications that remained unchanged during the study. The medications in the marathon school participants were antidepressant (1), anxiolytic (1), enalapril (1), estrogen for hormone replacement therapy (HRT) (1), topical estrogen (1), formoterol (1), glucocorticoid inhalation (2), hormonal intrauterine device (2), hypnotic (1), proton pump inhibitor (1), tamoxifen (1), thyroxine (2), and warfarin (1). The medications used by the controls were antidepressants (3), antihistamine (2), beclomethasone inhalation (1), estrogen for HRT (2), estrogen-progestin combination (6 for contraception, 1 for HRT), progestin for contraception (2), topical estrogen (1), hormonal intrauterine device (3), proton pump inhibitor (1), and thyroxine (1). There were no other differences in medication use between the groups, except for a higher prevalence of estrogen-progestin combination users in controls ($p = 0.002$). Excluding users of estrogen or progestin (alone or combined), or including their use as a covariate, altered the p-values but did not change the significance of the hemodynamic results reported below.

The proportions of male and female participants did not differ among the 43 controls and 45 marathon school participants (Table 1). The mean age, alcohol consumption, proportion of current smokers, height, initial weight, and initial body mass index (BMI) were similar in both groups. The time difference between the initial and final measurements was 37 weeks for the controls and 34 weeks for the marathon school participants ($p = 0.054$). Body weight and BMI were reduced by the marathon school training. Subsequently, final body weight and BMI were lower in the marathon school participants than in the controls (Table 1).

Initial blood hemoglobin, hematocrit, and plasma concentrations of CRP, potassium, creatinine, glucose, insulin, and insulin sensitivity as evaluated using QUICKI, did not differ between the controls and marathon school participants, while plasma sodium was 1.0 mmol/l lower in the latter group (Table 2). After 8 months of training, a reduction in fasting plasma insulin and an increase in insulin sensitivity were observed in the marathon group (Table 2). They also presented a 2.7% reduction in fat percentage, and moderate increases in the

	Control	Marathon school	*p*-value
Number	43	45	–
Male/Female	17/26	15/30	0.545†
Age (years)	42.2 (9.8)	40.9 (8.0)	0.647
Age range (years)	24.2–57.7	21.7–55.3	–
Post-menopausal participants (n)	6	5	0.547
Alcohol consumption (drinks/week)	3 [1–5]	2 [1–3]	0.285
Current smoker (n)	3	2	0.419†
Height (cm)	172 (11)	171 (9)	0.260
Time difference between measurements (weeks)	37 [19–41]	34 [32–35]	0.054
Body mass index (kg/m^2)			
Initial	25.8 (3.2)	25.1 (3.3)	0.350
Final	26.0 (3.1)	24.6 (2.8)	**0.030**
Change	+0.2 (1.0)	-0.5 (1.4)	**0.008**
Weight (kg)			
Initial	77.0 (13.4)	73.7 (13.2)	0.243
Final	77.4 (13.3)	72.0 (11.7)	**0.049**
Change	+0.4 (2.8)	-1.6 (4.0)	**0.008**
Auscultatory brachial systolic BP (mmHg)#			
Initial	122.2 (11.8)	119.5 (10.6)	0.279
Final	121.4 (9.8)	116.5 (10.4)	**0.038**
Change	-0.8 (9.8)	-3.0 (9.8)	0.341
Auscultatory brachial diastolic BP (mmHg)#			
Initial	76.1 (9.8)	73.8 (10.6)	0.300
Final	75.4 (6.9)	71.8 (8.2)	**0.045**
Change	-0.9 (7.3)	-2.0 (1.4)	0.540
Tonometric radial systolic BP (mmHg)‡			
Initial	119.8 (12.3)	115.5 (11.6)	0.100
Final	119.6 (12.8)	112.8 (9.8)	**0.006**
Change	-0.2 (10.1)	-2.7 (9.6)	0.229
Tonometric radial diastolic BP (mmHg)‡			
Initial	71.3 (9.7)	68.7 (7.8)	0.163
Final	71.5 (8.8)	67.2 (8.2)	**0.006**
Change	+0.2 (7.8)	-1.4 (7.4)	0.324

Table 1. Demographic and anthropometric characteristics of the study subjects. Mean (SD), median [25th -75th percentile], or number of subjects; BP, blood pressure; t-test or †chisquare test; ‡mean BP during 10-minute head-up tilt; $n = 33$ for the auscultatory BP measurements in controls. Significant values are in bold.

evaluated aerobic and anaerobic thresholds, and maximal oxygen uptake (Table 2). Plasma volume, evaluated from the initial and final hemoglobin and hematocrit values[35], did not significantly change in the marathon school participants [mean (SE) change + 0.26 (1.62) %].

Blood pressure results

Initial auscultatory measurements of brachial BP, and tonometric measurements of radial BP, did not differ between the groups, while final values of brachial BP and tonometric BP were lower in the marathon group (Table 1). In between-groups comparisons, the changes in brachial or radial BP during the follow-up did not significantly differ in the groups (Table 1).

In response to passive head-up tilt, systolic BP decreased, and diastolic BP increased similarly in both groups at the beginning and at the end of the study, i.e., no significant group × posture interactions were observed (Figs. 1 and 2; Table 3). Initial systolic and diastolic BPs at the aortic level were numerically but not significantly lower in the marathon group than in controls (-3.4/-2.3 mmHg, $p > 0.166$, Fig. 1a and d), while the final aortic systolic/diastolic BPs were -7.2/-4.5 mmHg lower in the marathon group ($p < 0.01$, Fig. 1b and e). The numerical decreases in mean aortic BPs were not significantly greater in the marathon group (-3.5/-3.1 mmHg) than in the control group, when calculated over the 10-minute recording period ($p > 0.074$, Fig. 1c and f). The within-group changes in aortic BP during the study were not significant in either group (Table 3).

Initial BPs at the finger level were also numerically, but not significantly, lower in the marathon school participants (by -5.5/-4.5 mmHg, $p > 0.075$, Fig. 2a and d). However, the final systolic/diastolic BPs were -10.9/-10.2 mmHg lower in the marathon group ($p < 0.001$, Fig. 2b and e). The 5.4 mmHg difference in the reduction of finger systolic BP was not significantly different between the groups ($p = 0.120$, Fig. 2c), whereas the -6.1 mmHg greater reduction in

	Initial values (month 0)			Marathon school follow-up analyses (month 8)[#]		
	Control	Marathon school	*p*-value	Final values	Change	*p*-value for change
Hemoglobin (g/l)	144 (12)	141 (13)	0.240	140 (13)	-1 (10)	0.535
Hematocrit (%)	41.7 (3.0)	40.6 (3.3)	0.117	41.2 (3.6)	0.6 (3.0)	0.204
Fasting plasma						
C-reactive protein (mg/l)	0.6 [0.5–1.7]	0.7 [0.5–1.4]	0.644[†]	0.8 [0.5–1.85]	0.0 [-0.2–0.5]	0.446[‡]
Potassium (mmol/l)	3.8 (0.2)	3.7 (0.3)	0.446	3.7 (0.3)	0.0 (0.3)	0.888
Sodium (mmol/l)	140.6 (1.8)	139.6 (1.5)	**0.003**	139.8 (1.8)	+0.3 (2.1)	0.423
Creatinine (µmol/l)	74 (13)	71 (11)	0.190	72 (12)	+1 (6)	0.958
Glucose (mmol/l)	5.3 (0.6)	5.2 (0.4)	0.314	5.1 (0.4)	-0.1 (0.35)	0.067
Insulin (mU/l)	8.1 (6.8)	6.1 (3.3)	0.092	5.2 (3.5)	-0.8 (2.5)	**0.030**
QUICKI	0.360 (0.033)	0.375 (0.039)	0.067	0.389 (0.048)	+0.013 (0.037)	**0.029**
eGFR (ml/min/1.72 m^2)	96 (12)	100 (12)	0.057	100 (13)	0 (8)	0.996
Fat percentage	n.d.	27.8 (7.0)	n.d.	24.4 (7.4)	-2.7 (3.0)	**< 0.001**
Evaluated aerobic threshold (ml/kg/min)	n.d.	24.5 (2.3)	n.d.	27.6 (3.2)	3.1 (2.0)	**< 0.001**
Evaluated anaerobic threshold (ml/kg/min)	n.d.	32.1 (4.5)	n.d.	35.8 (5.0)	3.7 (2.2)	**< 0.001**
Evaluated maximal oxygen uptake (ml/kg/min)	n.d.	40.0 (5.5)	n.d.	43.2 (6.3)	3.2 (3.2)	**< 0.001**

Table 2. Laboratory results in controls ($n = 43$) and marathon school participants ($n = 45$). Mean (SD) or median [25th -75th percentile]; [#]fat percentage was missing from 5 and other laboratory values were missing from one marathon school participant; independent t-test for comparisons between controls and marathon school participants, dependent t-test for changes among marathon school participants except for the following analyses: [†]Mann-Whitney U-test, [‡]Wilcoxon signed rank test. eGFR, estimated glomerular filtration rate; QUICKI, quantitative insulin sensitivity check index; n.d., not determined. Significant values are in bold.

finger diastolic BP was significantly more pronounced in the marathon group ($p = 0.034$, Fig. 2f). The within-group reductions in finger systolic and diastolic BP were also significant in the marathon group (Table 3).

Heart rate, stroke volume, cardiac output, and systemic vascular resistance

When shifting from supine to upright posture, heart rate and SVRI increased, while stroke index and cardiac index decreased (Figs. 3 and 4). Initial and final heart rates during head-up tilt were similar in both marathon and control groups (Fig. 3a, b and c). In between-group comparisons, initial stroke index values did not show differences, while the mean final stroke index was 4.4 ml/m^2 higher in the marathon than in the control group ($p = 0.017$). Also, the initial and final stroke indexes decreased more in response to head-up tilt in the marathon group ($p < 0.01$ for group × posture interactions, Fig. 3d and e). When calculated over the 10-minute recording period, the mean changes in stroke index during the study were not significantly different between the groups ($p = 0.07$, Fig. 3f). In within-group analyses, heart rate and stroke index decreased similarly in response to upright posture in the initial and final recordings (Table 3).

In between-group comparisons, initial and final cardiac index values did not differ between the study groups (Fig. 4a, b and c). However, in both the initial and final recordings, the decrease in cardiac index during upright posture was more pronounced in the marathon group ($p < 0.012$, Fig. 4a and b). In within-group analyses, cardiac index values did not change during the study in either group (Table 3). Initial SVRI values were not significantly different between the groups ($p = 0.141$), while the final mean SVRI was 286 dyn×s/cm^5×m^2 lower in the marathon group ($p = 0.002$) (Fig. 4d and e). In between-group analysis, the change in SVRI during the study was not significantly different (-146 dyn×s/cm^5×m^2, $p = 0.124$) (Fig. 4f). However, in the within-group analysis the reduction in SVRI in the marathon group was significant (Table 3).

Large arterial stiffness and extracellular water volume

There were no differences in the initial and final values of PWV (Fig. 5a and b), or the changes in PWV during follow-up (Fig. 5c; Table 3). The initial and final ECW volumes were not significantly different in the groups (Fig. 5d and e). However, in between-group comparisons, the decrease in ECW volume was -0.37 L ($p = 0.032$) in the marathon school participants compared to controls in unadjusted analysis, and -0.34 L ($p = 0.045$) in analysis adjusted for the parallel change in body weight (Fig. 5f). In within-group analyses, the changes in ECW volume were not significant (Table 3).

DISCUSSION

High BP is the most significant risk factor worldwide for increasing the burden of disease[2,3]. Therefore, non-pharmacological approaches to reducing BP are of major interest[1]. Regular physical activity has been recommended as a first-line treatment of elevated BP[36]. In the present study we examined the influences of supervised running training on BP, hemodynamics and volume balance in 45 participants versus 43 controls. The mean weekly exercise time of 214 min, monitored during the initial 6 months, is considered to provide substantial health benefits[36]. In order to avoid the effects of acute exercise on BP and ECW volume[29], the participants were instructed to abstain from strenuous exercise for 24 h prior to the recordings. When compared

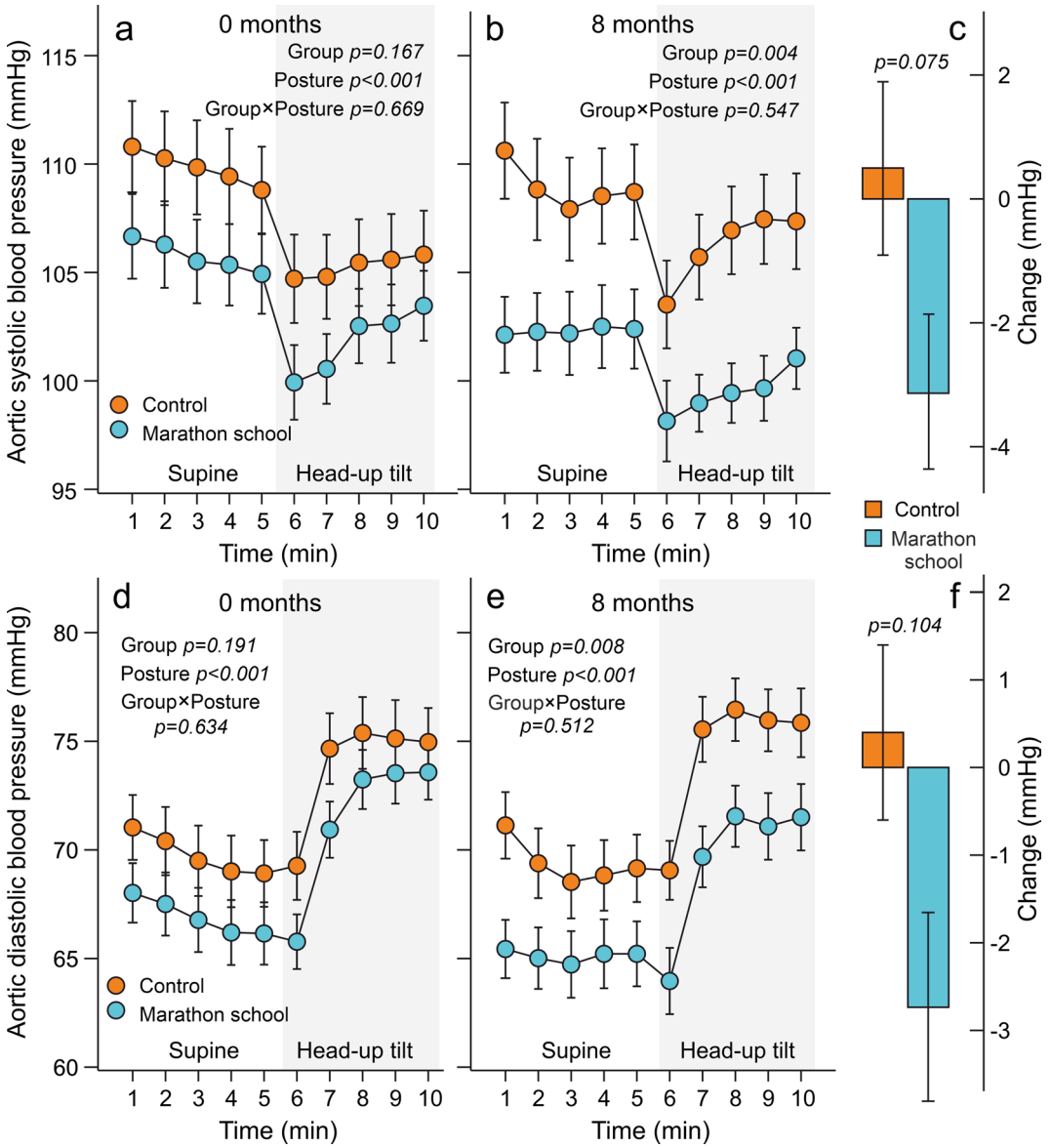

Fig. 1. Aortic systolic (**a**, **b**) and diastolic blood pressure (**d**, **e**) at 0 months and at 8 months in 43 controls and in 45 marathon school participants, along with between-group comparisons of the average changes in these variables (**c**, **f**) over the follow-up period during 10-minute recordings comprising both supine and upright postures. Statistical analyses were by generalized estimating equations, mean and SEM depicted.

with corresponding BP changes in the controls, 8 months of marathon training did not significantly reduce aortic BP (-3.5/-3.1 mmHg, ($p = 0.075$/$p = 0.138$). At the finger level, mean BP was reduced by -5.4/-6.1 mmHg ($p = 0.120$/0.034) over the 10-minute recording period, with a greater decrease in diastolic BP observed in the marathon group. When compared with controls, the above changes were accompanied by a -0.34-liter change in ECW volume ($p = 0.045$). Although all reductions in BP were not statistically significant, the more pronounced separation of BP values between the study groups was evident at the end of the study.

Many studies on the effects of exercise on BP have been performed in unsupervised participants[14,37,38]. Here, the marathon school consisted of regular weekly contacts with the instructor, and the adherence to the program was high with only four dropouts during the eight-month period. Weekly instructor-escorted 26-km-long running exercises during the last 3 months ensured that the participants adhered to the training program. Although information from individual exercise diaries was not complete, objective training effects were observed: mean weight, fat percentage, and BMI were decreased, and insulin sensitivity was increased. The measures of physical performance were improved, as evaluated aerobic and anaerobic thresholds and maximal oxygen uptake were increased in the marathon group. The control group presented with small non-significant increases in body weight and BMI (+0.4 kg and +0.2 kg/m^2, respectively). Previously, average weight gain in midlife has been reported to be about 0.75 kg per year[39], and average increase in fat mass about 0.6 kg/year[40].

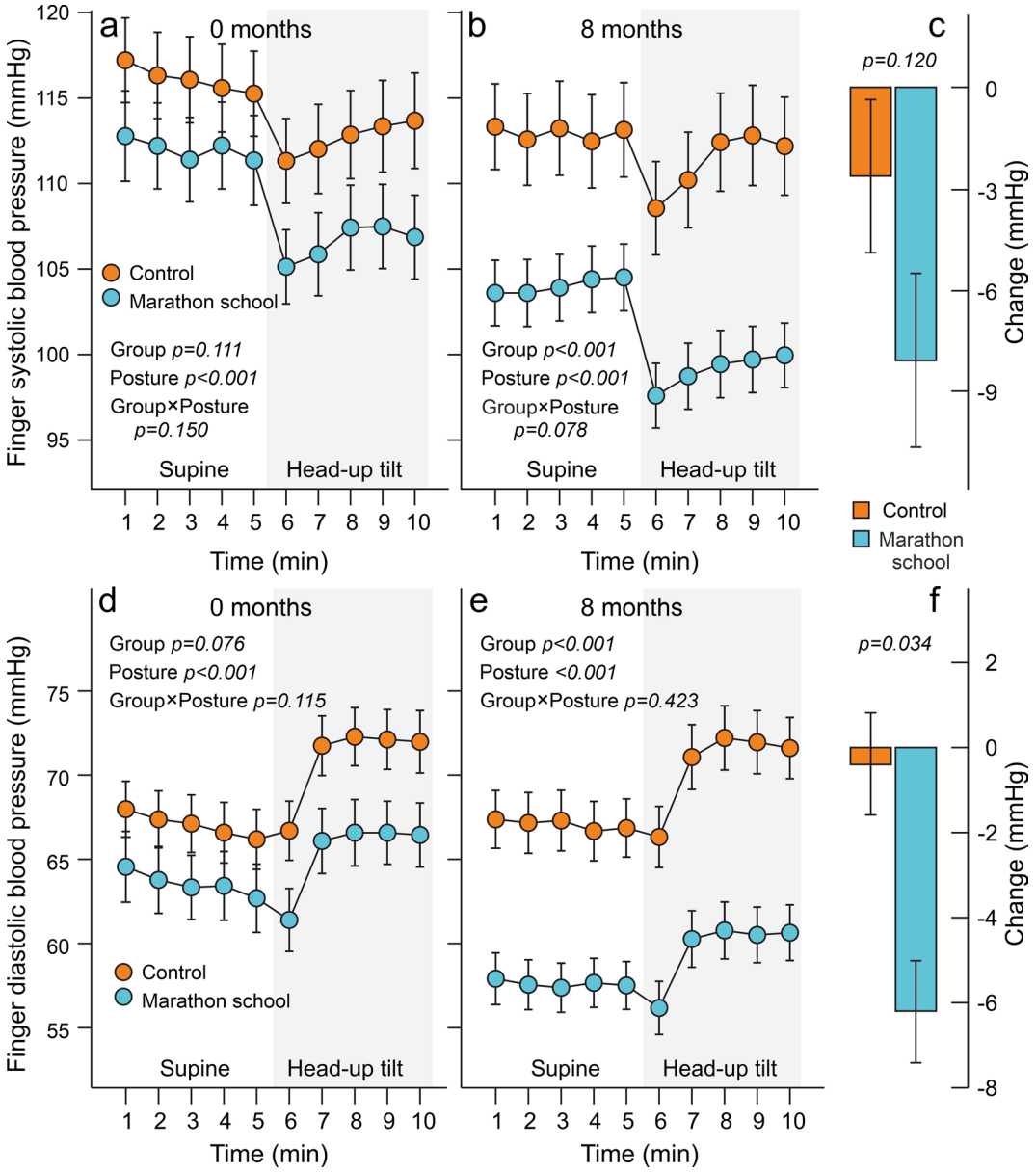

Fig. 2. Third finger systolic (**a**, **b**) and diastolic (**d**, **e**) blood pressure at 0 months and at 8 months in 43 controls and in 45 marathon school participants, and between-group comparisons of the average changes in these variables (**c**, **f**) over the follow-up period during 10-minute recordings. Statistics by generalized estimating equations, mean and SEM.

Based on previous studies, aerobic endurance exercise can induce several physiological adaptations, resulting in lower BP, decreased vascular resistance, alleviation of cardiovascular risk factors, and a reduced body weight[1,6]. Although exercise-induced reductions in BP have been relatively small, even minor decreases can have significant public health impacts due to the high prevalence of hypertension and its association with cardiovascular diseases[41,42]. A review comprising 394 exercise participants and 239 controls found that aerobic endurance training reduced ambulatory daytime BP by -3.2/-2.7 mmHg[43]. A European consensus document states that endurance training reduces BP by -7.4/-4.5 mmHg in hypertensive subjects and by -2.9/-1.9 mmHg in normotensive subjects[4]. In resistant hypertension, eight to twelve weeks of treadmill exercise reduced ambulatory 24-hour BP by -6/-3 mmHg and alleviated BP elevation during treadmill test in 24 patients versus 26 non-trained controls[9]. In the present study, the marathon school participants showed non-significant -3.5/-3.1 mmHg reductions in aortic BP, and more pronounced -5.4/-6.1 mmHg reductions in finger BP versus controls. It seems likely that with a larger sample size, which would increase statistical power and reduce variability, the observed changes in aortic BP could reach statistical significance. Overall, our BP findings are consistent with the previously reported results[4,9,43].

Initial hemodynamics were very similar in the present study groups. The only difference was the more pronounced decrease in the initial stroke index value during head-up tilt in the marathon group, a difference

Variable	Group	Within-group change in variable	*p*-value, comparison between 0- and 8-month visits	*p*-value, comparison of visit × posture interactions
Aortic systolic BP (mmHg)	Control	0.5 (18.1)	0.856	0.523
	Marathon school	-3.2 (10.6)	0.114	0.668
Aortic diastolic BP (mmHg)	Control	0.4 (13.0)	0.844	0.751
	Marathon school	-2.1 (11.3)	0.196	0.659
Finger systolic BP (mmHg)	Control	-2.6 (23.3)	0.464	0.639
	Marathon school	**-8.0 (19.9)**	**0.008**	0.698
Finger diastolic BP (mmHg)	Control	-0.4 (15.6)	0.852	0.307
	Marathon school	**-6.2 (15.9)**	**0.011**	0.981
Heart rate (1/min)	Control	0.7 (12.3)	0.716	0.371
	Marathon school	1.1 (9.9)	0.470	0.327
Stroke index (ml/m^2)	Control	-1.9 (12.3)	0.324	0.676
	Marathon school	1.0 (6.6)	0.318	0.624
Cardiac index (l/min/m^2)	Control	0.03 (0.52)	0.680	0.994
	Marathon school	0.10 (0.53)	0.225	0.971
SVRI (dyn×s/cm^5×m^2)	Control	-17 (655)	0.868	0.495
	Marathon school	**-167 (544)**	**0.041**	0.888
Pulse wave velocity (m/s)	Control	0.00 (1.88)	0.986	n.a.
	Marathon school	0.04 (1.39)	0.847	n.a.
Extracellular water volume (l)	Control	0.12 (2.40)	0.756	n.a.
	Marathon school	-0.21 (2.45)	0.567	n.a.

Table 3. Within-group changes in the hemodynamic variables from month 0 to month 8 in the study participants. Values are mean (SD); SD, standard deviation; BP, blood pressure; SVRI, systemic vascular resistance index; n.a., not applicable. Significant values are in bold.

that persisted in the final recordings. We monitored BP at the aortic, radial and finger levels, and found that the training-induced changes in different parts of the arterial tree were not uniform. There change in aortic BP was not significant (-3.5/-3.1 mmHg, $p = 0.075/p = 0.138$), while a significant decrease in finger diastolic BP was observed (-5.4/-6.1 mmHg, $p = 0.120/0.034$) compared to the control group. These deviations may be due to differences in vascular compliance and wave reflection[44]. Allan et al. reported that systolic BP values measured by finger plethysmography did not align well with brachial oscillometric BP values, while better agreement was observed between finger and brachial diastolic BPs[44]. Of note, central rather than peripheral BP may better reflect the pressure load on vital organs and be more relevant to the pathogenesis of cardiovascular diseases[45,46]. Moreover, the reduction in BP at the finger level may be partially explained by alterations in thermoregulation, as the hand functions as an important heat-exchange organ with arteriovenous anastomoses and dense vascularization[47]. In the fingers, blood flow can increase by up to fivefold, enabling the removal of excess heat through vasodilation when blood flow is directed to the anastomoses[47,48]. Regular training for a marathon can be expected to induce changes in thermoregulation.

In skeletal muscle, exercise increases capillary density and improves blood flow capacity by enlarging the caliber of arterial supply vessels[49]. In the cardiac muscle, regular physical exercise decreases β_1 and $\beta_2$receptor expression or sensitivity, and reduces sympathetic and increases parasympathetic tone to the heart[1,23,24]. Neurovascular coupling may also be altered by higher physical activity[50]. Ten physically active men and ten sedentary controls had similar MSNA at rest. However, during lower body negative pressure, only in sedentary men did forearm vascular resistance directly correlate with MSNA[50]. Here, we examined whether regular exercise training could induce hemodynamic changes during passive head-up tilt. This procedure activates the sympathetic nervous system, and increases heart rate and SVR to compensate for the effects of increased blood pooling to the lower extremities[18–20]. Despite previous findings indicating reduced sympathetic and increased parasympathetic tone following endurance training[1,23], eight months of supervised exercise did not induce significant changes in hemodynamics during autonomic challenge caused by upright posture in the present study. Therefore, other explanations for the training-induced reductions in BP should be considered.

Some previous investigations without a control group have reported reductions in BP after exercise training[34,37,38]. In laboratory measurements using two ten-second recordings of brachial BP in 138 participants, 6 months of unsupervised training for a marathon reduced aortic BP by -4/-3 mmHg when compared with baseline BP[37]. Among 68 participants, 17 weeks of unsupervised marathon training reduced BP by -4/-2 mmHg versus initial values, and induced 3–5% increases in left and right ventricular cavity sizes, respectively[38]. In 237 untrained healthy subjects volunteering for their first marathon, unsupervised training reduced aortic compliance by -7%, decreased SVR by -4%, and brachial BP by -4/-3 mmHg versus initial values, but no control group was included[34]. In the forementioned study, brachial BP was measured in semi-supine position in the laboratory during two ten-second-long recordings at baseline and after 6 months of training[34]. A control group is essential for the interpretation of the effects of interventions, as in studies focused on the treatment of hypertension, BP

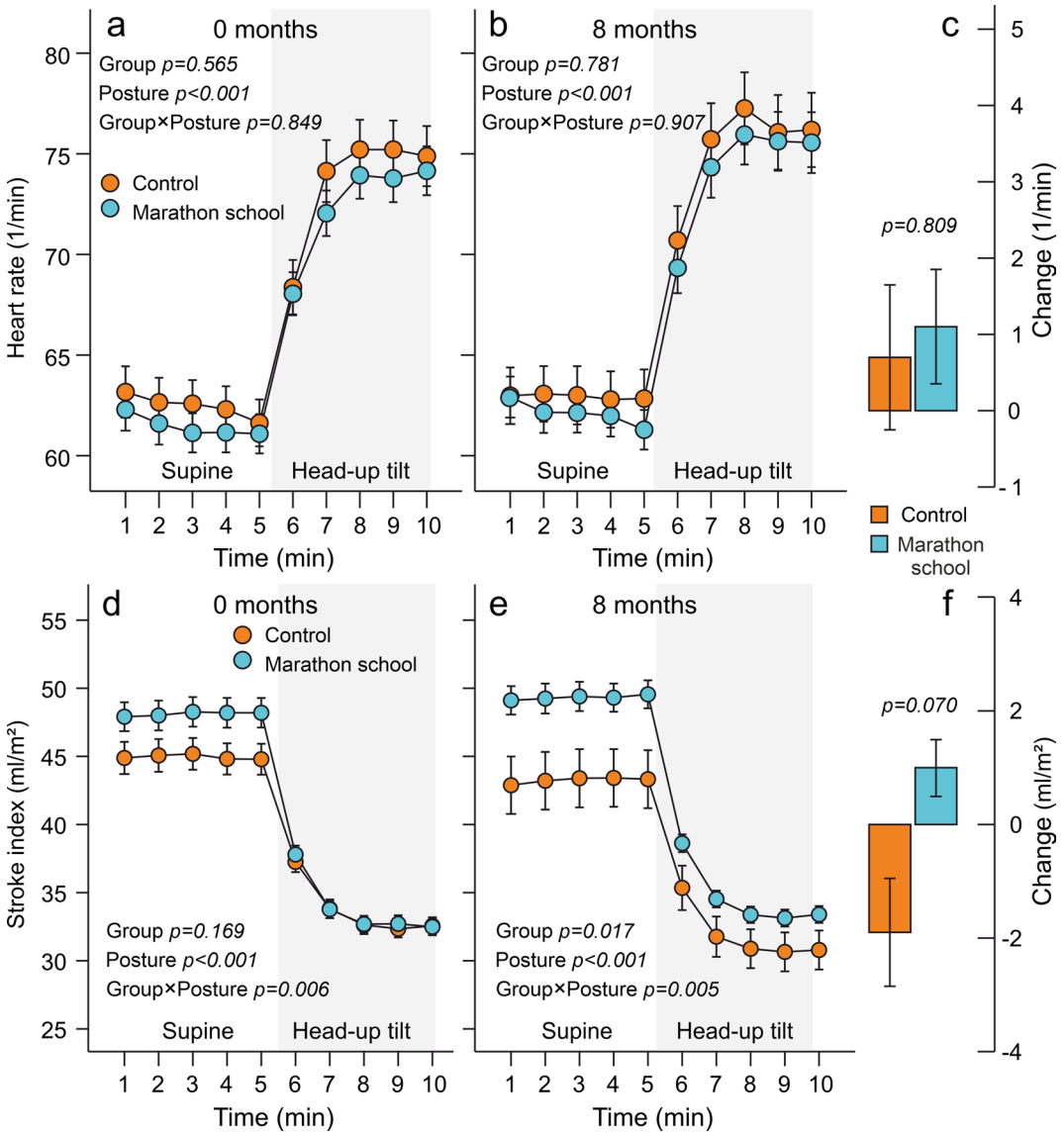

Fig. 3. Heart rate (**a**, **b**) and stroke index (**d**, **e**) at 0 months and at 8 months in 43 controls and in 45 marathon school participants, and between-group comparisons of the average changes in these variables (**c**, **f**) over the follow-up period during 10-minute recordings. Statistics by generalized estimating equations, mean and SEM.

usually decreases during the follow-up even in subjects of the placebo group[51,52]. Without controls the present -8.0/-6.0 mmHg reduction in finger BP versus initial values would have somewhat exaggerated the influence of marathon school training on the level of BP.

In bioimpedance measurements, ECW volume makes up to 35–45% of total body water[53]. ECW volume can influence blood volume: when ECW volume decreases, it may decrease plasma and blood volume, thus reducing BP[54]. Recently, Wolff et al. stated that the role of blood volume as a regulator of BP has been underrated[54]. Sodium homeostasis, volume status, and BP regulation are closely related[55]. Previously, sodium intake has been related to ECW volume in 510 subjects without cardiovascular medications[56]. The present non-significant -3.5/-3.1 mmHg change in central BP and -5.4/-6.1 mmHg change in finger BP were associated with a -0.34-litre reduction in ECW volume versus untrained controls, a finding that may be related to the impact of long-term training on sodium balance. Endurance training has been found to induce sodium losses of ~50 mmol/hour due to sweating in athletes[57].

Previously, acute heavy exercise was found to increase plasma volume[58,59]. Five hours of heavy exercise per day for 4 days increased plasma volume by 8.5% and decreased heart rate among 13 volunteers[58]. An extreme endurance trial was found to increase plasma albumin among six young men, and increase total body water in bioimpedance measurements[59]. However, these findings have limited applicability to the present long-term effects. The marathon school participants were instructed to avoid heavy exercise for 24 h before the measurements. We found no changes in the heart rate, evaluated plasma volume[35], or plasma sodium concentration in the marathon group, findings that rule out an increase in plasma volume in our long-term study.

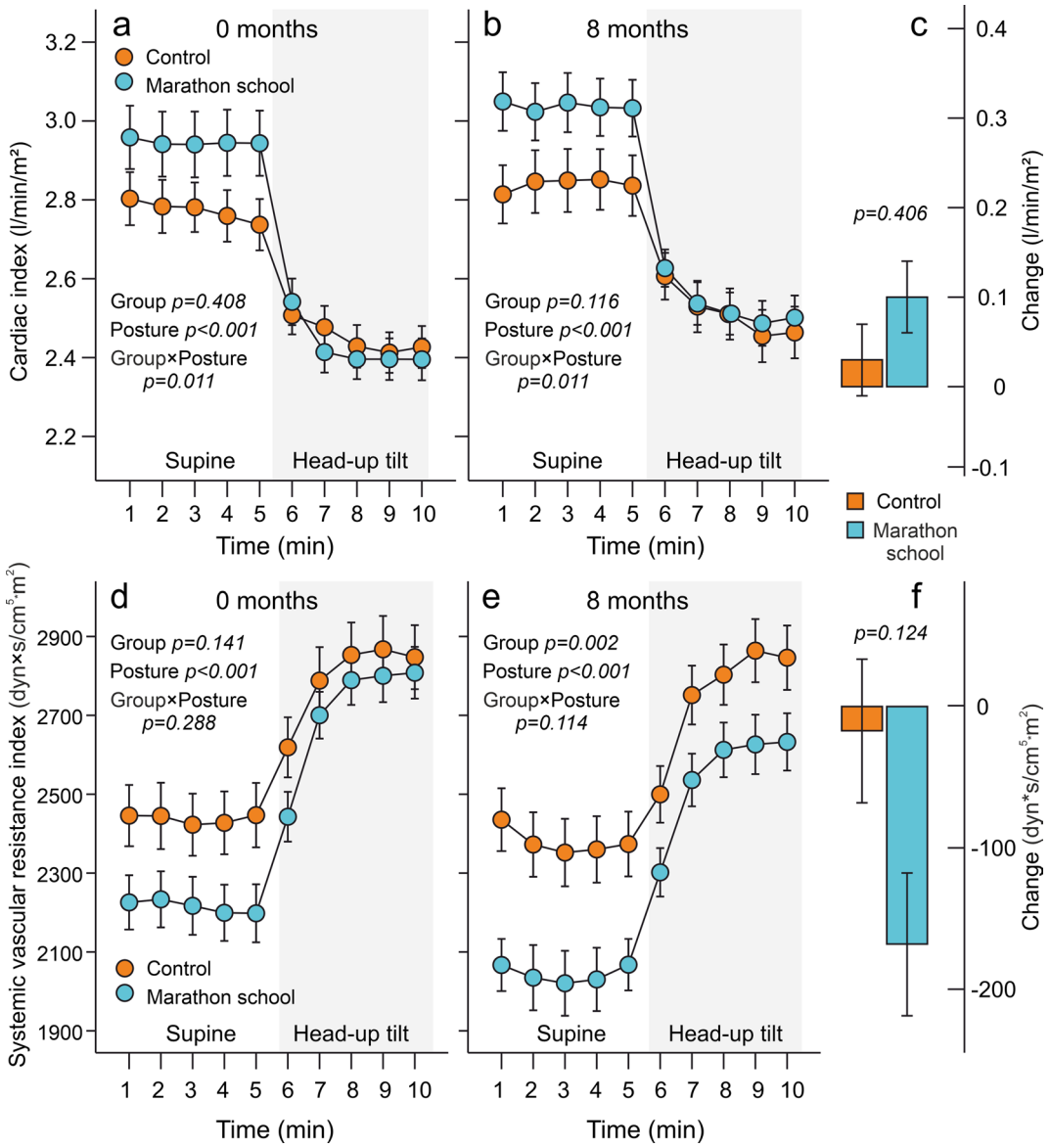

Fig. 4. Cardiac index (**a**, **b**) and systemic vascular resistance index (**d**, **e**) at 0 months and at 8 months in 43 controls and in 45 marathon school participants, and between-group comparisons of the average changes in these variables (**c**, **f**) over the follow-up period during 10-minute recordings. Statistics by generalized estimating equations, mean and SEM.

Increased large artery stiffness contributes to the age-related increase in systolic BP and pulse pressure[7]. The completion of a 246-km-long ultra-marathon race acutely increased arterial stiffness among 20 competitors, as judged by 22.6% elevation in carotid-femoral PWV, in the absence of significant changes in BP[60]. In contrast, 6 months of training reduced aortic stiffness versus initial values among 138 marathon completers[37]. However, no controls were included in the above study, and final BP was -4/-3 mmHg lower than the pre-training values[37]. The level of BP is an important determinant of the measures that evaluate aortic stiffness[61]. In the Whitehall II study comprising 5196 participants, higher physical activity level was related with a slower age-related progression of aortic stiffness, a finding that was independent of conventional vascular risk factors[62]. In our study, 8 months of marathon school did not affect PWV, indicating that large artery stiffness was not changed.

In the present study, the initial level of SVRI was not significantly different between the groups, but final SVRI was lower in the marathon group. Also, a within-group reduction in SVRI was observed in the marathon group, while cardiac output values were similar in the beginning and at the end of the study in both groups. Some reports have suggested that the beneficial effects of exercise training may be mediated via its effects on endothelium-mediated control of arterial tone and microvascular angiogenesis[63–65]. Such effects can be expected to reduce peripheral arterial resistance, supporting the view that a reduction in SVRI may explain the training-induced of lowering in BP.

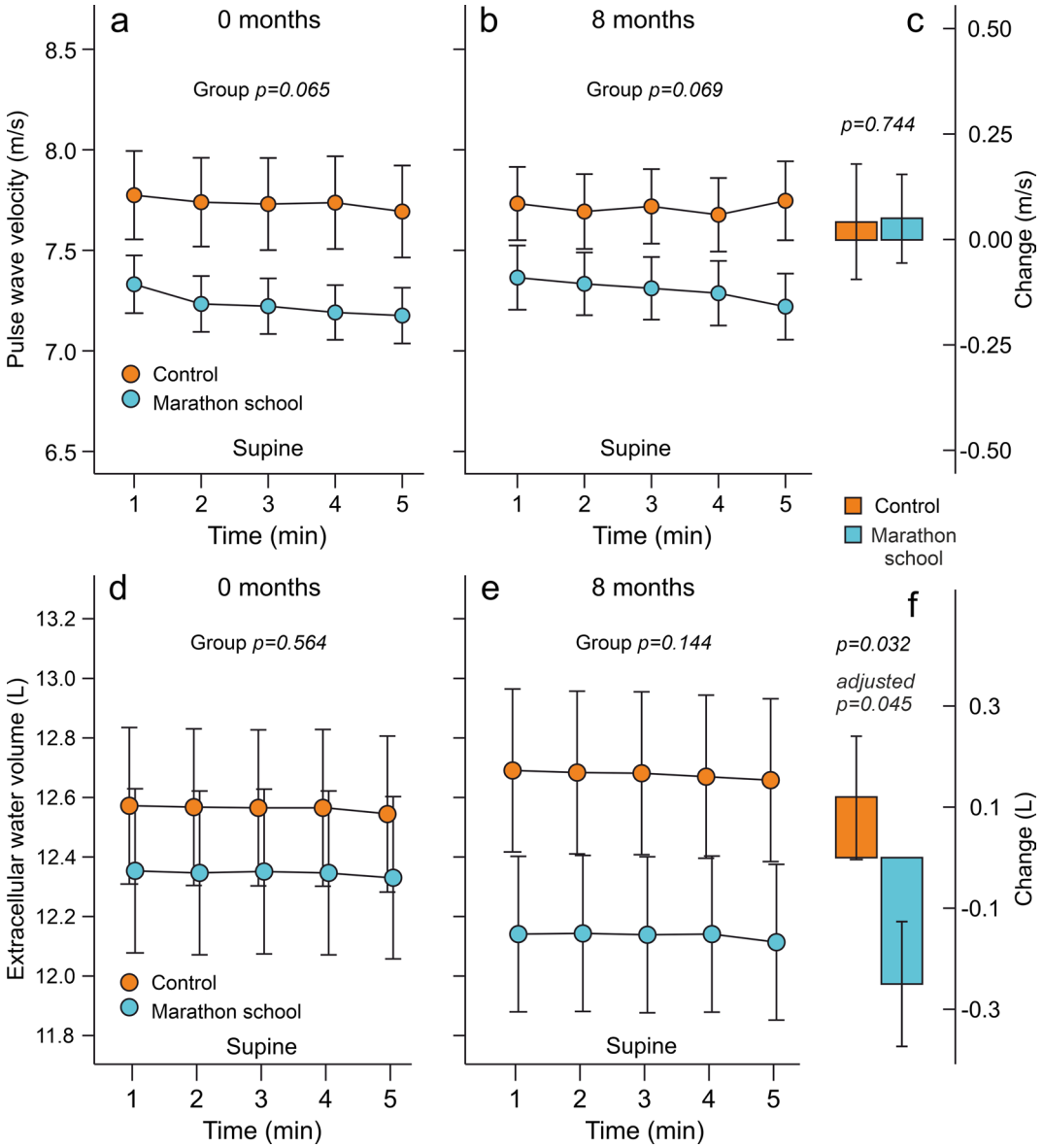

Fig. 5. Pulse wave velocity (**a**, **b**) and extracellular water volume (**d**, **e**) at 0 months and at 8 months in 43 controls and in 45 marathon school participants, and between-group comparisons of the average changes in these variables (**c**, **f**) over the follow-up period. For the changes in extracellular water volume, both the crude *p*-value, and the *p*-value adjusted for the parallel changes in body weight are shown. Generalized estimating equations, mean and SEM.

Our study has limitations. A selection bias caused by the recruitment of voluntary subjects cannot be excluded. Although comprehensive adjustment for confounders was performed, many of the clinical and biochemical variables are closely correlated, leading to a potential multicollinearity problem. We applied non-invasive methods for the hemodynamic measurements, while the results on stroke volume are also based on mathematical processing of the bioimpedance signal[32]. Moreover, central aortic BP and pulse wave reflections are mathematically derived from the tonometry signal[31]. Evaluation of aerobic and anaerobic thresholds and blood tests at the close of the study were not performed in the control group. The medications used by the participants may have affected the results, as the use of an estrogen-progestin combination was more prevalent in the controls. However, all medications remained stable throughout the study, which should alleviate potential confounding effects.

The strengths of our study are the broad analyses of biochemistry, and assessment of several hemodynamic variables so that both aortic and finger BP were simultaneously recorded. Men and women have been found to regulate BP through different physiological mechanisms[66], while central hemodynamics may be more strongly influenced by sympathetic activity in older women than in younger women[67]. A similar sex distribution, number of postmenopausal women, mean age, and age range among participants can be expected to have controlled for these confounding factors. As BP levels are not uniform in supine and upright postures[21], we included a head-

up tilt in the study protocol. The training was professionally supervised, and its impact on body composition, insulin sensitivity and physical performance was documented. Finally, fluid balance was considered as a possible mechanism of training-induced changes in hemodynamics.

To conclude, 8 months of supervised aerobic exercise training in a marathon school moderately reduced peripheral diastolic BP, a finding associated with reductions in SVRI and ECW volume. Our findings support the view that regular exercise serves as a moderate, non-pharmacological means of lowering BP.

Data availability

Analyses and generated datasets that support the current study are not available publicly. The datasets are available from the corresponding author on reasonable request.

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References

1. Sanchis-Gomar, F. et al. Exercise effects on cardiovascular disease: from basic aspects to clinical evidence. *Cardiovasc. Res.* **118**, 2253–2266 (2021).
2. Lim, S. S. et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the global burden of disease study 2010. *Lancet* **380**, 2224–2260 (2013).
3. Luyckx, V. A. et al. Mind the gap in kidney care: translating what we know into what we do. *Kidney Int.* **105**, 406–417 (2024).
4. Hanssen, H. et al. Personalized exercise prescription in the prevention and treatment of arterial hypertension: a consensus document from the European association of preventive cardiology (EAPC) and the ESC Council on hypertension. *Eur. J. Prev. Cardiol.* **29**, 205–215 (2022).
5. Carretero, O. A. & Oparil, S. Essential hypertension: part I: definition and etiology. *Circulation* **101**, 329–335 (2000).
6. Nystoriak, M. A. & Bhatnagar, A. Cardiovascular effects and benefits of exercise. *Front. Cardiovasc. Med.* **5**, 135 (2018).
7. Williams, B. et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur. Heart J.* **39**, 3021–3104 (2018).
8. Saco-Ledo, G. et al. Acute aerobic exercise induces short-term reductions in ambulatory blood pressure in patients with hypertension: a systematic review and meta-analysis. *Hypertension* **78**, 1844–1858 (2021).
9. Dimeo, F. et al. Aerobic exercise reduces blood pressure in resistant hypertension. *Hypertension* **60**, 653–658 (2012).
10. Pierce, D. R., Doma, K., Raiff, H., Golledge, J. & Leicht, A. S. Influence of exercise mode on post-exercise arterial stiffness and pressure wave measures in healthy adult males. *Front. Physiol.* **9**, 1468 (2018).
11. Ng, A. V., Dg, R. C. & Dr, S. J. Endurance exercise training is associated with elevated basal sympathetic nerve activity in healthy older humans. *J Appl. Physiol. Bethesda Md* **1985 77**, (1994).
12. Letnes, J. M. et al. Effect of 5 years of exercise training on the cardiovascular risk profile of older adults: the generation 100 randomized trial. *Eur. Heart J.* **43**, 2065–2075 (2021).
13. Bouchard, C. et al. Adverse metabolic response to regular exercise: is it a rare or common occurrence? *PLOS ONE.* **7**, e37887 (2012).
14. Sung, K. C. et al. Physical activity and the progression of coronary artery calcification. *Heart* **107**, 1710–1716 (2021).
15. Denton, K. M., Hilliard, L. M. & Tare, M. Sex-related differences in hypertension. *Hypertension* **62**, 674–677 (2013).
16. Hart, E. C., Joyner, M. J., Wallin, B. G. & Charkoudian, N. Sex, ageing and resting blood pressure: gaining insights from the integrated balance of neural and haemodynamic factors. *J. Physiol.* **590**, 2069–2079 (2012).
17. Chung, A. K. et al. Women have higher left ventricular ejection fractions than men independent of differences in left ventricular volume. *Circulation* **113**, 1597–1604 (2006).
18. Tikkakoski, A. J. et al. Hemodynamic alterations in hypertensive patients at rest and during passive head-up Tilt. *J. Hypertens.* **31**, 906–915 (2013).
19. Esler, M. et al. Consequences of the evolutionary cardiovascular challenge of human bipedalism: orthostatic intolerance syndromes, orthostatic hypertension. *J. Hypertens.* **37**, 2333–2340 (2019).
20. Reulecke, S. et al. Men and women should be separately investigated in studies of orthostatic challenge due to different gender-related dynamics of autonomic response. *Physiol. Meas.* **37**, 314–332 (2016).
21. Suojanen, L. J. et al. Individual changes of central blood pressure in response to upright posture: different hemodynamic phenotypes. *J. Hypertens.* **39**, 2403–2412 (2021).
22. Palatini, P., Mos, L., Saladini, F. & Rattazzi, M. Blood pressure hyperreactivity to standing: a predictor of adverse outcome in young hypertensive patients. *Hypertension* **79**, 984–992 (2022).
23. Fiuza-Luces, C. et al. Exercise benefits in cardiovascular disease: beyond Attenuation of traditional risk factors. *Nat. Rev. Cardiol.* **15**, 731–743 (2018).
24. Holycross, B. J. et al. Exercise training normalizes β-adrenoceptor expression in dogs susceptible to ventricular fibrillation. *Am. J. Physiol. -Heart Circ. Physiol.* **293**, H2702–H2709 (2007).
25. Oinonen, L. et al. Plasma total calcium concentration is associated with blood pressure and systemic vascular resistance in normotensive and never-treated hypertensive subjects. *Blood Press.* **29**, 137–148 (2020).
26. Goodwin, M. L., Harris, J. E., Hernández, A. & Gladden, L. B. Blood lactate measurements and analysis during exercise: A guide for clinicians. *J. Diabetes Sci. Technol. Online*. **1**, 558–569 (2007).
27. Hakanen, T. *Aerobisen ja anaerobisen kynnyssykkeen mallintaminen MARS-menetelmällä sekä liikunnan määrän ja laadun vaikutus kuntoarvioihin*. (2011). https://trepo.tuni.fi/handle/10024/82303
28. Katz, A. et al. Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. *J. Clin. Endocrinol. Metab.* **85**, 2402–2410 (2000).
29. de Brito, L. C. et al. Post-exercise hypotension and its mechanisms differ after morning and evening exercise: a randomized crossover study. *Plos One*. **10**, e0132458 (2015).
30. Tahvanainen, A. et al. Analysis of cardiovascular responses to passive head-up Tilt using continuous pulse wave analysis and impedance cardiography. *Scand. J. Clin. Lab. Invest.* **69**, 128–137 (2009).
31. Chen, C. H. et al. Estimation of central aortic pressure waveform by mathematical transformation of radial tonometry pressure. Validation of generalized transfer function. *Circulation* **95**, 1827–1836 (1997).
32. Kööbi, T., Kaukinen, S., Turjanmaa, V. M. & Uusitalo, A. J. Whole-body impedance cardiography in the measurement of cardiac output. *Crit. Care Med.* **25**, 779–785 (1997).
33. Kööbi, T., Kähönen, M., Iivainen, T. & Turjanmaa, V. Simultaneous non-invasive assessment of arterial stiffness and haemodynamics - a validation study. *Clin. Physiol. Funct. Imaging.* **23**, 31–36 (2003).
34. Torlasco, C. et al. Age matters: differences in exercise-induced cardiovascular remodelling in young and middle aged healthy sedentary individuals. *Eur. J. Prev. Cardiol.* **28**, 738–746 (2021).

35. Strauss, M. B., Davis, R. K., Rosenbaum, J. D. & Rossmeisl, E. C. Water diuresis produced during recumbency by the intravenous infusion of isotonic saline solution. *J. Clin. Invest.* **30**, 862–868 (1951).
36. Barone Gibbs, B. et al. Physical activity as A critical component of first-line treatment for elevated blood pressure or cholesterol: who, what, and how? A scientific statement from the American heart association. *Hypertension* **78**, e26–e37 (2021).
37. Bhuva, A. N. et al. Training for a first-time marathon reverses age-related aortic stiffening. *J. Am. Coll. Cardiol.* **75**, 60–71 (2020).
38. D'Silva, A. et al. Cardiovascular remodeling experienced by real-world, unsupervised, young novice marathon runners. *Front. Physiol.* **11**, 232 (2020).
39. Kapoor, E., Collazo-Clavell, L, M., Faubion & S, S. Weight gain in women at midlife: a concise review of the pathophysiology and strategies for management. *Mayo Clin. Proc.* **92**, 1552–1558 (2017).
40. Sowers, M. et al. Changes in body composition in women over six years at midlife: ovarian and chronological aging. *J. Clin. Endocrinol. Metab.* **92**, 895–901 (2007).
41. Canoy, D. et al. How much Lowering of blood pressure is required to prevent cardiovascular disease in patients with and without previous cardiovascular disease? *Curr. Cardiol. Rep.* **24**, 851–860 (2022).
42. Hardy, S. T. et al. Primary prevention of chronic kidney disease through population-based strategies for blood pressure control: the ARIC study. *J. Clin. Hypertens.* **20**, 1018–1026 (2018).
43. Cornelissen, V. A., Buys, R. & Smart, N. A. Endurance exercise beneficially affects ambulatory blood pressure: a systematic review and meta-analysis. *J. Hypertens.* **31**, 639–648 (2013).
44. Allan, P. D., O'Donnell, T. & Tzeng, Y. C. Agreement between finger plethysmography- and brachial oscillometry-derived blood pressure measurements. *Clin. Physiol. Funct. Imaging.* **38**, 439–446 (2018).
45. Kollias, A., Lagou, S., Zeniodi, M. E., Boubouchairopoulou, N. & Stergiou, G. S. Association of central versus brachial blood pressure with target-organ damage: systematic review and meta-analysis. *Hypertension* **67**, 183–190 (2016).
46. Agabiti-Rosei, E. et al. Central blood pressure measurements and antihypertensive therapy: a consensus document. *Hypertension* **50**, 154–160 (2007).
47. Romanovsky, A. A. Skin temperature: its role in thermoregulation. *Acta Physiol. Oxf. Engl.* **210**, 498–507 (2014).
48. Nagasaka, T., Cabanac, M., Hirata, K. & Nunomura, T. Control of local heat gain by vasomotor response of the hand. *J. Appl. Physiol. Bethesda Md. 1985.* **63**, 1335–1338 (1987).
49. Prior, B. M., Lloyd, P. G., Yang, H. T. & Terjung, R. L. Exercise-induced vascular remodeling. *Exerc. Sport Sci. Rev.* **31**, 26 (2003).
50. Notarius, C. F., Murai, H., Morris, B. L. & Floras, J. S. Effect of fitness on reflex sympathetic neurovascular transduction in middle-age men. *Med. Sci. Sports Exerc.* **44**, 232–237 (2012).
51. Ruilope, L. M. et al. Blood pressure and cardiorenal outcomes with finerenone in chronic kidney disease in type 2 diabetes. *Hypertension* **79**, 2685–2695 (2022).
52. Bhatt, D. L. et al. A controlled trial of renal denervation for resistant hypertension. *N Engl. J. Med.* **370**, 1393–1401 (2014).
53. Jaffrin, M. Y. & Morel, H. Body fluid volumes measurements by impedance: A review of bioimpedance spectroscopy (BIS) and bioimpedance analysis (BIA) methods. *Med. Eng. Phys.* **30**, 1257–1269 (2008).
54. Wolff, C. B., Green, D. W., Paton, J. F. R. & Collier, D. J. New Understanding of circulatory blood flow and arterial blood pressure mechanisms. *Cardiovasc. Res.* **118**, e29–e31 (2022).
55. Bie, P. Mechanisms of sodium balance: total body sodium, surrogate variables, and renal sodium excretion. *Am. J. Physiol. -Regul Integr. Comp. Physiol.* **315**, R945–R962 (2018).
56. Taurio, J. et al. Urine sodium excretion is related to extracellular water volume but not to blood pressure in 510 normotensive and never-treated hypertensive subjects. *Blood Press.* **32**, 2170869 (2023).
57. Barnes, K. A. et al. Normative data for sweating rate, sweat sodium concentration, and sweat sodium loss in athletes: an update and analysis by sport. *J. Sports Sci.* **37**, 2356–2366 (2019).
58. Mounier, R., Pialoux, V., Mischler, I., Coudert, J. & Fellmann, N. Effect of hypervolemia on heart rate during 4 days of prolonged exercises. *Int. J. Sports Med.* **24**, 523–529 (2003).
59. Mischler, I. et al. Human albumin synthesis is increased by an ultra-endurance trial. *Med. Sci. Sports Exerc.* **35**, 75–81 (2003).
60. Koutlianos, N. et al. Arterial function after a 246 Km ultra-marathon running race. *Int. J. Sports Med.* **42**, 1167–1173 (2021).
61. Townsend, R. R. et al. Recommendations for improving and standardizing vascular research on arterial stiffness: a scientific statement from the American heart association. *Hypertension* **66**, 698–722 (2015).
62. Ahmadi-Abhari, S. et al. Physical activity, sedentary behavior, and long-term changes in aortic stiffness: the Whitehall II study. *J. Am. Heart Assoc.* **6**, e005974 (2017).
63. Twerenbold, S. et al. Short-term high-intensity interval training improves micro- but not macrovascular function in hypertensive patients. *Scand. J. Med. Sci. Sports.* **33**, 1231–1241 (2023).
64. Liang, J. et al. Promotion of aerobic exercise induced angiogenesis is associated with decline in blood pressure in hypertension: result of EXCAVATION-CHN1. *Hypertension* **77**, 1141–1153 (2021).
65. Arvola, P. et al. Exercise enhances vasorelaxation in experimental obesity associated hypertension. *Cardiovasc. Res.* **43**, 992–1002 (1999).
66. Briant, L. J. B., Charkoudian, N. & Hart, E. C. Sympathetic regulation of blood pressure in normotension and hypertension: when sex matters. *Exp. Physiol.* **101**, 219–229 (2016).
67. Harvey, R. E. et al. Influence of sympathetic nerve activity on aortichemodynamics and pulse wave velocity in women. *Am. J. Physiol. Heart Circ. Physiol.* **312**, H340–H346 (2017).

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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