Exercise heat acclimation has minimal effects on left ventricular volumes, function and systemic hemodynamics in euhydrated and dehydrated trained humans

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Keywords: Heat stress, hypohydration, stroke volume, ventricular filling

Running Head: Heat acclimation, hydration, and cardiac function

Abstract

Heat acclimation (HA) may improve the regulation of cardiac output ($\dot{Q}$) through increased blood volume (BV) and left ventricular (LV) diastolic filling, and attenuate reductions in $\dot{Q}$ during exercise-induced dehydration; however, these hypotheses have never been directly tested. Before and following 10-days exercise HA, eight males completed two trials of submaximal exercise in 33°C and 50% relative humidity while maintaining pre-exercise euhydrated body mass (EUH; -0.6±0.4%) or becoming progressively dehydrated (DEH; -3.6±0.7%). Rectal (T_{re}) and skin (T_{sk}) temperatures, heart rate (HR), LV volumes and function, systemic hemodynamics and BV were measured at rest and during bouts of semi-recumbent cycling (55% $\dot{V}O_{2max}$) at 20, 100 and 180 min, interspersed by periods of upright exercise. T_{re}, BV, HR, LV volumes, LV systolic and diastolic function and systemic hemodynamics were similar between trials at rest and during the first 20 min of exercise (all $P>0.05$). These responses were largely unaffected by HA at 180 min in either hydration state. However, DEH induced higher T_{re} (0.6±0.3°C) and HR (16±7 beats·min^{-1}) and lower stroke volume (26±16 ml), end-diastolic volume (29±16 ml) and $\dot{Q}$ (2.1±0.8 L·min^{-1}) compared to EUH at 180 min (all $P<0.05$), yet LV twist and untwisting rate were increased or maintained ($P=0.028$ and 0.52, respectively). Findings indicate HA has minimal effects on LV volumes, LV mechanical function and systemic hemodynamics during submaximal exercise in moderate heat where HR and BV are similar. In contrast, DEH evokes greater hyperthermia and tachycardia, reduces BV, and impairs diastolic LV filling, lowering $\dot{Q}$, regardless of HA state.

New and noteworthy

This study demonstrates that 10 days of exercise heat acclimation has minimal effects on left ventricular volumes, intrinsic cardiac function and systemic hemodynamics during prolonged, repeated semi-recumbent exercise in moderate heat, where heart rate and blood volume are similar to pre-acclimation levels. However, progressive dehydration is consistently associated with similar degrees of hyperthermia and tachycardia, and reductions in blood volume, diastolic filling of the left ventricle, stroke volume and cardiac output, regardless of acclimation state.

Introduction

Cardiovascular adaptations to heat acclimation (HA) are considered integral for the regulation of cardiac output ($\dot{Q}$), blood pressure and peripheral blood flow, such that exercise tolerance/performance can be enhanced in hot conditions (40, 54). The available evidence, however, indicates that the $\dot{Q}$ response to HA varies widely; decreasing (60), remaining unchanged (19, 24, 27, 35, 43, 61) or increasing (36) during exercise in the heat. This discrepancy in the literature, which may reflect differences in exercise intensity, type and severity of heat stress, training or hydration status (40), and the number of participants between HA conditions (35, 36), questions whether HA *per se* enhances cardiovascular function during exercise.

According to classic models of cardiovascular control, HA could modulate cardiac function during exercise by altering preload, afterload, and/or intrinsic cardiac function (23). However, evidence directly supporting these mechanisms is limited. Firstly, heart rate (HR) is lowered, while stroke volume (SV) and blood volume (BV) are reportedly enhanced (49, 61), but central blood volume (43) and exercising leg and forearm blood flows are unchanged with HA during submaximal exercise (35, 36). It is therefore unclear whether enhanced preload of the heart may be a mechanism increasing SV with HA, independently of the confounding effects of exercise training (37). Secondly, there is limited and conflicting data regarding the effects of HA on mean arterial pressure (MAP; 13, 21, 24), and no data on effective arterial elastance, which is indicative of net arterial load or afterload. While resting MAP may be reduced in sedentary healthy individuals following passive heat therapy (5), exercising MAP has been shown to be reduced (13), unaltered (19, 21) or increased (24) following exercise HA. Lastly, evidence of the intrinsic cardiac function responses to exercise HA is scant. In the rodent model, cardiac muscle exhibits a transient increase in autonomic excitability, enhanced left ventricular (LV) compliance and contractility, and lowered myocardial oxygen consumption with prolonged passive HA (>1 month; 17,18). HA studies in humans to date have quantified $\dot{Q}$ and derived SV (19, 24, 27, 35, 36, 43, 60, 61), therefore, the direct effects of HA on intrinsic cardiac contractile function and the filling and emptying of the LV at rest and during intense dynamic exercise in the heat are yet to be determined. Acutely, SV is maintained under heat stress at rest and during small muscle mass exercise while $\dot{Q}$ is increased, despite a reduction in diastolic filling pressure and end-diastolic volume (EDV; 4, 51). To compensate for reductions in filling pressure, LV systolic twisting and diastolic untwisting are enhanced in proportion to the magnitude of heat stress to support the emptying and filling of the LV, respectively (34, 51). In addition, observations during dobutamine infusion (38) suggest that LV contractility may be enhanced in response to heat stress and increased sympathetic tone. Whether LV function is enhanced during dynamic exercise in response to HA-induced adaptations such as reduced body temperature, heart rate and perhaps sympathetic nervous activity (20, 36), is unknown.

HA increases the sensitivity and rate of sweating, improving evaporative heat exchange from the body to the environment (40, 54). However, profuse sweating during prolonged exercise in the heat results in progressive dehydration when fluid replacement is inadequate. Dehydration leads to decreases in BV and elevations in body temperature, which are associated with reductions in $\dot{Q}$, SV and to a lesser extent arterial pressure, compared to euhydrated exercise, with parallel increases in peripheral vascular resistance (17). The reductions in $\dot{Q}$ and SV occur in proportion to the deficit in total body water (29), but the overall degree of cardiovascular strain depends on the environmental conditions and the intensity and mode of exercise (31, 50, 59). Recently, Watanabe et al. (59) postulated that dehydration reduces SV and $\dot{Q}$ during intense whole-body exercise in the heat via impaired cardiac filling and venous return, as intrinsic LV diastolic and systolic function tends to be enhanced, but brain and exercising, and non-exercising limb blood flow and beat-volume are compromised (16, 56, 59). Similar dehydration-induced impairments in thermoregulatory and cardiovascular function have been observed acutely in partially heat acclimated individuals (16, 17). However, the extent to which HA status influences cardiovascular and thermoregulatory responses to dehydration is unclear. Moderate exercise-induced dehydration following long-term HA has been shown to result in smaller increases in HR and core temperature compared to pre-HA levels (39). HR during exercise-heat stress following overnight dehydration (~3-5%) has also been shown to be reduced (46) or unchanged (7) after HA. Similar to the mechanisms discussed above, a blunting of the HR and thermal responses to exercise post-HA may attenuate impairments to venous return with mild dehydration and therefore improve central hemodynamics. However, $\dot{Q}$ and SV responses during brief periods of exercise following diuretic administration are similarly reduced compared to euhydrated controls before and after short-term HA (22). Therefore, despite indications that hypohydration acutely influences the thermoregulatory and cardiovascular responses to exercise-heat stress following HA, the effects of HA on mild and more pronounced exercise-induced dehydration warrants further investigation.

The aim of this study was to directly determine the diastolic and systolic LV volumes and function and systemic hemodynamics during dynamic exercise under moderate heat stress with distinct hydration status. By doing so, the study sought to generate further insight into the mechanisms underpinning the cardiovascular responses to HA and the potential interaction with acute changes in hydration. Echocardiographic and hematological measurements were conducted during repeated bouts of semi-recumbent cycling before and after exercise-HA. Responses were determined while euhydration was maintained and during matched levels of dehydration before and following HA. It was hypothesized that SV during exercise would be increased following HA with both maintained euhydration and progressive dehydration, via an increased EDV and BV, and decreased HR. However, pronounced dehydration following HA would result in lower exercising $\dot{Q}$ compared to euhydration, associated in part with a reduced BV and impaired diastolic ventricular filling, rather than a blunted LV function.

Methods

Participants

Eight males with an average age, height, body mass and $\dot{V}O_{2max}$ of 33 ± 5 years, 176 ± 5 cm, 75.4 ± 4.7 kg and 3.89 ± 0.47 $L{\cdot}min^{-1}$ volunteered to take part in this study. Participants were all trained cyclists and triathletes regularly training ≥5 h per week and were free from illness or injury. Participants provided written informed consent for their participation prior to undergoing a pre-screening procedure that involved a health questionnaire and resting echocardiographic assessment. All participants had a structurally and functionally normal heart as confirmed by an experienced sonographer. The study was approved by Anti-Doping Lab Qatar Research Ethics Committee (Approval no. F201500105) and conducted in accordance with the Declaration of Helsinki.

Experimental design

A within participant, repeated measures study was completed whereby participants underwent two trials of prolonged dynamic exercise in the heat (Figure 1). Throughout each trial, euhydrated pre-exercise body mass was either maintained (EUH) or decreased with progressive exercise-induced dehydration (DEH). The order of trials was randomized and counterbalanced and trials were repeated following a 10-day exercise HA intervention at a controlled HR. The current experiments are part of a larger project and the adaptations associated with HA and their effects on performance published elsewhere (57). Briefly, HA consisted of 90 min of EUH cycling exercise in environmental conditions of 40°C and 40% relative humidity. The initial 15 min period was conducted at a workload eliciting 65% $\dot{V}O_{2max}$, thereafter workload was altered to maintain a HR corresponding to that intensity (147 ± 6 beats·min^{-1}). Absolute red cell volume, PV and BV were determined prior to each experimental trial. Food and fluid intakes were recorded over the 24 h period prior to the first experimental trial and were replicated prior to each subsequent experiment.

Pre-experimental procedures

Participants attended the laboratory on four separate occasions prior to the commencement of the first experimental trial. During two visits separated by a minimum of 24 h, maximal incremental tests to exhaustion were conducted during upright (Lode Excalibur Sport, Groningen, The Netherlands) and semi-recumbent (Ergoselect, Ergoline, GMbH, Germany) cycling exercise, respectively. Each test was used to determine the workloads and target HR for the experimental trials and HA sessions. Tests were conducted in a temperate environment (19.2 ± 1.9°C and 63 ± 10% relative humidity) and participants wore cycling shorts, socks and shoes throughout. Following completion of the semi-recumbent test, participants rested in the laboratory for 30 min to allow their body temperature to return to pre-exercise levels. Thereafter, they entered an environmental chamber with target ambient conditions of 33°C and 50% relative humidity (TEMI 1000, Sanwood Environmental Chambers co., Taiwan) and completed 60 min of upright cycling exercise at a workload equivalent to 65% $\dot{V}O_{2max}$ (171 ± 21 W). *Ad libitum* fluid intake was recorded and used to correct for changes in nude body mass for the calculation of hourly sweat rate.

On two separate visits, hemoglobin mass (Hb_{mass}) was determined via a modified optimized carbon monoxide rebreathing technique (48). In any case where Hb_{mass} differed by >2% between measurements, the test was repeated before the study progressed. The typical error associated with this technique was 0.63%. Carbon monoxide rebreathing was repeated once 24 h following the final day of HA to account for potential changes in Hb_{mass}.

Experimental trials

The experimental procedures are outlined in Figure 1. Participants arrived at the laboratory at similar times of day ≥2 hrs post-prandial and provided a urine sample before a measurement of nude body mass was recorded to the nearest 100 g (SECA 798, Germany). A urine specific gravity ≤1.020 was considered indicative of euhydration (1) and was measured using a refractometer (PAL-10s, ATAGO, Tokyo, Japan). Participants then self-inserted a rectal thermistor (DM 852, Ellab, A/S, Hillerød, Denmark) and donned a HR monitor (RS800CX, T31-Coded Transmitter, Polar Electro, Kempele, Finland), cycling shorts, socks and shoes before lying supine in the main laboratory. A cannula was inserted into a right antecubital vein and flushed with 2 ml of saline before electrocardiogram sensor electrodes and skin temperature thermistors (iButtons, Maxim Integrated Products, Sunnyvale, CA, USA) were applied. After a period of 10 min rest, HR was recorded over a 2 min period before a duplicate measurement of blood pressure was manually assessed using a sphygmomanometer. A resting blood sample was collected before participants entered an environmental chamber and mounted the semi-recumbent cycle ergometer. Environmental conditions in the chamber averaged 33.0 ± 0.3°C and 50 ± 4% relative humidity throughout experimentation. The ergometer was tilted longitudinally, and participants adopted the left lateral decubitus position for 5 min before resting measurement of LV volumes and function were recorded. Once completed, participants were returned to a semi-recumbent position and began exercising at a workload equivalent to 55% $\dot{V}O_{2max}$ (135 ± 18 W) for a period of 5 min to ensure a steady state was achieved. Participants continued to cycle while blood pressure was recorded, the ergometer was again tilted, and echocardiographic assessments and blood sampling were repeated over a further 15 min.

Following initial resting and exercising measurements, participants transferred to the upright cycle ergometer and exercised for 60 min at 65% $\dot{V}O_{2max}$. Fluid intake was prescribed over this period and consisted of a 0.1% electrolyte drink (HIGH5 ZERO, H5, Bardon, UK) divided into four equal aliquots to the nearest 1 ml. The total volume consumed was equivalent to either 90% (EUH) or 10% (DEH) of expected hourly sweat loss and was calculated from the pre-experimental visit and the final day of HA for pre- and post-HA trials, respectively. Intake began at the onset of upright exercise and subsequent aliquots were provided after 15, 30 and 45 min of cycling. A fan directed at participants throughout all periods of exercise provided 3 $m \cdot s^{-1}$ convective airflow. At the end of each period of upright exercise, participants removed all clothing except instrumentation and towel dried non-evaporated sweat before body mass was measured within the chamber to determine changes in total body water. Participants then re-dressed, mounted the semi-recumbent ergometer and completed the exercising measurement period. This process was then repeated a final time before the end of the trial. Thus, measurements of blood pressure, BV and LV volumes and function were conducted at rest and after 20, 100 and 180 min of dynamic exercise in the heat (Figure 1). Experimental trials were separated by a period of 1-2 days of complete rest that was standardized within-participants pre- and post-HA.

Measurement procedures

Rectal temperature (T_{re}) was measured via an individualized re-usable thermistor placed 15 cm beyond the anal sphincter. Mean skin temperature (T_{sk}) was calculated as an area weighted mean from measures taken from the chest, upper arm, thigh and lower leg as previously described (41). T_{sk} and T_{re} were recorded at rest and at the beginning and end of each semi-recumbent exercise period. HR, T_{sk} and T_{re} were also recorded every 5 min and the rating of perceived exertion (3) and thermal comfort (2) every 10 min during periods of upright cycling.

Venous blood samples were drawn into 2 ml lithium heparinized syringes (PICO 50, Radiometer) following a 2 ml discharge immediately after echocardiographic measurements. The cannula was then flushed with ~5 ml of saline. Whole blood was immediately analyzed in triplicate for measurements of metabolite, electrolyte and hemoglobin concentration and hematocrit (ABL90 FLEX, Radiometer, BrØnshØj, Denmark). Absolute BV was measured as HB_{mass}/venous hemoglobin concentration x 100, where Hb_{mass} and hemoglobin concentration are in g and $g \cdot dl^{-1}$, respectively. Red cell volume was calculated as percentage hematocrit/100 x BV. Plasma volume (PV) was then calculated by subtracting red cell volume from BV. The measurement error for Hb_{mass}, hemoglobin concentration and hematocrit were 0.63%, 0.30% and 0.20%, respectively.

Echocardiographic images were recorded by an experienced sonographer at a standardized order and depth for each participant. All images were collected using a commercially available ultrasound machine (CX50 POC, Philips Healthcare, The Netherlands) and 5 MHz sector array probe (S5-1, Philips Healthcare). Frame rate was fixed at 60 Hz for 2D image acquisition, the maximal achievable from the ultrasound machine. A minimum of six images were recorded of each view and analysis was conducted over three consecutive cardiac cycles where possible. All images were conducted at the end of expiration. Initial recordings of the short axis base and apex were made before apical 2- and 4-chamber images were acquired. Pulsed-wave tissue Doppler recordings of the septal mitral and lateral annulus were also recorded at rest. All images were exported, de-identified and analysed offline (Q Station 3.0, Philips Healthcare, The Netherlands) at the end of the data collection period as to avoid confirmation bias. LV mass was calculated pre- and post-HA from images acquired at rest as previously described (47). Diastolic and systolic LV volumes were determined using the Simpson's method of bi-plane disc summation while HR was recorded via a 3-lead electrocardiogram inherent in the ultrasound. The co-efficient of variation for repeated exercising hemodynamics using echocardiography was between 6-10%. $\dot{Q}$ was calculated as the product of HR and SV.

MAP was calculated as ((2 x DBP) + SBP)/3, where DBP and SBP are diastolic and systolic blood pressures, respectively. Total peripheral resistance (TPR) was calculated as MAP/ $\dot{Q}$. Effective arterial elastance, an indirect measurement of the net arterial load imposed on the LV, was calculated as 0.9 x SBP/SV (8, 9). LV end-systolic elastance, considered an integrated measure of LV performance (45) was calculated as 0.9 x SBP/ESV (9), where ESV is end-systolic volume. Ventricular-arterial coupling was calculated as the quotient of end-systolic elastance and effective arterial elastance (53).

2D speckle tracking of the short-axis base and apex was used to derive circumferential strain, strain rates and rotational parameters, while longitudinal strain was determined from the apical 4-chamber view as described previously (50, 51). Briefly, diastolic and systolic frame-by-frame data were normalized to their respective percentage of duration and interpolated separately to 300 data points using cubic spline interpolation (GraphPad Prism 5, San Diego, CA). Twist, untwisting and the respective velocities were obtained by subtraction of basal rotation/velocity data from apical rotation/velocity data. Peak untwisting velocity was determined as the greatest negative deflection following peak twisting velocity.

Statistical analyses

Two-way ANOVA (hydration x HA) with repeated measures analyses were used to compare measurements recorded at rest and at the end of upright cycling exercise. Separate three-way (hydration x time x HA) ANOVA's were used to compare measurements during semi-recumbent cycling exercise. Mauchley's test was used to test the assumption of Sphericity. In cases where this assumption was violated a Greenhouse-Geisser correction factor was applied. Bonferroni *post-hoc* testing was employed to determine where differences occurred. Wilcoxon signed rank tests were used to analyse ordinal rating of perceived exertion and thermal comfort data. Relationships between selected physiological variables pre- and post-HA were evaluated using Pearson's product-moment correlation. All statistical analyses were conducted using

SPSS (Version 21, IBM, Armonk, US). Results are reported as mean ± SD. The level of significance was set at $P<0.05$.

Results

Heat acclimation intervention summary

Resting T_{re} and HR were similar during the 10-days of HA (P = 0.438 and 0.34, respectively, Supplemental Figure S1). T_{re} after 15 min of fixed workload exercise was unaffected by HA, averaging 37.5 ± 0.3°C on day 1 and 37.4 ± 0.2°C on day 10, respectively (P = 0.29). However, over the same period, HR was 11 ± 8 beats·min^{-1} lower on day 10 compared to day 1 (P = 0.002). During the 75 min of exercise at a target HR, total work increased by 112 ± 16 kJ (18 ± 7%) over the 10 days of HA (P < 0.001). Exercise at a controlled HR resulted in an elevated T_{re}, which averaged 38.5 ± 0.3°C for the final 60 min of exercise each day of HA. Sweat rate increased by 13 ± 12% between day 1 and 10 of HA (P = 0.01). Full responses to the 10 day HA protocol are published in detail elsewhere (57).

Resting responses to heat acclimation

Participants attended the laboratory in a well-hydrated state as indicated by similar urine specific gravity (1.013 ± 0.008, P = 0.24) and nude body mass (75.2 ± 4.7 kg, P = 0.21) measurements between trials. There was a 2.1% decrease in Hb_{mass} from 882 ± 69 g pre-HA to 863 ± 78 g 24 h following day 10 of the HA intervention (P = 0.03). Post-HA hematological responses were therefore calculated using this value. Resting red cell volume tended to be slightly reduced following HA (31 ± 37 ml, P = 0.052). No other effects of HA were observed on resting venous blood constituents, absolute BV and PV, which did not differ between trials (all P > 0.05, Table 1, Figure 3).

HA did not alter resting T_{re} or T_{sk} (both P > 0.05, Figure 2). There was no main effect of HA on resting HR (P = 0.14) which averaged 60 ± 7 beats·min^{-1} in pre-HA trials and 56 ± 4 beats·min^{-1} in post-HA trials, respectively (Figure 3). There was main effect of HA on resting SV (P = 0.003) which was only slightly greater (6 ± 5 ml) post-HA, however resting $\dot{Q}$ was not altered, averaging 5.31 ± 0.65 in the pre- and 5.33 ± 0.77 L·min^{-1} in the post-HA trials, respectively (P = 0.93). Systolic and diastolic LV volumes also did not differ between trials (all P > 0.05, Figure 3). Resting SBP and DBP were 120 ± 13 and 63 ± 15 mmHg pre-HA and 118 ± 8 and 61 ± 10 mmHg post-HA (P = 0.241 and 0.271, respectively). Resting MAP was not altered by HA (P = 0.21, Figure 4). There was a main effect of HA on decreasing resting effective arterial elastance (0.10 ± 0.11 mmHg·ml^{-1}, P = 0.014). Resting LV systolic elastance (P = 0.85) and ventricular-arterial coupling (P = 0.085) were not altered by HA (Figure 5).

LV mass was unchanged by HA, averaging 174 ± 10 g pre-HA and 175 ± 9 g post-HA, respectively (P = 0.80). Similarly, LV systolic and diastolic function was largely unaltered by HA as there were no differences in basal, apical or longitudinal strain and strain rate parameters, and LV rotation and rotational velocities were also similar between trials (all P > 0.05, Tables 2-4, Figure 6).

Responses to initial 20 min semi-recumbent cycling

Throughout the initial 20 min of semi-recumbent exercise, thermal and peripheral hemodynamic responses and BV were similar between all four trials as participants were still euhydrated (all P > 0.05, Figures 2-4). Initial exercising $\dot{Q}$ was unaltered by HA and was associated with similar HR and LV volumes, mechanical and strain responses between trials (Figures 3-6, Tables 3 and 4).

Upright exercise, hydration status and acclimation

Greater fluid intake was prescribed post-HA, increasing from 2.7 ± 0.5 L to 3.2 ± 0.4 L in EUH, and from 0.7 ± 0.1 L to 0.8 ± 0.4 L in DEH trials (both P < 0.05) to account for increases in sweat rate throughout the 10-day HA period (P = 0.01). This resulted in similar body mass changes during exercise pre- and post-HA (P = 0.28). Body mass was generally maintained in EUH trials, averaging -0.6 ± 0.4% of pre-exercise values at 180 min. In contrast, fluid restriction resulted in average body mass deficits of 1.8 ± 0.3% at 100 min and 3.6 ± 0.7% at 180 min, respectively (both P < 0.001).

During the EUH trial, average T_{re} during upright exercise decreased from 38.4 ± 0.2°C pre-HA to 38.3 ± 0.1°C post-HA (P = 0.006) and was 0.2 ± 0.1°C lower at the end of the upright exercise period post-HA (P = 0.014). Average exercising HR was also lowered from 156 ± 8 to 149 ± 6 beats·min^{-1} with EUH following HA (P = 0.012) and was 7 ± 8 beats·min^{-1} lower at the end of upright exercise (P = 0.04). In contrast, average T_{re} during upright exercise with DEH (38.5 ± 0.2°C) was not altered post-HA (38.5 ± 0.3, P = 0.41). Average upright exercising HR with DEH was also unaltered, averaging 160 ± 6 and 157 ± 7 beats·min^{-1} pre- and post-HA, respectively (P = 0.19). Rating of perceived exertion at the end of upright exercise decreased with HA, averaging 15 ± 2 pre-HA and 13 ± 2 units post-HA with EUH (*P* = 0.016) and 16 ± 2 units pre-HA and 15 ± 2 units post-HA with DEH (*P* = 0.03), respectively. Thermal comfort was not altered by HA in either condition, averaging 5.2 ± 0.8 units at the end of upright exercise (all *P* > 0.05).

Heat acclimation effects on semi-recumbent exercise bouts at 100 and 180 min

The T_{re} responses to periods of semi-recumbent exercise were not altered by HA in either condition (*P* = 0.10), averaging 38.3 ± 0.2°C and 38.9 ± 0.4°C at 180 min with EUH and DEH, respectively. There were also no HA (*P* = 0.18) or time (*P* =0.78) effects on T_{sk} during exercise, which averaged 34.1 ± 0.8°C throughout all periods of semi-recumbent exercise (Figure 2). Similar to resting responses, there was no effect of HA on BV responses during exercise in either hydration state (both *P* > 0.05, Table 1, Figure 3). HR during semi-recumbent exercise was also unaltered by HA (*P* = 0.17), and was 139 ± 7 pre- and 135 ± 8 beats$\cdot$min^{-1} post-HA with EUH (*P* = 0.07) and 150 ± 10 pre- and 151 ± 10 beats$\cdot$min^{-1} post-HA with DEH (*P* = 1.00) at 180 min, respectively (Figure 3).

There was a main effect of HA on $\dot{Q}$ (*P* = 0.04) and a tendency for a HA-time interaction effect (*P* = 0.053). Pairwise analyses indicated $\dot{Q}$ was ~5% greater post-HA with EUH (0.7 ± 0.7 L$\cdot$min^{-1}, *P* = 0.031), reaching 15.1 ± 1.6 L$\cdot$min^{-1} prior to the end of exercise (Figure 4). This was associated with a slightly greater SV at 180 min with EUH exercise post-HA (9 ± 6 ml, *P* = 0.013). Despite the increase in SV there was no effect of HA on diastolic or systolic LV volumes (both *P* > 0.05). However, a HA-hydration-time effect was observed for EDV (*P* = 0.015). Pairwise analyses identified a slight 7 ± 5 ml decline in EDV with EUH pre-HA (*P* = 0.01) which was otherwise maintained post-HA (*P* = 1.0). There was also little to no effect of HA on LV function during exercise. A main effect of HA was observed in peak systolic apical strain (*P* = 0.026), but no pairwise differences were identified between trials (all *P* > 0.05). All other systolic and diastolic rotation, twist and strain parameters were similar pre- to post-HA with EUH (all *P* > 0.05, Tables 3 and 4, Figure 6).

There was a main effect of time on exercising SBP and DBP (both *P* < 0.01). Exercising SBP responses were similar pre- and post-HA (*P* = 0.499) and a significant main effect of HA was observed on DBP (*P* = 0.015). Pairwise analyses indicated a 6 ± 5 mmHg decline in SBP from 20 to 180 min of EUH exercise post-HA (*P* = 0.049), while DBP was 3 ± 3 mmHg lower at 180 min compared to pre-HA (*P* = 0.018). MAP tended to decrease with HA (*P* = 0.06), but no pairwise differences were observed between pre- and post-HA responses to exercise (all $P > 0.05$). There were main effects of time and HA (both $P < 0.001$) on TPR as well as a hydration-time interaction effect ($P = 0.007$), which was significantly lower post-HA with EUH from 100 min ($P < 0.05$, Figure 4). Similarly, there was also a main effect of HA ($P = 0.048$) and time ($P = 0.007$) on effective arterial elastance, which was significantly lower post-HA at 180 min with EUH (0.10 ± 0.11 $mmHg \cdot ml^{-1}$, $P = 0.03$, Figure 5). LV end-systolic elastance remained stable during exercise and was not altered by hydration or HA status (all $P > 0.05$, Figure 5). There was a main effect of HA ($P = 0.024$) and time ($P < 0.001$) on ventricular-arterial coupling, which was significantly greater with EUH post-HA at 180 min (0.38 ± 0.39, $P = 0.027$ Figure 5).

Exercise-induced dehydration following acclimation

Exercise-induced dehydration was associated with significant declines in PV ($11 \pm 4\%$, $P = 0.001$) and BV ($6 \pm 2\%$, $P = 0.001$) between 20- and 180-min post-HA (Table 1, Figure 3B). DEH also resulted in significantly greater increases in T_{re} (0.6 ± 0.4°C, $P = 0.004$) and HR (16 ± 7 $beats \cdot min^{-1}$, $P < 0.001$) compared to EUH post-HA at 180 min (Figures 2 and 3).

$\dot{Q}$ was maintained pre-HA with mild DEH at 100 min despite greater increases in T_{re} and HR and lower SV compared to EUH (all $P < 0.05$). In contrast, T_{re}, HR and SV were similar between trials at 100 min post-HA (all $P > 0.05$, Figures 2-3). However, no effect of HA was observed on the DEH responses to exercise ($P > 0.05$). Instead, $\dot{Q}$ declined from 100 min with DEH post-HA (1.3 ± 0.7 $L \cdot min^{-1}$, $P = 0.004$) and was 2.1 ± 0.8 $L \cdot min^{-1}$ lower compared to EUH at 180 min ($P < 0.001$, Figure 4). This was associated with a 26 ± 9 ml lower SV and 29 ± 16 ml lower EDV at the end of exercise compared to EUH (both $P = 0.001$, Figure 3). There was a main effect of hydration status on SBP ($P = 0.029$), which was 9 ± 9 mmHg lower with DEH compared to EUH at 180 min post-HA ($P = 0.034$). Exercising DBP was not altered by hydration status ($P = 0.218$). There was also a tendency for a main effect of hydration ($P = 0.08$) and a significant main effect of time ($P = 0.001$) on MAP. Pairwise analyses identified MAP declined slightly during DEH exercise and tended to be 6 ± 8 mmHg lower with DEH compared to EUH after 180 min post-HA ($P = 0.07$). No differences in TPR were observed between EUH and DEH exercise post-HA (all $P > 0.05$, Figure 4). Effective arterial elastance increased with progressive dehydration post-HA ($P < 0.001$) and was 0.29 ± 0.18 $mmHg \cdot ml^{-1}$ greater compared to EUH post-HA at 180 min ($P = 0.003$). Ventricular-arterial coupling was not altered by hydration status ($P = 0.693$, Figure 5).

There was a significant correlation between a decline in SV and reductions in EDV both pre- ($r = 0.664$, $P < 0.001$) and post-HA ($r = 0.691$, $P < 0.001$). Similarly, there were significant correlations for progressive declines in EDV during exercise and reductions in BV ($r = 0.484$ pre- and 0.528 post-HA, respectively; both $P < 0.001$) and increases in HR ($r = 0.467$ pre- and 0.464 post-HA, respectively; both $P < 0.001$; Figure 7).

Despite the decline in $\dot{Q}$ and SV, LV twist mechanics and strain were mostly unchanged or slightly enhanced by DEH (Tables 3 and 4, Figure 6). Peak systolic basal circumferential and longitudinal strains were slightly lower post-HA with DEH compared to EUH at 180 min ($P < 0.05$, Table 3). However, basal and apical systolic rotation and systolic and diastolic rotational velocities all increased with DEH from 20 min post-HA (all $P < 0.05$, Tables 3 and 4). Similarly, there was no effect of hydration post-HA on twist parameters (all $P > 0.05$), with peak twist increasing slightly ($P = 0.022$) and peak untwisting velocity maintained ($P = 0.20$) from 20 min with DEH (Figure 6).

Discussion

The main findings of the study are that i) HA has minimal effects on LV diastolic and systolic function, LV volumes and systemic hemodynamics at rest and during brief (20 min) submaximal exercise under moderate heat stress while euhydrated where BV and HR are similar pre- and post-HA and, ii) when euhydrated exercise is protracted these responses remain largely unaltered. However, iii) progressive dehydration >3% was associated with a lower $\dot{Q}$ and SV and greater elevations in T_{re} and HR compared to euhydration, regardless of HA state. Finally, iv) the lower $\dot{Q}$ and SV during exercise with dehydration appears to be largely driven by a reduction in BV and impairment in the diastolic filling of the LV, as the fall in EDV was similar to the decline in SV, while LV systolic and diastolic mechanical function and integrated LV performance were maintained or slightly enhanced. Collectively, these findings indicate that exercise HA has minimal effects on LV volumes, LV systolic and diastolic function and systemic hemodynamics in euhydrated and dehydrated trained humans.

Independent effects of heat acclimation on cardiovascular function

An important observation of this study is that systemic hemodynamics were largely unaffected by HA as $\dot{Q}$, MAP and TPR were relatively unaltered at rest and during exercise under moderate heat stress while EUH was maintained (Figure 4). Previous findings suggest $\dot{Q}$ is unaltered at rest (19) and during submaximal exercise (43, 61) following HA, while others report a significant increase (36) or decrease (60) during exercise in hot-dry heat, possibly reflecting differences in the severity of heat stress, intensity of exercise or training and hydration status (40). The effects of HA on blood pressure are also varied (13, 21, 24) with minimal data to determine the integrated hemodynamic responses to dynamic exercise, and therefore the mechanisms that may underpin changes in cardiovascular function, if they indeed occur. In this study, echocardiography was used to quantify intrinsic myocardial function and LV volumes. This was paired with measurements of absolute BV and MAP. As such, the cardiovascular responses to exercise and the effects of HA and hydration can be interpreted using two classic cardiovascular models. The first is the cardiac model, where cardiac function is determined by intrinsic (i.e. contractility) and extrinsic (i.e. preload and afterload) factors. The second is the systemic model based on the hydrodynamic equivalent of Ohm's law, where systemic perfusion pressure (MAP assuming right atrial pressure is 0 mmHg) is equal to the product of systemic blood flow (i.e. $\dot{Q}$) and resistance (i.e. TPR), and can be used alongside BV and estimates of effective arterial elastance, LV end-systolic elastance and ventricular arterial coupling to address potential systemic factors affecting cardiac preload and afterload with HA.

Intrinsically, SV is influenced by cardiac contractility. Findings of previous studies are limited to indications that HA may decrease sympathetic nerve activity (20, 36), perhaps altering the inotropic state of the myocardium. Direct evidence of the effects of passive HA on intrinsic cardiac function is limited to the rodent model and indicates that periods of 1-2 months result in several integrated molecular responses that improve contractility of the LV (25, 28). In the present study, tissue doppler and speckle tracking echocardiography were used to provide insight into human myocardial diastolic and systolic function at rest and during exercise in response to HA. A pertinent finding was that HA did not affect LV systolic or diastolic mechanical function. Resting early and late diastolic tissue velocities of the medial and lateral annulus, which correlate with early diastolic filling pressure and atrial function, respectively (52, 55), were similar between trials (Table 2). In addition, there were no differences in any rotational, twist, untwist or strain parameters at rest or during euhydrated exercise following HA (Tables 3 and 4, Figure 6), which may otherwise be suggestive of altered myocardial efficiency in the absence of changes in LV structure (52), as LV mass was also unaffected. Typically, evidence of LV remodelling or functional adaptations, such as increased chamber dimensions, wall thickness, or systolic and diastolic function may be apparent following periods of ~6 months of regular exercise in healthy humans (26, 52). As such, it appears that a 10-day HA regimen is not a sufficient stimulus to induce changes in cardiac structure and intrinsic function at rest or during submaximal exercise in the heat in endurance-trained individuals.

Extrinsically, LV volumes are influenced by afterload and preload. In the present study, HA had no effect on resting MAP, which was largely similar throughout EUH exercise, with only a tendency to be slightly (~4 mmHg) lower post-HA. Furthermore, TPR was similar at rest and 20 min of exercise between trials, with a small decrease post-HA noted from 100 min onward (Figure 4). Together with only slight differences in effective arterial elastance at rest and 180 min (Figure 5), it appears the relatively similar LV volumes and $\dot{Q}$ during EUH pre- and post-HA were not associated with a substantial reduction in afterload. An increase in PV and therefore total circulating BV is an often-reported response to HA (12, 54), but is not consistently observed (e.g. 14, 33). The prevailing view is that a greater BV increases the filling pressure of the LV and SV, which would permit $\dot{Q}$ to increase following HA (40, 49, 54), assuming no other changes occur. Studies supporting this view have reported increases in SV, with an unchanged or increased $\dot{Q}$ in conjunction with PV expansion in the region of 7-9% (19, 36, 61). However, the assumption that increased PV and therefore BV alone with HA would enhance $\dot{Q}$ is largely unsupported in the literature (19, 24, 43, 60). For example, a ~6% PV expansion pre- to post-HA does not appear to alter $\dot{Q}$ responses to incremental exercise in the heat (24). Furthermore, acute ~600-800 ml increases in BV have been shown to increase $\dot{Q}$ and SV during cycling exercise (11) or have no effect on $\dot{Q}$, SV, leg blood flow or oxygen uptake (18) at rest and during single leg knee-extensor exercise. Therefore, the independent role of PV and BV expansion with HA on cardiovascular control is unclear and indicates numerous factors act to modulate $\dot{Q}$ responses following HA. In contrast to the observations of Nielsen et al. (36) and in disagreement with the present hypothesis, $\dot{Q}$ was unaltered at rest, 20 and 100 min, with only a slight (0.7 $L \cdot min^{-1}$) increase observed at 180 min with EUH post-HA in the present study. Compared to pre-HA, BV and diastolic filling of the LV was similar and was associated with a largely unaltered SV at rest and during exercise (+6-9 ml). HR was also unaltered by HA during submaximal semi-recumbent cycling under moderate heat stress (Figure 3). A reduction in HR with HA may increase the diastolic filling time of the LV. Further work exploring the relationship between lowered HR, enhanced BV, and greater LV preload, such as during different modalities of exercise and in a range of populations, is warranted. Nonetheless, the observations that HR, BV, LV volumes, LV intrinsic mechanical function, integrated LV performance, ventricular-arterial coupling and systemic hemodynamics were similar between trials indicate that 10 days of exercise HA in the present study did not significantly alter cardiovascular function and its regulation at rest and during submaximal exercise in euhydrated trained individuals.

Acute exercise-induced dehydration and cardiovascular function

A second major finding of the present study was that HA did not attenuate the deleterious effects of dehydration on LV filling and systemic hemodynamics or altered intrinsic diastolic and systolic mechanical function. In this study, fluid intake was manipulated so that similar mild (~1.8%) and moderate (~3.6%) reductions in body mass occurred before and after HA, permitting the effects of HA on standardized levels of dehydration via exercise-induced heat stress to be determined. In the dehydration trial, $\dot{Q}$ was ~2.1 $L \cdot min^{-1}$ lower than euhydration at 180 min post-HA, and was associated with a disproportionately larger fall in SV compared to the increase in HR. The SV decline does not appear to be related to increased afterload, when considering the MAP responses to dehydration. Similar to previous studies (15, 17, 56), MAP decreased during exercise with DEH and tended to be lower than EUH pre- and post-HA (Figure 4). However, the parallel increase in effective arterial elastance is suggestive of an elevation in the net arterial load imposed on the LV and thus the possibility remains that elevated afterload might have contributed to the lowering in SV. Notwithstanding, the observation that ESV and end-systolic elastance did not change with DEH (Figures 3 and 5) indicate that the integrated performance of the LV was preserved and thus the impact of the elevated afterload on SV was negligible (59).

The lower $\dot{Q}$ and SV with DEH were also unrelated to a blunting of intrinsic LV function. The present findings agree with recent observations during exercise-induced dehydration in that LV diastolic and systolic mechanical performance are generally maintained or enhanced as exercise progresses (59) (Tables 3 and 4, Figures 3 and 6). Nevertheless, there was a relatively small reduction in basal and longitudinal strain at 180 min, which has been shown to occur with dehydration (50) and hemodialysis (10), indicating an influence of preload on this parameter. However, rotation, rotational velocities, systolic twist and diastolic untwisting rate were either maintained or significantly increased with dehydration, suggesting a slight enhancement in myocardial contractility, possibly due to enhanced sympathetic nerve activity (15). As such, it appears that dehydration and concomitant hyperthermia are associated with a general maintenance or slight improvement in the intrinsic systolic and diastolic function of the LV, and HA does not appear to influence these responses.

Instead the present findings indicate that the preload of the heart is diminished with acute moderate DEH, but HA does not alter this response. The ~0.6°C and ~16 beats·min^{-1} greater T_{re} and HR and the ~360 ml lower BV at the end of exercise were strikingly similar post- and pre-HA. This finding does not support our hypothesis that HA would attenuate the effects of exercise-induced dehydration on the thermal, intervascular and cardiac volume responses to moderate heat stress exercise (39, 46). Interestingly, the unaltered HR and BV with HA were associated with comparable LV filling responses, with DEH similarly impairing preload (~29 ml) and SV (~26 ml) at the end of exercise pre- and post-HA. Both a diminished BV and elevated HR, and thus lower diastolic filling time, were associated with the decline in EDV (Figure 3 and 7), with each likely interacting with other factors such as compromised peripheral blood flow (i.e. brain, skin and non- and exercising muscle) (16, 17, 29, 31, 56, 59) to diminish LV preload. In support of an interactive effect of several factors modulating cardiovascular function, acute blood withdrawal alone (20% BV or ~1.2 L/min) does not alter SV and $\dot{Q}$ at rest and during leg extension exercise (6, 18). Similarly, acute elevations in HR via atrial pacing lowers EDV and SV, but does not alter $\dot{Q}$ at rest (42, 44) and during submaximal or maximal exercise (32, 42), nor changes leg blood flow or other hemodynamic variables in these conditions (32). In contrast, during dynamic exercise in dehydrated and hyperthermic individuals, dextran infusion halves the reduction in SV and attenuates the increase in HR compared to fluid restriction alone, such that $\dot{Q}$ (30) and thus peripheral blood flow are restored. Collectively, the present and previous findings reveal that moderate dehydration reduces BV and peripheral blood flow (16, 17, 30, 31, 56, 59) during exercise-heat stress and exacerbates the increase in T_{re} and HR, with these responses interacting to impair the diastolic filling of the LV (Figure 8).

Limitations

Given the similarities in T_{re} and HR during bouts of semi-recumbent cycling, it may appear the HA intervention did not induce significant adaptation in this study. However, these similarities may be explained by the experimental procedures used, as T_{re}, HR and RPE were ~0.2°C, ~7 beats·min^{-1} and 2 units lower at the end of upright exercise with euhydration post-HA, respectively. Instead, the similar responses noted during semi-recumbent cycling may result from periods of brief rest for the assessment of body mass, moderate environmental heat stress, semi-recumbent cycling position and submaximal exercise intensity, or a combination thereof. This experimental approach was chosen to minimise participant discomfort, ensure adequate echocardiographic image quality and the standardization of hydration status between trials. Future studies should determine the peripheral and central haemodynamic responses to continuous dynamic exercise to elucidate the influence of peripheral vascular factors on cardiac function following HA. Secondly, from a cardiac perspective, the present study was limited to echocardiographic speckle tracking and LV volume assessments. Future studies should seek to determine intra-ventricular pressure gradients and/or assess the effects of HA on right heart volume and function, which may provide any indication of alterations in diastolic ventricular filling or pulmonary blood flow, respectively. Finally, some of the peak systolic and diastolic parameters appear to be somewhat lower than previous studies adopting similar protocols (59). Every effort was taken to ensure the short-axis apical images were standardized and collected as caudal as possible. However, it seems likely these images were collected off-axis, which is known to underestimate peak systolic apical rotation (58) and thus velocity and twist parameters. However, values were similar at rest and during the initial 20 min bouts of exercise between pre-HA trials. Furthermore, there was a consistent effect of DEH on apical rotation and rotational velocity (Table 3). Therefore, these parameters are adequately reproducible and are valid reflections of potential differences occurring due to HA or dehydration.

Conclusions

Heat acclimation did not notably increase SV and $\dot{Q}$ at rest or during prolonged dynamic euhydrated exercise in the heat through increased BV or diastolic filling of the LV. Similarly, systolic and diastolic LV function were largely unaffected following 10 days of heat acclimation during euhydrated exercise. In contrast, dehydration beyond 3% of body mass was associated with greater hyperthermia, elevated HR, reduced BV and a decline in the LV diastolic filling, which reduced $\dot{Q}$, regardless of HA state. This occurred in the face of a general maintenance or even slight enhancement of LV mechanical function and performance. Together, these findings indicate the cardiovascular system is highly responsive to stress evoked by acute dehydration but is largely unaffected by exercise-heat acclimation when HR and BV are not altered.

Acknowledgements

The authors wish to thank Mr Salam Abourafeh, Mr Sean McCrudden, Dr Ihsan Mohammed, Mrs Elena Procopciuc and Dr Nathan Townsend for their assistance in data collection. We would also like to thank Dr Carmen Adamuz, Dr Victoria Watt, Mr DeWet van der Westhuizen and Prof. Mathew Wilson for their technical expertise. The authors also extend a special thank you to the participants who made this study possible.

Funding

This study was funded by Aspetar Orthopaedic and Sports Medicine Hospital, Doha, Qatar.

Conflicts of interest

The authors have no conflicts of interest to declare.

Author contributions

GT, JP and JG-A designed the study. GT, NR, AS and DN collected the data. GT, JP, JG-A, AS, NE and DN interpreted and analysed the data. All authors contributed to drafting the work, revising it critically for important intellectual content and approved the final manuscript.

References

1. **Armstrong LE**, **Maresh CM**, **Castellani JW**, **Bergeron MF**, **Kenefick RW**. Urinary indices of hydration status. *Int J Sport Nutr* 4: 265–279, 1994. doi: 10.1123/ijsn.8.4.345.

2. **Bedford T**. *The warmth factor in comfort at work*. 1936.

3. **Borg GA.** Pyshophysical bases of perceived exertion. *Med Sci Sports Exerc* 14: 377–381, 1982. doi: 10.1249/00005768-198205000-00012.

4. **Brothers RM**, **Bhella PS**, **Shibata S**, **Wingo JE**, **Levine BD**, **Crandall CG**. Cardiac systolic and diastolic function during whole body heat stress. *Am J Physiol - Hear Circ Physiol* 296: 1150–1156, 2009. doi: 10.1152/ajpheart.01069.2008.

5. **Brunt VE**, **Howard MJ**, **Francisco MA**, **Ely BR**, **Minson CT**. Passive heat therapy improves endothelial function, arterial stiffness and blood pressure in sedentary humans. *J Physiol* 594: 5329–5342, 2016. doi: 10.1113/JP272453.

6. **Burns AT**, **Gerche A La**, **Prior DL**, **MacIsaac AI**. Left ventricular torsion parameters are affected by acute changes in load. *Echocardiography* 27: 407–414, 2010. doi: 10.1111/j.1540-8175.2009.01037.x.

7. **Buskirk ER**, **Iampietro PF**, **Bass DE**. Work performance after dehydration: effects of physical conditioning and heat acclimatization. *J Appl Physiol* 12: 189–194, 1958. doi: 10.1152/jappl.1958.12.2.189.

8. **Chantler PD**, **Lakatta EG**. Arterial-ventricular coupling with aging and disease. *Front Physiol* 3 MAY: 1–13, 2012. doi: 10.3389/fphys.2012.00090.

9. **Chantler PD**, **Lakatta EG**, **Najjar SS**. Arterial-ventricular coupling: Mechanistic insights into cardiovascular performance at rest and during exercise. *J Appl Physiol* 105: 1342–1351, 2008. doi: 10.1152/japplphysiol.90600.2008.

10. **Choi JO**, **Shin DH**, **Cho SW**, **Song Y Bin**, **Kim JH**, **Kim YG**, **Lee SC**, **Park SW**. Effect of preload on left ventricular longitudinal strain by 2D speckle tracking. *Echocardiography* 25: 873–879, 2008. doi: 10.1111/j.1540-8175.2008.00707.x.

11. **Fortney SM**, **Nadel ER**, **Wenger CB**, **Bove JR**. Effecet of acute alterations of blood

volume on circulatory performance in humans. *J Appl Physiol* 50: 292–298, 1981. doi: 10.1152/jappl.1981.50.2.292.

12. **Fox RH**, **Goldsmith R**, **Kidd DJ**, **Lewis HE**. Acclimatization to heat in man by controlled elevation of body temperature. *J Physiol* 166: 530–547, 1963. doi: 10.1113/jphysiol.1963.sp007121.

13. **Fujii N**, **Honda Y**, **Ogawa T**, **Tsuji B**, **Kondo N**, **Koga S**, **Nishiyasu T**. Short-term exercise-heat acclimation enhances skin vasodilation but not hyperthermic hyperpnea in humans exercising in a hot environment. *Eur J Appl Physiol* 112: 295–307, 2012. doi: 10.1007/s00421-011-1980-6.

14. **Garrett AT**, **Goosens NG**, **Rehrer NG**, **Patterson MJ**, **Cotter JD**. Induction and decay of short-term heat acclimation. *Eur J Appl Physiol* 107: 659–670, 2009. doi: 10.1007/s00421-009-1182-7.

15. **González-Alonso J**. Separate and combined influences of dehydration and hyperthermia on cardiovascular responses to exercise. *Int J Sports Med* 19: 6–9, 1998. doi: 10.1055/s-2007-971972.

16. **González-Alonso J**, **Calbet JAL**, **Nielsen B**. Muscle blood flow is reduced with dehydration during prolonged exercise in humans. *J Physiol* 513: 895–905, 1998. doi: 10.1111/j.1469-7793.1998.895ba.x.

17. **Gonzalez-Alonso J**, **Mora-Rodriguez R**, **Below PR**, **Coyle EF**. Dehydration reduces cardiac output and increases systemic and cutaneous vascular resistance during exercise. *J Appl Physiol* 79: 1487–1496, 1995. doi: 10.1152/jappl.1995.79.5.1487.

18. **González-Alonso J**, **Mortensen SP**, **Dawson EA**, **Secher NH**, **Damsgaard R**. Erythrocytes and the regulation of human skeletal muscle blood flow and oxygen delivery: Role of erythrocyte count and oxygenation state of haemoglobin. *J Physiol* 572: 295–305, 2006. doi: 10.1113/jphysiol.2005.101121.

19. **Goto M**, **Okazaki K**, **Kamijo YI**, **Ikegawa S**, **Masuki S**, **Miyagawa K**, **Nose H**. Protein and carbohydrate supplementation during 5-day aerobic training enhanced plasma volume expansion and thermoregulatory adaptation in young men. *J Appl Physiol* 109: 1247–1255, 2010. doi: 10.1152/japplphysiol.00577.2010.

20. **Hodge D**, **Jones D**, **Martinez R**, **Buono MJ**. Time course of the attenuation of sympathetic nervous activity during active heat acclimation. *Auton Neurosci Basic Clin* 177: 101–103, 2013. doi: 10.1016/j.autneu.2013.02.017.

21. **Ichinose TK**, **Inoue Y**, **Hirata M**, **Shamsuddin AKM**, **Kondo N**. Enhanced heat loss responses induced by short-term endurance training in exercising women. *Exp Physiol* 94: 90–102, 2009. doi: 10.1113/expphysiol.2008.043810.

22. **Ikegawa S**, **Kamijo YI**, **Okazaki K**, **Masuki S**, **Okada Y**, **Nose H**. Effects of hypohydration on thermoregulation during exercise before and after 5-day aerobic training in a warm environment in young men. *J Appl Physiol* 110: 972–980, 2011. doi: 10.1152/japplphysiol.01193.2010.

23. **Joyce W**, **Wang T**. What determines systemic blood flow in vertebrates? *J Exp Biol* 223, 2020. doi: 10.1242/jeb.215335.

24. **Keiser S**, **Flück D**, **Hüppin F**, **Stravs A**, **Hilty MP**, **Lundby C**. Heat training increases exercise capacity in hot but not in temperate conditions: A mechanistic counter-balanced cross-over study. *Am J Physiol - Hear Circ Physiol* 309: H750–H761, 2015. doi: 10.1152/ajpheart.00138.2015.

25. **Levi E**, **Vivi A**, **Hasin Y**, **Tassini M**, **Navon G**, **Horowitz M**. Heat acclimation improves cardiac mechanics and metabolic performance during ischemia and reperfusion. *J Appl Physiol* 75: 833–839, 1993. doi: 10.1152/jappl.1993.75.2.833.

26. **Levy WC**, **Cerqueira MD**, **Abrass IB**, **Schwartz RS**, **Stratton JR**. Endurance exercise training augments diastolic filling at rest and during exercise in healthy young and older men. *Circulation* 88: 116–126, 1993. doi: 10.1161/01.CIR.88.1.116.

27. **Lorenzo S**, **Halliwill JR**, **Sawka MN**, **Minson CT**. Heat acclimation improves exercise performance. *J Appl Physiol* 109: 1140–1147, 2010. doi: 10.1152/japplphysiol.00495.2010.

28. **Mirit E**, **Gross C**, **Hasin Y**, **Palmon A**, **Horowitz M**. Changes in cardiac mechanics with heat acclimation: Adrenergic signaling and SR-Ca regulatory proteins. *Am J Physiol - Regul Integr Comp Physiol* 279: 77–85, 2000. doi: 10.1152/ajpregu.2000.279.1.r77.

29. **Montain SJ**, **Coyle EF**. Influence of graded dehydration on hyperthermia and cardiovascular drift during exercise. *J Appl Physiol* 73: 1340–1350, 1992. doi: 10.1152/jappl.1992.73.4.1340.

30. **Montain SJ**, **Coyle EF**. Fluid ingestion during exercise increases skin blood flow independent of increases in blood volume. *J Appl Physiol* 73: 903–910, 1992. doi: 10.1152/jappl.1992.73.3.903.

31. **Montain SJ**, **Sawka MN**, **Latzka WA**, **Valeri CR**. Thermal and cardiovascular strain from hypohydration: Influence of exercise intensity. *Int J Sports Med* 19: 87–91, 1998. doi: 10.1055/s-2007-971887.

32. **Munch GDW**, **Svendsen JH**, **Damsgaard R**, **Secher NH**, **González-Alonso J**, **Mortensen SP**. Maximal heart rate does not limit cardiovascular capacity in healthy humans: Insight from right atrial pacing during maximal exercise. *J Physiol* 592: 377–390, 2014. doi: 10.1113/jphysiol.2013.262246.

33. **Neal RA**, **Corbett J**, **Massey HC**, **Tipton MJ**. Effect of short-term heat acclimation with permissive dehydration on thermoregulation and temperate exercise performance. *Scand J Med Sci Sport* 26: 875–884, 2016. doi: 10.1111/sms.12526.

34. **Nelson MD**, **Altamirano-Diaz LA**, **Petersen SR**, **DeLorey DS**, **Stickland MK**, **Thompson RB**, **Haykowsky MJ**. Left ventricular systolic and diastolic function during tilt-table positioning and passive heat stress in humans. *Am J Physiol - Hear Circ Physiol* 301: 599–608, 2011. doi: 10.1152/ajpheart.00127.2011.

35. **Nielsen B**, **Strange S**, **Christensen NJ**, **Warberg J**, **Saltin B**. Acute and adaptive responses in humans to exercise in a warm, humid environment. *Pflugers Arch Eur J Physiol* 434: 49–56, 1997. doi: 10.1007/s004240050361.

36. **Nielsen BYB**, **Hales JRS**, **Strange S**, **Christensen NJ**, **Warberg J**, **Saltin B**. Human circulatory and thermoregulatory adaptations with heat acclimation and exercise in a hot, dry environment. *J Physiol* 460: 467–485, 1993. doi: 10.1113/jphysiol.1993.sp019482.

37. **Oberholzer L**, **Siebenmann C**, **Mikkelsen CJ**, **Junge N**, **Piil JF**, **Morris NB**, **Goetze JP**, **Meinild Lundby A-K**, **Nybo L**, **Lundby C**. Hematological Adaptations to

Prolonged Heat Acclimation in Endurance-Trained Males. *Front Physiol* 10: 1–8, 2019. doi: 10.3389/fphys.2019.01379.

38. **Opdahl A**, **Helle-Valle T**, **Remme EW**, **Vartdal T**, **Pettersen E**, **Lunde K**, **Edvardsen T**, **Smiseth OA**. Apical Rotation by Speckle Tracking Echocardiography: A Simplified Bedside Index of Left Ventricular Twist. *J Am Soc Echocardiogr* 21: 1121–1128, 2008. doi: 10.1016/j.echo.2008.06.012.

39. **Patterson MJ**, **Stocks JM**, **Taylor NAS**. Humid heat acclimation does not elicit a preferential sweat redistribution toward the limbs. *Am J Physiol - Regul Integr Comp Physiol* 286: 512–518, 2004. doi: 10.1152/ajpregu.00359.2003.

40. **Périard JD**, **Racinais S**, **Sawka MN**. Adaptations and mechanisms of human heat acclimation: Applications for competitive athletes and sports. *Scand J Med Sci Sport* 25: 20–38, 2015. doi: 10.1111/sms.12408.

41. **Ramanathan NL**. a New Weighting System for Mean Surface Temperature of the Human Body. *J Appl Physiol* 19: 531–533, 1964. doi: 10.1152/jappl.1964.19.3.531.

42. **Ross J**, **Linhart JW**, **Brauwald E**. Effects of changing heart rate in man by electrical stimulation of the right atrium. studies at rest, during exercise, and with isoproterenol. *Circulation* 32: 549–558, 1965. doi: 10.1161/01.CIR.32.4.549.

43. **Rowell LB**, **Kraning KK**, **Kennedy JW**, **Evans TO**. Central circulatory responses to work in dry heat before and after acclimatization. *J Appl Physiol* 22: 509–518, 1967. doi: 10.1152/jappl.1967.22.3.509.

44. **Rozenman Y**, **Weiss AT**, **Atlan H**, **Gotsman MS**. Left ventricular function during atrial pacing: A radionuclide angiographic study. *Clin Cardiol* 7: 349–355, 1984. doi: 10.1002/clc.4960070606.

45. **Sagawa K**, **Suga H**, **Shoukas AA**, **Bakalar KM**. End-systolic pressure/volume ratio: A new index of ventricular contractility. *Am J Cardiol* 40: 748–753, 1977. doi: 10.1016/0002-9149(77)90192-8.

46. **Sawka MN**, **Toner MM**, **Francesconi RP**, **Pandolf KB**. Hypohydration and exercise: Effects of heat acclimation, gender, and environment. *J Appl Physiol Respir Environ*

Exerc Physiol 55: 1147–1153, 1983. doi: 10.1152/jappl.1983.55.4.1147.

47. **Schiller NB**, **Shah PM**, **Crawford M**, **DeMaria A**, **Devereux R**, **Feigenbaum H**, **Gutgesell H**, **Reichek N**, **Sahn D**, **Schnittger I**, **Silverman NH**, **Tajik AJ**. Recommendations for Quantitation of the Left Ventricle by Two-Dimensional Echocardiography. *J Am Soc Echocardiogr* 2: 358–367, 1989. doi: 10.1016/S0894-7317(89)80014-8.

48. **Schmidt W**, **Prommer N**. The optimised CO-rebreathing method: A new tool to determine total haemoglobin mass routinely. *Eur J Appl Physiol* 95: 486–495, 2005. doi: 10.1007/s00421-005-0050-3.

49. **Senay LC**. An inquiry into the role of cardiac filling pressure in acclimatization to heat. *Yale J Biol Med* 59: 247–256, 1986.

50. **Stöhr EJ**, **González-Alonso J**, **Pearson J**, **Low DA**, **Ali L**, **Barke H**, **Shave R**. Dehydration reduces left ventricular filling at rest and during exercise independent of twist mechanics. *J Appl Physiol* 111: 891–897, 2011. doi: 10.1152/japplphysiol.00528.2011.

51. **Stöhr EJ**, **González-Alonso J**, **Pearson J**, **Low DA**, **Ali L**, **Barker H**, **Shave R**. Effects of graded heat stress on global left ventricular function and twist mechanics at rest and during exercise in healthy humans. *Exp Physiol* 96: 114–124, 2011. doi: 10.1113/expphysiol.2010.055137.

52. **Stöhr EJ**, **McDonnell B**, **Thompson J**, **Stone K**, **Bull T**, **Houston R**, **Cockcroft J**, **Shave R**. Left ventricular mechanics in humans with high aerobic fitness: Adaptation independent of structural remodelling, arterial haemodynamics and heart rate. *J Physiol* 590: 2107–2119, 2012. doi: 10.1113/jphysiol.2012.227850.

53. **Takeuchi M**, **Igarashi Y**, **Tomimoto S**, **Odake M**, **Hayashi T**, **Tsukamoto T**, **Hata K**, **Takaoka H**, **Fukuzaki H**. Single-beat estimation of the slope of the end-systolic pressure - volume relation in the human left ventricle. *Circulation* 83: 202–212, 1991. doi: 10.1161/01.CIR.83.1.202.

54. **Taylor NAS**. Human heat adaptation. *Compr Physiol* 4: 325–365, 2014. doi: 10.1002/cphy.c130022.

55. **Thomas L**, **Levett K**, **Boyd A**, **Leung DYC**, **Schiller NB**, **Ross DL**. Changes in regional left atrial function with aging: Evaluation by doppler tissue imaging. *Eur J Echocardiogr* 4: 92–100, 2003. doi: 10.1053/euje.2002.0622.

56. **Trangmar SJ**, **Chiesa ST**, **Llodio I**, **Garcia B**, **Kalsi KK**, **Secher NH**, **González-Alonso J**. Dehydration accelerates reductions in cerebral blood flow during prolonged exercise in the heat without compromising brain metabolism. *Am J Physiol - Hear Circ Physiol* 309: H1598–H1607, 2015. doi: 10.1152/ajpheart.00525.2015.

57. **Travers G**, **Nichols D**, **Riding N**, **González-Alonso J**, **Périard JD**. Heat Acclimation with Controlled Heart Rate: Influence of Hydration Status. *Med Sci Sport Exerc* 52: 1815–1824, 2020. doi: 10.1249/MSS.0000000000002320.

58. **van Dalen BM**, **Vletter WB**, **Soliman OII**, **ten Cate FJ**, **Geleijnse ML**. Importance of Transducer Position in the Assessment of Apical Rotation by Speckle Tracking Echocardiography. *J Am Soc Echocardiogr* 21: 895–898, 2008. doi: 10.1016/j.echo.2008.02.001.

59. **Watanabe K**, **Stöhr EJ**, **Akiyama K**, **Watanabe S**, **González-Alonso J**. Dehydration reduces stroke volume and cardiac output during exercise because of impaired cardiac filling and venous return, not left ventricular function. *Physiol Rep* 8, 2020. doi: 10.14814/phy2.14433.

60. **Wyndham CH**. Effect of Acclimatization on Circulatory Responses to High Environmental Temperatures. *J Appl Physiol* 4: 383–395, 1951. doi: 10.1152/jappl.1951.4.5.383.

61. **Wyndham CH**, **Benade AJ**, **Williams CG**, **Strydom NB**, **Goldin A**, **Heyns AJ**. Changes in central circulation and body fluid spaces during acclimatization to heat. *J Appl Physiol* 25: 586–593, 1968. doi: 10.1152/jappl.1968.25.5.586.

Figure legends

Figure 1. Schematic representation of the euhydration (EUH) and progressive dehydration (DEH) experimental trials separated by 10 days of heat acclimation (HA) with controlled heart rate (HR) (Top section). Blood volume (BV) was determined via carbon monoxide rebreathing. Upright and semi-recumbent cycling maximal oxygen uptake ($\dot{V}$O2max) as well as unacclimated sweat rate were determined pre-HA. Truncations indicate a minimum of 24 h between trials. Experimental trials (Bottom left) with EUH or DEH were conducted in a randomized counterbalanced order. Grey arrows indicate measurements of nude body mass. Black arrows indicate measurements of blood pressure and volume and left ventricular function. Measurements were conducted in the left-lateral decubitus position at rest and during sub-maximal cycling exercise (Bottom right).

Figure 2. Rectal (A and B) and mean skin (C and D) temperatures at rest and during discontinuous bouts of semi-recumbent cycling exercise under moderate heat stress pre- and post-heat acclimation (HA). Exercise was conducted with maintained euhydration (left) or with progressive dehydration (right) via fluid restriction. Data are means ± SD for 8 participants. *$P < 0.05$ vs. 20 min. $^{\dagger}P < 0.05$ vs. 100 min. $^{\ddagger}P < 0.05$ vs. euhydration.

Figure 3. Blood volume (BV; A and B), heart rate (HR; C and D), stroke volume (SV; E and F), end-diastolic (EDV; G and H) and end-systolic volumes (ESV; I and J) at rest and during bouts of semi-recumbent exercise under moderate heat stress pre- and post-heat acclimation (HA). Responses were measured while euhydration was maintained (left) or during progressive dehydration (right) via fluid restriction. Data are means ± SD for 8 participants. *$P < 0.05$ vs. 20 min. $^{\dagger}P < 0.05$ vs. 100 min. $^{\ddagger}P < 0.05$ vs. euhydration. #$P < 0.05$ vs. pre-HA.

Figure 4. Mean arterial pressure (MAP; A and B), cardiac output (C and D) and total peripheral resistance (TPR; E and F) at rest and during semi-recumbent cycling exercise under moderate heat stress pre- and post-heat acclimation (HA). Responses were measured while euhydration was maintained (left) or during progressive dehydration (right) via fluid restriction. Data are means ± SD for 8 participants. *$P < 0.05$ vs. 20 min. $^{\dagger}P < 0.05$ vs. 100 min. $^{\ddagger}P < 0.05$ vs. euhydration. #$P < 0.05$ vs. pre-HA.

Figure 5. Effective arterial elastance (A and B), left ventricular end-systolic elastance (C and D) and ventricular-arterial coupling (E and F) at rest and during exercise under moderate heat

stress pre- and post-heat acclimation (HA). Responses were measured while euhydration was maintained throughout (left) or during progressive dehydration (right) via fluid restriction. Data are means ± SD for 8 participants. *$P < 0.05$ vs. 20 min. $^{\dagger}P < 0.05$ vs. 100 min. $^{\ddagger}P < 0.05$ vs. euhydration. #$P < 0.05$ vs. pre-HA.

Figure 6. Left ventricular systolic twist (A and B) and diastolic untwisting velocity (C and D) at rest and during semi-recumbent exercise under moderate heat stress pre- and post-heat acclimation (HA). Responses were measured while euhydration was maintained (left) or during progressive dehydration (right) via fluid restriction. Data are means ± SD for 8 participants. *$P < 0.05$ vs. 20 min.

Figure 7. Relationships between stroke volume and end-diastolic volume (A) and between end-diastolic volume and blood volume (B) or heart rate (C). Data are for means ± SD responses for euhydrated and progressive dehydration trials pre- (open circles) and post-heat acclimation (closed circles), respectively. Lines are regression lines.

Figure 8. Summary of the effects of HA on cardiovascular adjustments to prolonged (180 min) dynamic exercise under moderate heat stress with maintained euhydration (A) and the influence of acute dehydration >3% on responses post-HA (B). Data are mean ± SD for 8 participants. With euhydration, cardiac output ($\dot{Q}$) and stroke volume (SV) are only slightly enhanced where blood volume, heart rate (HR), left ventricular (LV) mechanical function and diastolic filling of the LV (EDV) are similar. The slightly greater $\dot{Q}$ is associated with reduced Total peripheral resistance (TPR) as mean arterial pressure (MAP) is similar post-HA. In contrast, dehydration following HA results in a reduction in $\dot{Q}$ due to a fall in SV and is associated with a decline in MAP and increasing TPR. The post-HA fall in SV occurs as a result of a lower EDV, second to reductions in blood volume and ventricular filling time as end-systolic volume (ESV) and LV diastolic and systolic mechanical function are maintained or slightly enhanced, respectively throughout exercise. Grey arrows indicate relationships between variables and associated mechanisms.

Table 1. Hematological responses at rest and during repeated bouts of semi-recumbent cycling under moderate heat stress with euhydration (EUH) or progressive dehydration (DEH) before and after heat acclimation (HA).

	Trial	HA	Time (min) Rest	20	100	180
Red cell volume (ml)	EUH	Pre	2701 ± 213	2704 ± 213	2703 ± 212	2701 ± 210
		Post	2671 ± 223	2667 ± 222§	2668 ± 221§	2667 ± 222§
	DEH	Pre	2701 ± 212	2701 ± 213	2705 ± 212	2702 ± 212
		Post	2668 ± 222	2668 ± 222§	2668 ± 220§	2667 ± 222§
Plasma volume (ml)	EUH	Pre	3323 ± 294	2952 ± 278	2971 ± 270	2977 ± 247
		Post	3378 ± 295	3076 ± 294	3099 ± 307	3097 ± 269
	DEH	Pre	3341 ± 347	2970 ± 326	2827 ± 276*	2663 ± 249*†‡
		Post	3427 ± 254	3068 ± 219	2930 ± 189*	2716 ± 163*†‡
Hemoglobin ($g \cdot dl^{-1}$)	EUH	Pre	14.6 ± 0.6	15.6 ± 0.6	15.5 ± 0.6	15.5 ± 0.6
		Post	14.4 ± 0.8	15.2 ± 0.9§	15.1 ± 0.9§	15.1 ± 0.9§
	DEH	Pre	14.6 ± 0.8	15.6 ± 0.8	16.0 ± 0.8*	16.4 ± 0.7*†‡
		Post	14.3 ± 0.8	15.2 ± 0.7§	15.5 ± 0.8*	16.2 ± 0.8*†‡
Hematocrit (%)	EUH	Pre	45 ± 2	48 ± 2	48 ± 2	48 ± 2
		Post	44 ± 3	46 ± 3§	46 ± 3§	46 ± 3§
	DEH	Pre	45 ± 2	48 ± 2	49 ± 2*	50 ± 2*†‡
		Post	44 ± 2	47 ± 2§	48 ± 3*§	50 ± 2*†‡
Lactate ($mmol \cdot L^{-1}$)	EUH	Pre	1.3 ± 0.5	2.5 ± 0.8	2.3 ± 0.7	2.4 ± 0.4
		Post	1.2 ± 0.3	1.9 ± 0.5§	1.9 ± 0.5§	1.9 ± 0.3§
	DEH	Pre	1.2 ± 0.4	2.6 ± 0.9	2.1 ± 0.7*	2.3 ± 0.6
		Post	1.3 ± 0.4	2.2 ± 0.8§	1.7 ± 0.5*§	2.1 ± 0.2
Sodium ($mmol \cdot L^{-1}$)	EUH	Pre	140 ± 2	142 ± 2	143 ± 2	143 ± 2*
		Post	140 ± 2	141 ± 2	142 ± 2	142 ± 1
	DEH	Pre	140 ± 2	141 ± 2	145 ± 2*‡	148 ± 2*†‡
		Post	140 ± 2	142 ± 2	145 ± 2*‡	149 ± 3*†‡

*$P < 0.05$ vs. 20 min. †$P < 0.05$ vs. 100 min. ‡$P < 0.05$ vs. EUH. §$P < 0.05$ vs. pre-HA.

Table 2. Resting systolic and diastolic tissue velocities and timings before and after heat acclimation.

	Euhydration trial		Dehydration trial	
	Pre	Post	Pre	Post
Medial s' ($cm·s^{-1}$)	9 ± 1	9 ± 1	9 ± 1	9 ± 1
Medial e' ($cm·s^{-1}$)	12 ± 1	12 ± 2	12 ± 1	12 ±2
Medial a' ($cm·s^{-1}$)	8 ± 1	8 ± 1	8 ± 1	8 ± 2
Lateral e' ($cm·s^{-1}$)	16 ± 3	16 ± 3	16 ± 3	16 ± 2
Lateral a' ($cm·s^{-1}$)	7 ± 2	6 ± 1	7 ± 2	7 ± 3
IVRT (ms)	88 ± 7	94 ± 9	85 ± 12	93 ± 9*

IVRT: iso-volumetric relaxation time. *$P < 0.05$ vs. pre-acclimation.

Table 3. Peak systolic left ventricular strain and rotation parameters at rest and during exercise under moderate heat stress with maintained euhydration (EUH) and progressive dehydration (DEH) before and after heat acclimation (HA).

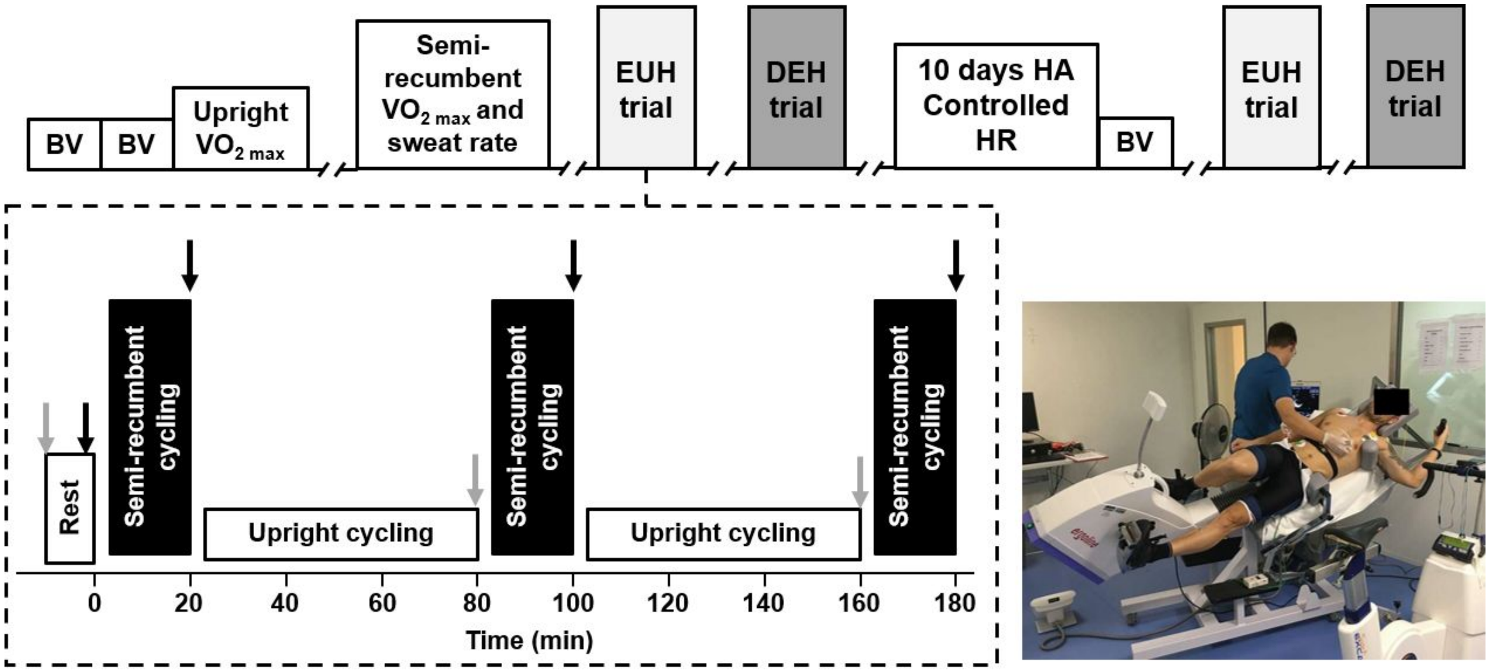
			Time (min)			
	Trial	**HA**	**Rest**	**20**	**100**	**180**
Basal rot. (deg.)	EUH	Pre	-3.9 ± 1.4	-6.0 ± 2.6	-6.0 ± 2.6	-6.7 ± 2.6
		Post	-3.2 ± 1.8	-3.9 ± 2.1	-5.6 ± 2.3	-5.2 ± 1.3
	DEH	Pre	-3.3 ± 1.6	-5.4 ± 3.0	-5.4 ± 3.4	-5.4 ± 2.1
		Post	-3.5 ± 1.3	-3.5 ± 1.7	-7.0 ± 2.2†	-6.5 ± 2.2†
Apical rot (deg.)	EUH	Pre	5.1 ± 1.9	7.1 ± 1.5	7.3 ± 1.7	9.4 ± 1.5
		Post	4.9 ± 1.0	7.4 ± 1.6	7.5 ± 1.4	8.3 ± 1.7
	DEH	Pre	5.1 ± 0.9	7.0 ± 1.1	8.1 ± 2.2	9.0 ± 2.9
		Post	5.3 ± 2.0	6.8 ± 1.6‡	8.5 ± 1.5	11.1 ± 2.0*†‡
Longitudinal strain (%)	EUH	Pre	-17.7 ± 1.1	-17.0 ± 2.1	-16.4 ± 2.0	-16.5 ± 2.0
		Post	-18.3 ± 2.4	-17.8 ± 1.8	-17.3 ± 1.6	-16.9 ± 2.1
	DEH	Pre	-17.5 ± 2.4	-18.2 ± 2.2	-14.7 ± 2.2†‡	-14.7 ± 2.0†‡
		Post	-18.2 ± 1.0	-17.9 ± 2.3	-17.1 ± 2.4	-14.5 ± 1.8†‡
Basal circ. strain (%)	EUH	Pre	-19 ± 4	-15 ± 4	-13 ± 3	-13 ± 2
		Post	-17 ± 3	-16 ± 3	-15 ± 3	-14 ± 4
	DEH	Pre	-19 ± 3	-17 ± 2	-13 ± 2†‡	-12 ± 3†‡
		Post	-21 ± 2	-15 ± 4	-14 ± 3	-12 ± 2†‡
Apical circ. strain (%)	EUH	Pre	-23 ± 5	-16 ± 4	-15 ± 3	-18 ± 5
		Post	-24 ± 6	-17 ± 4	-19 ± 4	-20 ± 5
	DEH	Pre	-23 ± 7	-18 ± 6	-14 ± 4	-15 ± 3
		Post	-23 ± 5	-18 ± 4	-17 ± 5	-19 ± 7
Basal rot. vel. (deg·s^{-1})	EUH	Pre	-50 ± 10	-123 ± 25	-131 ± 25	-142 ± 34
		Post	-61 ± 20	-96 ± 34	-107 ± 35	-124 ± 27
	DEH	Pre	-57 ± 13	-111 ± 36	-128 ± 40	-155 ± 50†
		Post	-57 ± 15	-103 ± 23	-140 ± 19†	-174 ± 39†‡
Apical rot. vel. (deg·s^{-1})	EUH	Pre	67 ± 25	161 ± 50	175 ± 28	201 ± 55
		Post	74 ± 21	144 ± 46	189 ± 80	173 ± 32
	DEH	Pre	75 ± 26	148 ± 46	166 ± 58	238 ± 47†‡
		Post	60 ± 20	154 ± 37	191 ± 42	252 ± 69†‡
Strain rate (s^{-1})						
Longitudinal	EUH	Pre	-0.9 ± 0.1	-1.3 ± 0.1	-1.3 ± 0.1	-1.4 ± 0.2
		Post	-0.9 ± 0.1	-1.3 ± 0.2	-1.3 ± 0.2	-1.4 ± 0.2
	DEH	Pre	-0.9 ± 0.1	-1.4 ± 0.2	-1.3 ± 0.1	-1.4 ± 0.2
		Post	-0.9 ± 0.1	-1.2 ± 0.1	-1.4 ± 0.2	-1.4 ± 0.2
Circ. basal	EUH	Pre	-1.3 ± 0.3	-1.5 ± 0.4	-1.5 ± 0.3	-1.5 ± 0.3
		Post	-1.3 ± 0.1	-1.5 ± 0.5	-1.4 ± 0.4	-1.5 ± 0.3
	DEH	Pre	-1.3 ± 0.2	-1.7 ± 0.3	-1.5 ± 0.4	-1.7 ± 0.5
		Post	-1.3 ± 0.2	-1.3 ± 0.3*	-1.5 ± 0.3	-2.1 ± 0.7‡
Circ. apical	EUH	Pre	-1.3 ± 0.3	-1.4 ± 0.4	-1.5 ± 0.2	-1.9 ± 0.5
		Post	-1.4 ± 0.3	-1.5 ± 0.4	-1.9 ± 0.5	-2.0 ± 0.6
	DEH	Pre	-1.4 ± 0.4	-1.6 ± 0.5	-1.5 ± 0.4	-2.1 ± 0.8
		Post	-1.4 ± 0.2	-1.6 ± 0.5	-1.8 ± 1.0	-2.3 ± 1.1

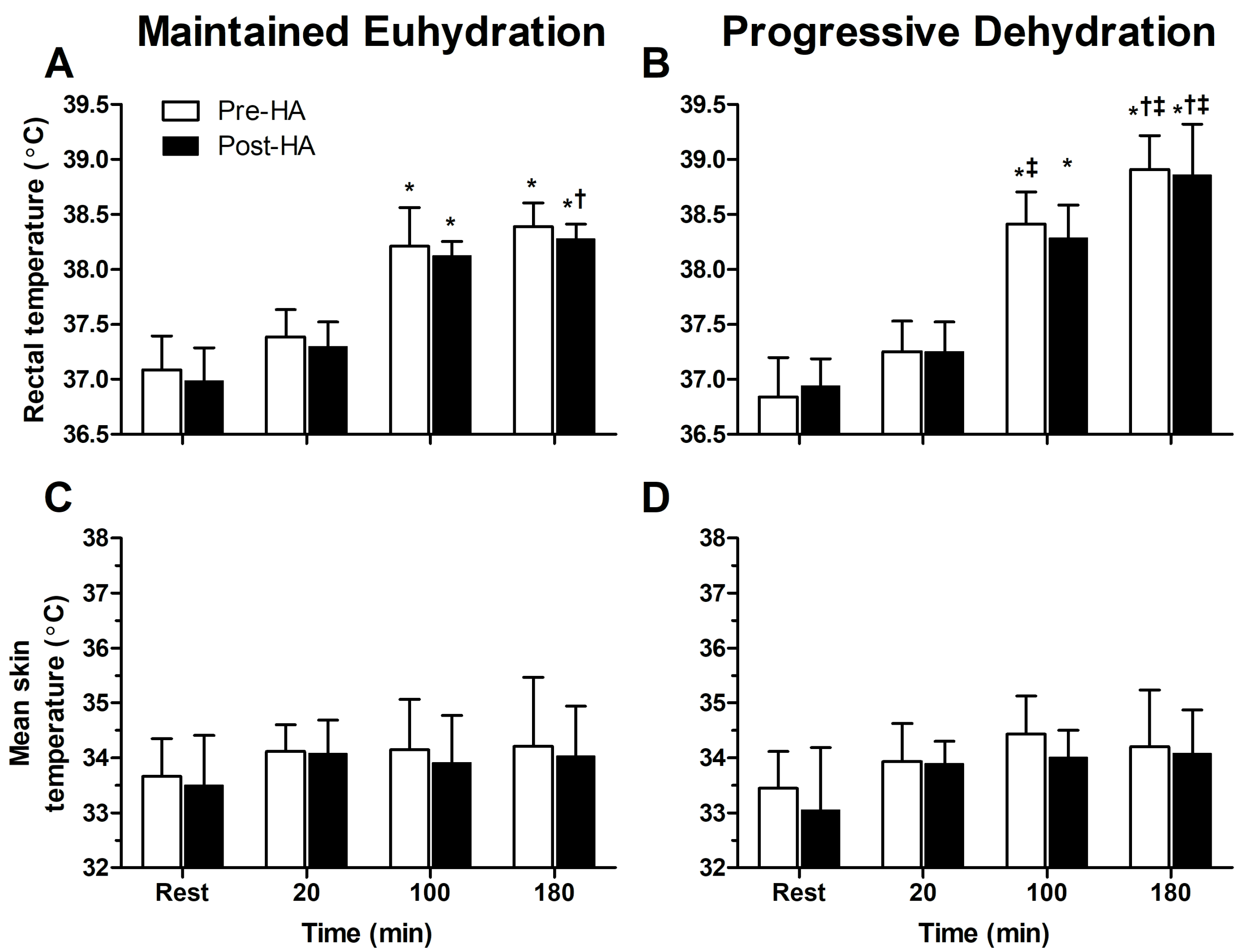
rot.: rotation, vel.: velocity, deg.: degrees, circ.: circumferential. *$P < 0.05$ vs. pre-HA. †$P < 0.05$ vs. 20 min. ‡$P < 0.05$ vs. EUH.

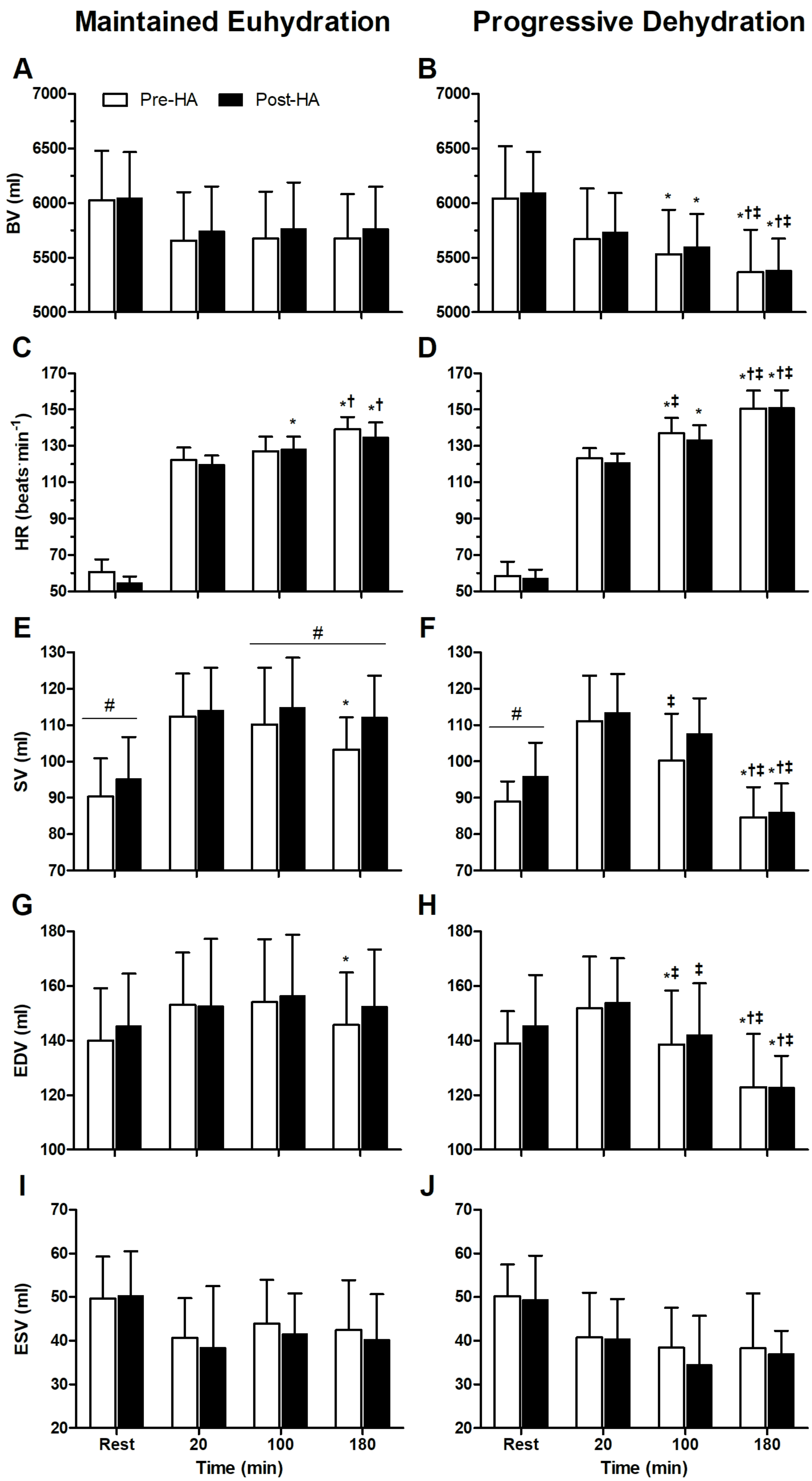
Table 4. Peak diastolic strain and rotation parameters at rest and during exercise under moderate heat stress with maintained euhydration (EUH) and progressive dehydration (DEH) before and after heat acclimation (HA).

			Time (min)			
			Rest	**20**	**100**	**180**
Basal rot. vel. (deg·s^{-1})	EUH	Pre	46 ± 14	97 ± 43	111 ± 40	107 ± 36
		Post	50 ± 24	83 ± 24	95 ± 18	93 ± 28
	DEH	Pre	48 ± 12	86 ± 39	98 ± 33	115 ± 64
		Post	49 ± 12	76 ± 18	104 ± 28	128 ± 41†
Apical rot. vel. (deg·s^{-1})	EUH	Pre	-51 ± 22	-97 ± 36	-92 ± 24	-115 ± 33
		Post	-55 ± 36	-105 ± 56	-139 ± 51	-119 ± 82
	DEH	Pre	-47 ± 13	-92 ± 29	-145 ± 62	-127 ± 43
		Post	-47 ± 19	-81 ± 37	-111 ± 55	-149 ± 59†
Strain rate (s^{-1})						
Longitudinal	EUH	Pre	1.02 ± 0.13	1.45 ± 0.23	1.48 ± 0.22	1.49 ± 0.16
		Post	1.04 ± 0.12	1.36 ± 0.25	1.52 ± 0.17	1.53 ± 0.23
	DEH	Pre	1.07 ± 0.19	1.56 ± 0.18	1.33 ± 0.20	1.38 ± 0.31
		Post	1.08 ± 0.13	1.42 ± 0.18	1.38 ± 0.21	1.41 ± 0.19
Circ. basal	EUH	Pre	1.33 ± 0.40	1.63 ± 0.36	1.62 ± 0.37	1.66 ± 0.31
		Post	1.41 ± 0.28	1.57 ± 0.41	1.62 ± 0.24	1.69 ± 0.33
	DEH	Pre	1.42 ± 0.44	1.77 ± 0.35	1.58 ± 0.43	2.01 ± 0.73
		Post	1.64 ± 0.64	1.64 ± 0.59	1.64 ± 0.28	1.71 ± 0.33
Circ. apical	EUH	Pre	1.54 ± 0.39	1.49 ± 0.44	1.47 ± 0.23	1.92 ± 0.29†
		Post	2.16 ± 1.05	1.61 ± 0.33	1.79 ± 0.43	1.96 ± 0.37
	DEH	Pre	1.71 ± 0.52	1.65 ± 0.52	1.66 ± 0.81	2.07 ± 0.81
		Post	1.50 ± 0.13	1.57 ± 0.24	1.68 ± 0.58	2.55 ± 1.67

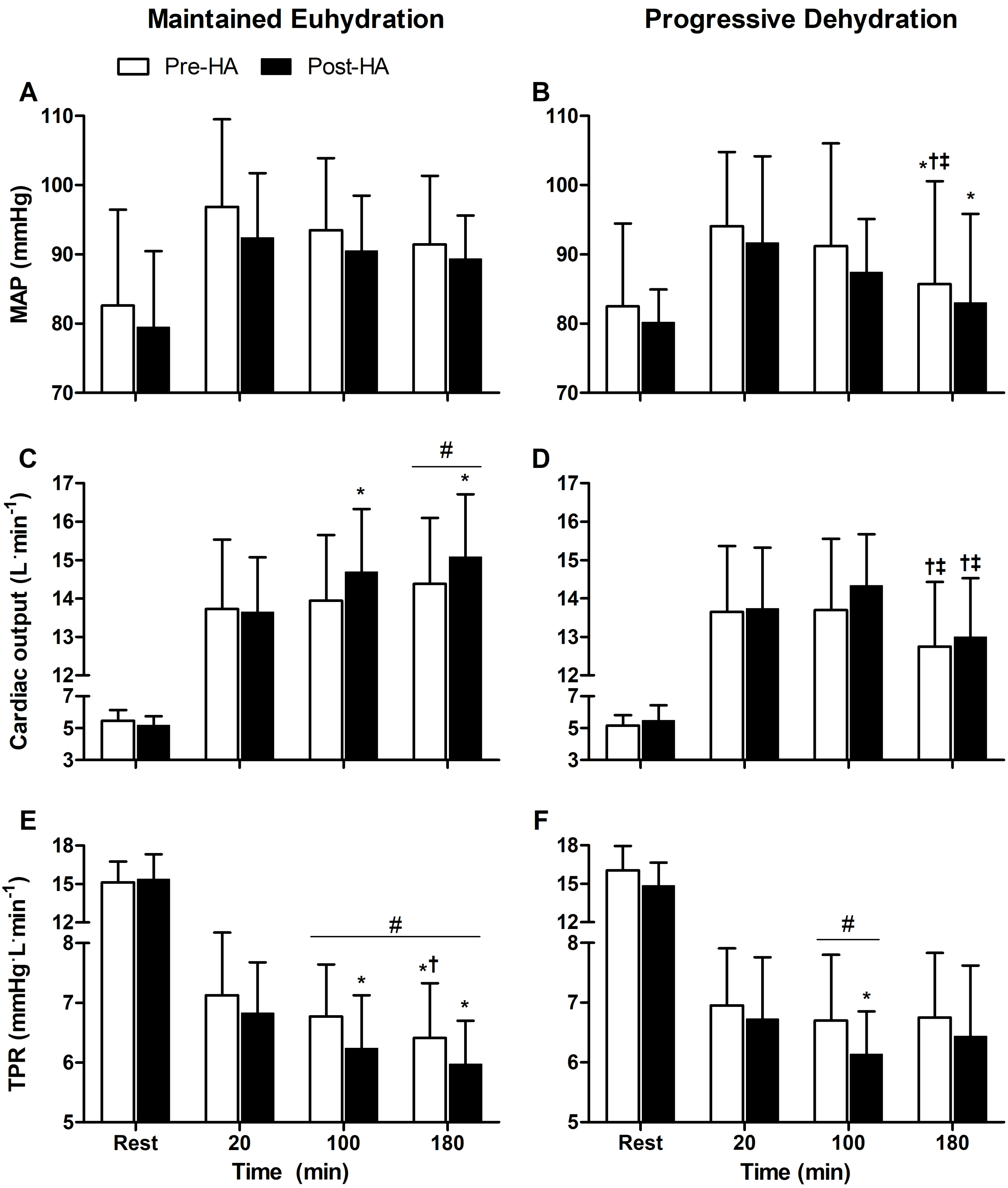
deg.: degrees, rot.: rotation, vel.: velocity, circ.: circumferential. †P<0.05 vs. 20 min

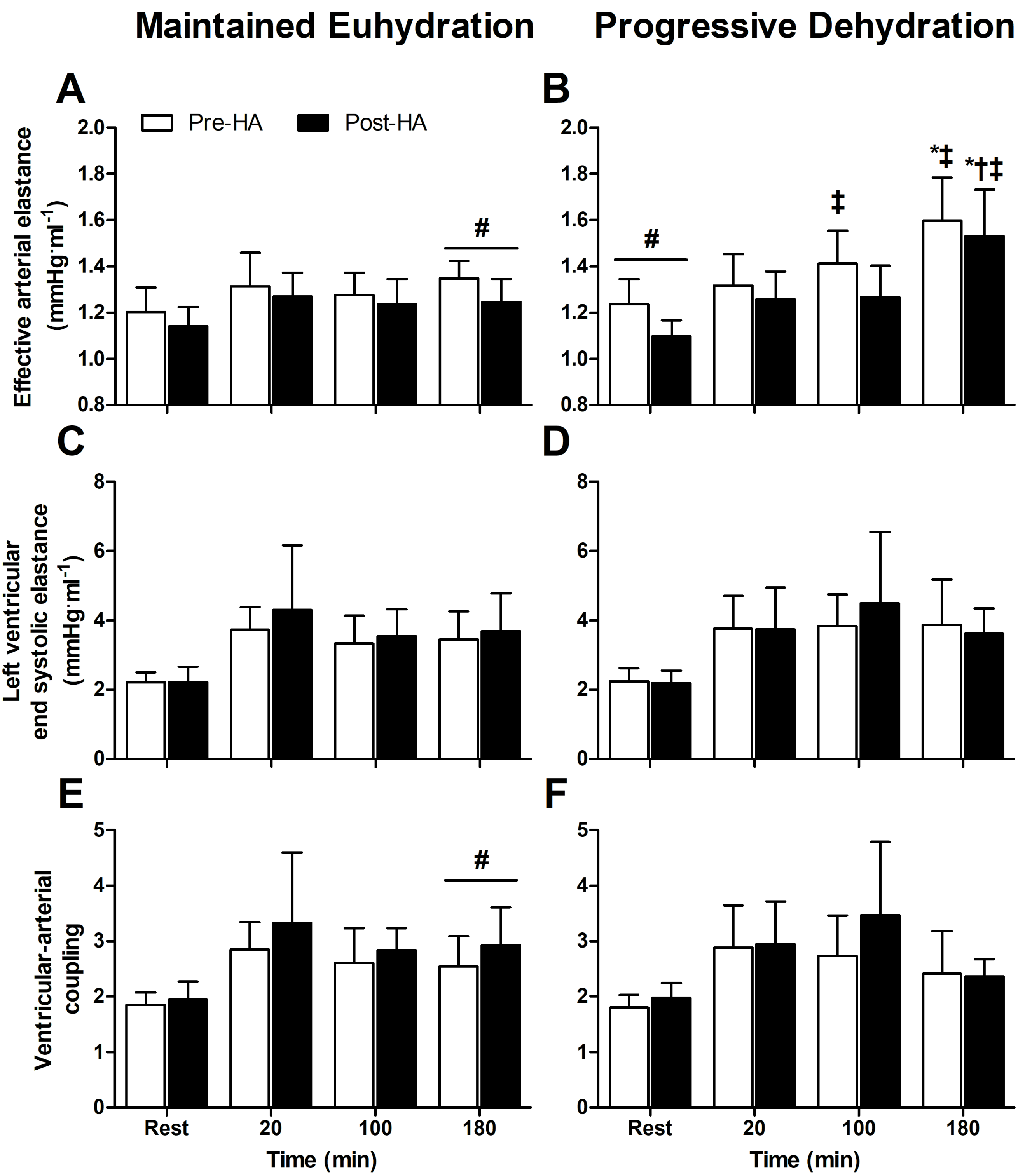

BV
BV
Upright VO2 max
Semi-recumbent VO2 max and sweat rate
EUH trial
DEH trial
10 days HA Controlled HR
BV
EUH trial
DEH trial
Rest
Semi-recumbent cycling
Upright cycling
Semi-recumbent cycling
Upright cycling
Semi-recumbent cycling
0
20
40
60
80
100
120
140
160
180
Time (min)

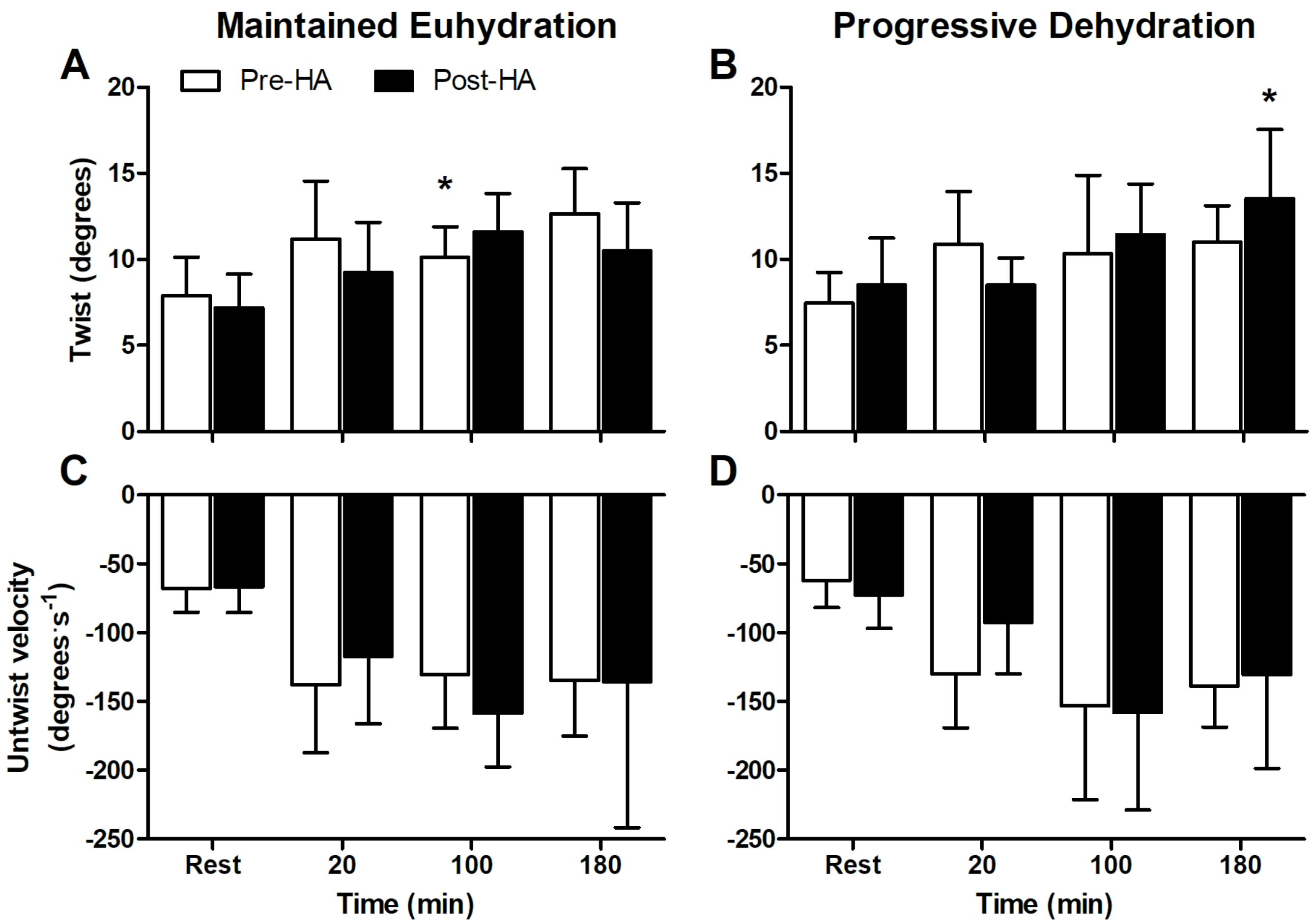

Maintained Euhydration
Progressive Dehydration
A
B
C
D
Pre-HA
Post-HA
Rectal temperature (°C)
Mean skin temperature (°C)
39.5
39.0
38.5
38.0
37.5
37.0
36.5
38
37
36
35
34
33
32
*
*†
*‡
*†‡
Rest
20
100
180
Time (min)



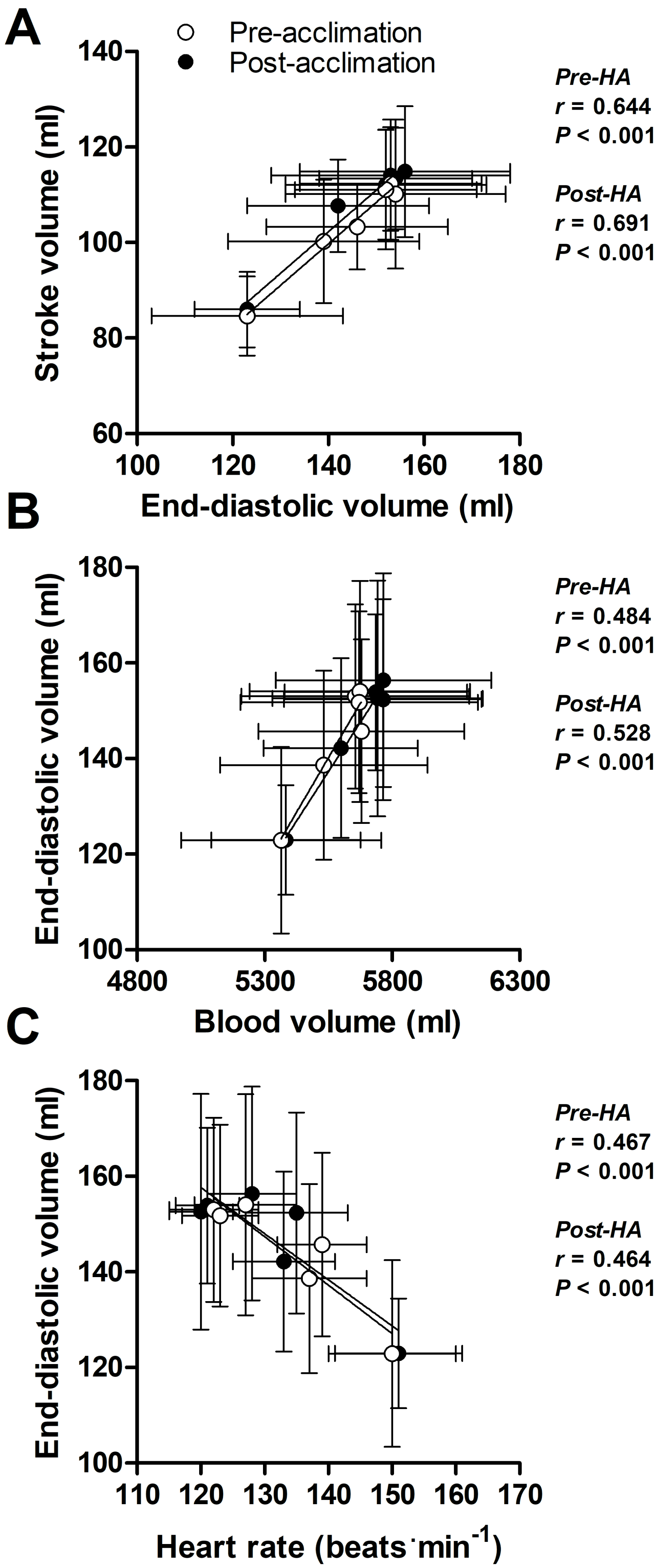
Maintained Euhydration
Progressive Dehydration
A
B
C
D
E
F
G
H
I
J
Pre-HA
Post-HA
BV (ml)
HR (beats·min-1)
SV (ml)
EDV (ml)
ESV (ml)
Rest
20
100
180
Time (min)
*
†
‡
#


Maintained Euhydration
Progressive Dehydration
Pre-HA
Post-HA
A
B
C
D
E
F
MAP (mmHg)
Cardiac output (L·min-1)
TPR (mmHg·L·min-1)
*†‡
*
#
*†
†‡
Rest
20
100
180
Time (min)

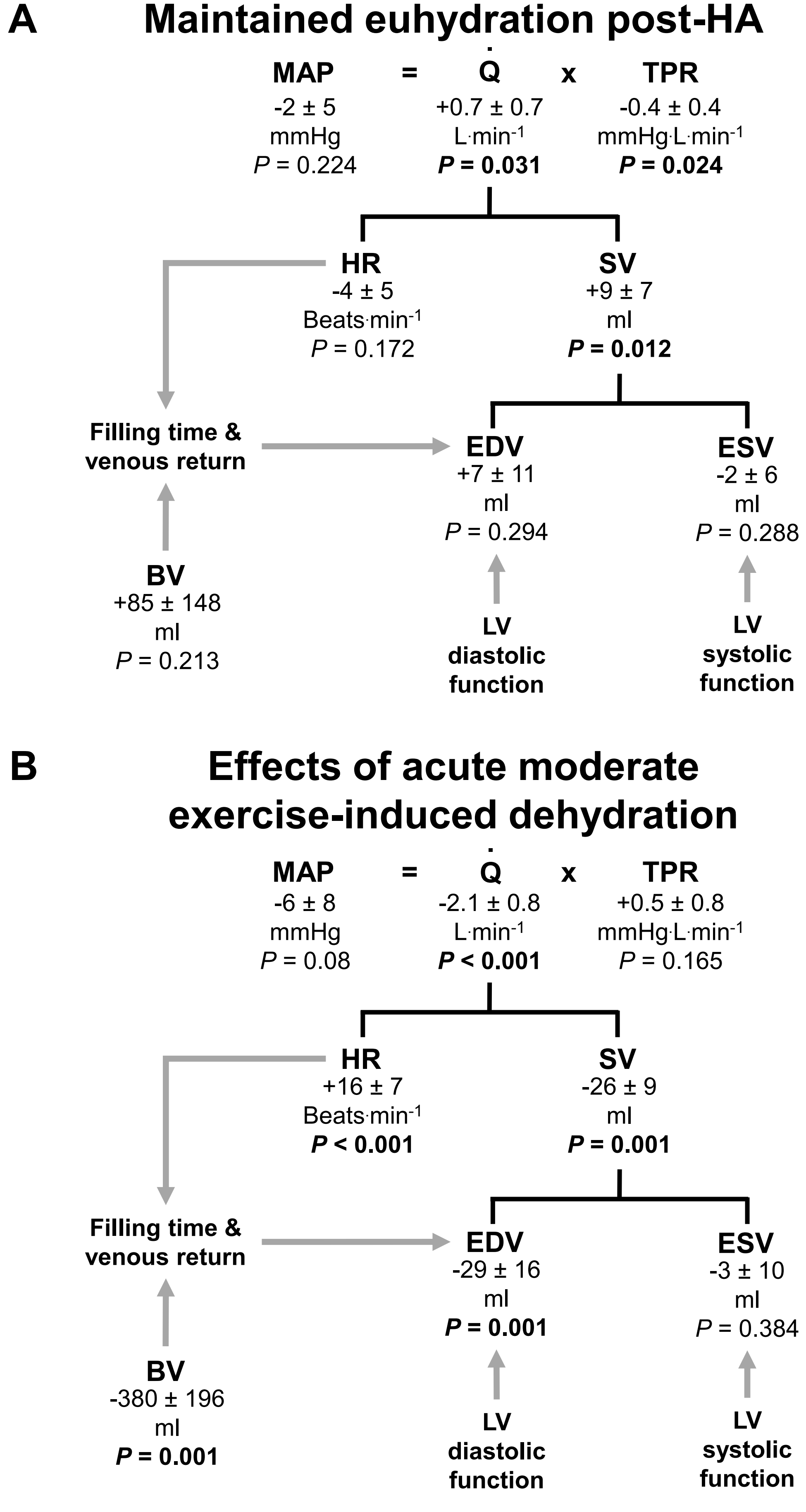

Maintained Euhydration
Progressive Dehydration
A
B
C
D
E
F
Pre-HA
Post-HA
Effective arterial elastance (mmHg·ml-1)
Left ventricular end systolic elastance (mmHg·ml-1)
Ventricular-arterial coupling
#
‡
*‡
*†‡
Rest
20
100
180
Time (min)



Maintained Euhydration
Progressive Dehydration
A
B
C
D
Pre-HA
Post-HA
Twist (degrees)
Untwist velocity (degrees·s-1)
20
15
10
5
0
-50
-100
-150
-200
-250
*
Rest
20
100
180
Time (min)



A
Pre-acclimation
Post-acclimation
140
120
100
80
60
Stroke volume (ml)
100
120
140
160
180
End-diastolic volume (ml)
Pre-HA
r = 0.644
P < 0.001
Post-HA
r = 0.691
P < 0.001
B
180
160
140
120
100
End-diastolic volume (ml)
4800
5300
5800
6300
Blood volume (ml)
Pre-HA
r = 0.484
P < 0.001
Post-HA
r = 0.528
P < 0.001
C
180
160
140
120
100
End-diastolic volume (ml)
110
120
130
140
150
160
170
Heart rate (beats·min-1)
Pre-HA
r = 0.467
P < 0.001
Post-HA
r = 0.464
P < 0.001


A
Maintained euhydration post-HA
MAP = Q x TPR
-2 ± 5
mmHg
P = 0.224
+0.7 ± 0.7
L·min-1
P = 0.031
-0.4 ± 0.4
mmHg·L·min-1
P = 0.024
HR
-4 ± 5
Beats·min-1
P = 0.172
SV
+9 ± 7
ml
P = 0.012
Filling time &
venous return
EDV
+7 ± 11
ml
P = 0.294
ESV
-2 ± 6
ml
P = 0.288
BV
+85 ± 148
ml
P = 0.213
LV
diastolic
function
LV
systolic
function
B
Effects of acute moderate
exercise-induced dehydration
MAP = Q x TPR
-6 ± 8
mmHg
P = 0.08
-2.1 ± 0.8
L·min-1
P < 0.001
+0.5 ± 0.8
mmHg·L·min-1
P = 0.165
HR
+16 ± 7
Beats·min-1
P < 0.001
SV
-26 ± 9
ml
P = 0.001
Filling time &
venous return
EDV
-29 ± 16
ml
P = 0.001
ESV
-3 ± 10
ml
P = 0.384
BV
-380 ± 196
ml
P = 0.001
LV
diastolic
function
LV
systolic
function