Dehydration reduces left ventricular filling at rest and during exercise independent of twist mechanics

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Submitted 27 April 2011; accepted in final form 16 June 2011

Stöhr EJ, González-Alonso J, Pearson J, Low DA, Ali L, Barker H, Shave R. Dehydration reduces left ventricular filling at rest and during exercise independent of twist mechanics. J Appl Physiol 111: 891–897, 2011. First published June 23, 2011; doi:10.1152/japplphysiol.00528.2011.—The purpose of this study was to determine whether the reduction in stroke volume (SV), previously shown to occur with dehydration and increases in internal body temperatures during prolonged exercise, is caused by a reduction in left ventricular (LV) function, as indicated by LV volumes, strain, and twist (“LV mechanics”). Eight healthy men [age: 20 ± 2, maximal oxygen uptake (VO2max): 58 ± 7 ml·kg−1·min−1] completed two, 1-h bouts of cycling in the heat (35°C, 50% peak power) without fluid replacement, resulting in 2% and 3.5% dehydration, respectively. Conventional and two-dimensional speckle-tracking echocardiography was used to determine LV volumes, strain, and twist at rest and during one-legged knee-extensor exercise at baseline, both levels of dehydration, and following rehydration. Progressive dehydration caused a significant reduction in end-diastolic volume (EDV) and SV at rest and during one-legged knee-extensor exercise (rest: Δ − 33 ± 14 and Δ − 21 ± 14 ml, respectively; exercise: Δ − 30 ± 10 and Δ − 22 ± 9 ml, respectively, during 3.5% dehydration). In contrast to the marked decline in EDV and SV, systolic and diastolic LV mechanics were either maintained or even enhanced with dehydration at rest and during knee-extensor exercise. We conclude that dehydration-induced reductions in SV at rest and during exercise are the result of reduced LV filling, as reflected by the decline in EDV. The concomitant maintenance of LV mechanics suggests that the decrease in LV filling, and consequently ejection, is likely caused by the reduction in blood volume and/or diminished filling time rather than impaired LV function.

METHODS

Study population. Following ethical approval from Brunel University’s Research Ethics Committee, eight healthy, active males [age 20 ± 2 years; height 177 ± 5 cm; body mass 72.7 ± 9.6 kg; peak oxygen consumption (VO2peak) 58 ± 7 ml·kg−1·min−1; peak power 336 ± 27 work (W)] provided verbal and written informed consent to take part in the study.

Familiarization and habituation. Participants attended the laboratory a total of five times for initial familiarization and determination of their VO2peak, heat habituation (three times) and for the main investigation. During the first visit, participants were familiarized with one-legged knee-extensor exercise. Participants then completed an incremental knee-extension exercise test with exercise intensity in-
increasing by 5 W every minute until volitional fatigue. Following 10 min of recovery, all participants performed an incremental exercise test on an upright cycle ergometer (Excalibur Sport, Lode, Groningen, Netherlands) to determine peak power output and VO2 peak.

The second, third, and fourth visits served as heat-stress and dehydration habituation sessions with participants cycling in a heat chamber (35°C, 55% humidity) for 60 min at 50% of the individual peak power achieved during the incremental test in the first visit. During exercise, participants did not ingest any fluids. Throughout all habituation sessions, core temperature was monitored using a rectal thermistor (TH-5 Thermalert, Physitemp, Clifton, NJ), and sweat rate was indexed as the body mass lost (kg). The three habituation sessions were separated by 48–72 h.

Experimental procedures. On arrival at the laboratory on the fifth visit, participants were weighed and placed in a semirecumbent position with their left foot strapped into a custom-built knee-extensor ergometer. After 10 min of supine rest, baseline body temperatures, blood pressure, and echocardiographic images were recorded within a 10-min period according to current guidelines (19). Following resting measurements, participants performed 15 min of one-legged knee-extensor exercise (23 ± 2 W; body temperatures, blood pressure, and cardiac function were recorded during the last 10 min of exercise. After completion of these normothermic and euhydrated control measurements, participants performed two separate, 1-h bouts of cycling exercise (50% peak power) in the heat (35°C, 55% humidity) without any fluid ingestion. The first bout of exercise in the heat resulted in ~3% dehydration, as determined by reductions in body mass. Total dehydration following the second bout of exercise was ~3.5%. Each bout of cycling exercise in the heat was followed by a 10- to 15-min semirecumbent resting period, after which, the measurements of body temperatures, blood pressure, and echocardiography were repeated, both at rest and during one-legged knee-extensor exercise. Following the 15 min of one-legged knee-extensor exercise at ~3.5% dehydration, participants gradually rehydrated over a period of 1 h by ingesting a chilled carbohydrate-electrolyte drink (4.5% carbohydrates, 3.3% sodium, 0.67% potassium). The volume of fluid ingested in liters matched the body mass lost in kilograms. Participants were allowed to urinate during the rehydration period; any volume of urine lost was replaced by adding the same volume of carbohydrate-electrolyte drink to the total amount of fluid ingested during the rehydration phase. Twenty minutes following rehydration, cardiovascular measurements were repeated at rest and during one-legged knee-extensor exercise. The experimental protocol is shown in Fig. 1.

Instrumentation. Throughout the study, mean skin temperature and core temperature were calculated from the weighted mean of six sites (33) and using a rectal thermistor (TH-5 Thermalert, Physitemp), respectively. Absolute blood volume was estimated at control, based on the results from previous studies (31). Changes in blood volume consequent to dehydration were calculated from the hemoglobin and hematocrit concentration obtained from venous blood samples as described previously (4). Arterial blood pressure was obtained either invasively from pressure transducers (Pressure Monitoring Kit, Baxter-Edwards, Irvine, CA) connected to a catheter (Leader-Cath +, Vygon, Ecouen, France) in the radial artery (n = 6) or noninvasively from a digit using photoplethysmography (n = 2) (Finometer PRO, Finapres Measurement Systems, The Netherlands) and was recorded continuously for offline analysis (PowerLab, ADInstruments, Oxford, UK). Mean arterial pressure (MAP) was calculated as the average blood pressure obtained from the beat-by-beat pressure waveforms during acquisition of echocardiographic images (Chart Application, Version 5.5.6, ADInstruments). Heart rate (HR) was recorded via ECG (Vivid 7 Dimension, GE Medical Systems, Norway).

Echocardiography. Echocardiographic images for the assessment of systolic and diastolic LV volumes and LV mechanics were acquired and analyzed as described previously (32). Briefly, images were recorded at rest and during the last 10 min of one-legged knee-extensor exercise on a commercially available ultrasound system (Vivid 7 Dimension, GE Medical Systems) in accordance with current guidelines (19). Five consecutive cardiac cycles were saved for offline analysis. LV parasternal long-axis images were analyzed for end-diastolic volume (EDV), end-systolic volume (ESV), SV, and ejection fraction (EF) (34). Cardiac output was calculated as the product of HR and SV. Isovolumic relaxation time was assessed using pulsed-wave tissue Doppler of the septal mitral annulus.

Two-dimensional strain and twist mechanics. Parasternal short-axis images at the basal level, with the mitral valve leaflets visible, and on the apical level just “proximal to the level with end-systolic LV luminal obliteration” (36), as well as apical four-chamber views, were acquired at 70–90 frames/s. Frame rate was kept constant within subjects, and images were analyzed offline (EchopAC, GE Medical Systems) for two-dimensional (2D) strain (radial, circumferential, and longitudinal), strain rates, and rotation. To adjust for inter- and intrasubject variability of HR, the raw data were normalized to the percentage of systolic and diastolic duration (2). Systolic and diastolic frame-by-frame data were separately interpolated to 300 data points using cubic spline interpolation (GraphPad Prism 5 for Windows, GraphPad Software, San Diego, CA). To obtain twist and twist velocity values at all systolic and diastolic data points, basal rotation/rotation velocity data were subtracted from apical rotation/rotation velocity data. Peak untwisting velocity was defined as the “first negative deflection after aortic valve closure” (AVC) (28), with AVC automatically determined by the EchopAC software (GE Medical Systems) and confirmed by tissue Doppler timings. The time from the onset of systole to the moment of mitral valve opening and peak diastolic untwisting velocity was determined from tissue Doppler and speckle-tracking analysis, respectively, and expressed in milliseconds. Reliability data of speckle-tracking-derived twist parameters for the same sonographer have been reported previously (32).

Statistical analysis. Systemic hemodynamic and echocardiographic variables at rest and during exercise were analyzed using two-way repeated measures ANOVA. All repeated measures ANOVA analyses included the rehydration condition. To identify statistical differences between hydration status and resting vs. exercise conditions, we used the Bonferroni post hoc test. The α level was set a priori to 0.05, and statistical analyses were performed using STATISTICA Version 6, 2002 (StatSoft, Tulsa, OK).

RESULTS

Hemodynamics and global LV function at rest with dehydration and following rehydration. Core and mean skin temperature increased with the first level of dehydration (2% loss in body mass) and remained at this level during the following level of dehydration (3.5% loss in body mass). Similarly, blood

![Fig. 1. Schematic representation of the experimental procedure. 2% DEHY: 2% dehydration; 3.5% DEHY: 3.5% dehydration; REHY: rehydration; ↓: echocardiographic image acquisition, blood pressure and heart rate assessment, determination of body temperatures and venous blood sample at rest and during one-legged knee-extensor exercise.](http://jap.physiology.org/)
volume was decreased significantly during the 2% dehydration condition ($P < 0.01$) but did not reduce significantly more with 3.5% dehydration. EDV, ESV, and SV also decreased significantly (all $P < 0.01$; Fig. 2), whereas cardiac output and EF were maintained (both $P > 0.05$). Dehydration did not significantly change MAP from control rest ($P > 0.05$). Following rehydration, body mass, core temperature, EDV, ESV, and SV were restored ($P > 0.05$ vs. control rest), while there was a small increase in blood volume, and HR remained slightly elevated ($P < 0.01$). The higher HR was associated with a small but significant increase in cardiac output following rehydration at rest ($P < 0.01$). Data are summarized in Table 1.

There was a significant increase in LV twist at rest with the highest level of dehydration ($P = 0.016$). This was the result of progressive increases in basal rotation with dehydration ($P < 0.01$), while apical rotation was maintained ($P > 0.05$; Fig. 3). Similarly, the increase in peak twist velocity ($P = 0.017$) with dehydration at rest was underpinned by progressive increases in basal rotation velocity ($P < 0.01$), whereas apical rotation velocity was maintained ($P > 0.05$). Peak untwisting velocity was unaltered with progressive dehydration at rest ($P > 0.05$). Furthermore, there was a small but significant reduction in peak longitudinal strain with 2% dehydration ($P = 0.018$), whereas peak radial and circumferential strain was maintained across all resting conditions ($P > 0.05$). In line with this, peak diastolic longitudinal strain rate also decreased with both levels of dehydration at rest and remained significantly lower following rehydration compared with control rest (all $P < 0.01$). All other diastolic strain rates were maintained across conditions ($P > 0.05$). In systole, peak longitudinal, radial, and basal circumferential strain rates were unaltered with dehydration ($P > 0.05$). However, systolic apical circumferential strain rate increased with 3.5% dehydration ($P = 0.014$) and returned to control levels when participants were rehydrated. Data are summarized in Table 2.

**Hemodynamics and global LV function during exercise with dehydration and following rehydration.** During exercise, dehydration caused a reduction in EDV, ESV, and SV (all $P < 0.01$). However, ESV was significantly lower than at rest. Cardiac output and EF were maintained throughout exercise conditions (both $P > 0.05$). The decrease in total blood volume during exercise was not statistically significant ($P > 0.05$). In contrast to resting conditions, during exercise, MAP declined progressively with each stage of dehydration ($P < 0.01$) and remained lower than control exercise following rehydration ($P < 0.01$).

Unlike rest, dehydration during exercise did not alter systolic or diastolic LV twist indices (all $P > 0.05$). While peak LV untwisting velocity occurred prior to mitral valve opening at control rest ($P > 0.01$), with dehydration, and following rehydration at rest and during one-legged knee-extensor exercise, peak LV untwisting velocity tended to be delayed (Fig. 4). Dehydration during exercise reduced peak longitudinal strain ($P < 0.01$), whereas radial and circumferential strain was maintained ($P > 0.05$). Furthermore, diastolic longitudinal strain rate decreased and remained lower following rehydration ($P < 0.01$). All other systolic and diastolic strain rates were maintained ($P > 0.05$).

**DISCUSSION**

The main aim of this study was to examine whether the decline in SV, caused by dehydration and mildly elevated body temperatures at rest and during exercise, would be in part underpinned by impaired LV mechanics. This study provides five novel findings: 1) dehydration significantly reduces EDV at rest and during one-legged knee-extensor exercise; 2) systolic twist mechanics are slightly enhanced with dehydration at rest and maintained during exercise; 3) diastolic twist mechanics are maintained with dehydration at rest and during exercise; 4) systolic longitudinal strain and diastolic longitudinal strain rates are slightly reduced with dehydration at rest and during exercise; and 5) peak LV untwisting velocity tends to be delayed with dehydration at rest and during exercise. Together, the findings show that dehydration at rest and during small muscle mass exercise results in a large decline in SV caused by...
a reduced EDV, whereas LV twist mechanics are maintained or even slightly enhanced. This suggests that the decline in SV is likely caused by factors such as the reduced blood volume and/or the diminished filling time and not by a reduction in LV function per se.

**Global LV function.** The present study shows for the first time that dehydration at rest and during small muscle mass exercise results in a significant reduction in EDV, which is not compensated for by the smaller decline in ESV, causing a decrease in SV of ~20 ml. Thus the decline in SV is exclusively the result of reduced LV filling as EF was maintained. Dehydration has been shown to independently reduce venous return, as indicated by lower cardiac filling pressures at rest (17). It is likely that the large reduction in EDV and SV is related to a decrease in venous return. In accordance with the previously observed restoration of SV with fluid replacement during exercise (14, 21), rehydration in the present study fully reinstated body mass, core temperature, EDV, ESV, and SV to baseline levels, suggesting that the observed effects of dehydration were transient in nature and probably unrelated to the preceding exercise.

While the maintenance of resting cardiac output following exercise-induced dehydration agrees with previous studies (20), the maintenance of cardiac output during small muscle mass exercise and dehydration differed from previous studies (10, 11, 14, 21). The differential response during exercise can likely be attributed to the relatively low exercise intensities and small muscle mass exercise intensity in the present study, which enabled a compensatory increase in HR. However, despite these differences, the ~20-ml decline in SV, observed at rest and during exercise in this study, was comparable with that previously seen with similar levels of dehydration during whole-body exercise (10, 11). Thus a similar magnitude of dehydration appears to result in comparable, absolute reductions in SV, irrespective of exercise modality and intensity.

**Systolic LV mechanics.** Further to the observed decline in EDV, ESV, and SV, this study shows that except for a small but significant reduction in longitudinal strain, systolic LV mechanics are maintained or even significantly enhanced with progressive dehydration at rest and during one-legged knee-extensor exercise. Longitudinal strain has previously been shown to be sensitive to reductions in preload (3). The small reduction in longitudinal strain in the present study was, therefore, likely caused by lower venous return rather than a reflection of impaired intrinsic myocardial function. Moreover, systolic radial and circumferential strains were maintained with dehydration at rest and during exercise. In the face of reduced EDV, this maintenance of strain and systolic strain rates further suggests that intrinsic myocardial contractility was actually enhanced, and the overall contractile state was maintained with dehydration. Thus a reduction in myocardial shortening, which may have been expected due to the decrease in EDV, appears to be compensated for by an increase in sympathetic activity induced by dehydration, as previously shown (12).

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**Table 1. Changes in body temperature and cardiac function at control, two levels of dehydration, and following rehydration**

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Exercise</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Control rest</td>
<td>2% DEHY</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>72.7 ± 9.6</td>
<td>71.5 ± 9.5*</td>
</tr>
<tr>
<td>Core temp. (°C)</td>
<td>37.1 ± 0.1</td>
<td>38.0 ± 0.5*</td>
</tr>
<tr>
<td>Mean skin temp. (°C)</td>
<td>33.9 ± 0.5</td>
<td>34.7 ± 0.8</td>
</tr>
<tr>
<td>Blood volume (ml)</td>
<td>5251 ± 504</td>
<td>5072 ± 626*</td>
</tr>
<tr>
<td>Cardiac output (L · min⁻¹)</td>
<td>4.7 ± 0.8</td>
<td>5.5 ± 0.9</td>
</tr>
<tr>
<td>IVRT (ms)</td>
<td>74 ± 16</td>
<td>73 ± 8</td>
</tr>
<tr>
<td>EF (%)</td>
<td>66 ± 7</td>
<td>66 ± 5</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>98 ± 12</td>
<td>92 ± 13</td>
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</table>

DEHY: dehydration; REHY: rehydration; HR: heart rate; IVRT: isovolumic relaxation time; EF: ejection fraction; MAP: mean arterial pressure. *P < 0.01 from control; †P < 0.01 from 2% DEHY; ‡P < 0.01 from 3.5% DEHY; §P < 0.01 compared with the same condition at rest.
The increase in systolic LV twist observed with progressive dehydration at rest was probably also mediated by enhanced sympathetic activity. This finding is in contrast with the previous observation of a significant reduction in LV mechanics at rest following ultraendurance exercise, which was accompanied by ~4.5% dehydration (26). In the present investigation, SV was lower, and HR was higher compared with the study by Nottin et al. (26). Despite the more pronounced alterations in LV hemodynamics in the present study, LV mechanics were maintained or even enhanced. Consequently, the significant reduction in LV mechanics reported by Nottin et al. (26) may well have been a consequence of the prolonged exercise rather than that of ensuing dehydration. Conversely, in the present setting, the observed changes in systolic LV mechanics were likely caused by dehydration, as rehydration fully restored global function and LV mechanics.

Fig. 4. Time-to-peak LV untwisting velocity in relation to mitral valve opening (MVO) (n = 8). Although the effect was small, there was a general trend for peak LV untwisting velocity to occur after mitral valve opening. This was not fully reversed following rehydration. *P < 0.01 from control; †P < 0.01 from 2% dehydration; ‡P < 0.01 from 3.5% dehydration; §P < 0.01 compared with the same condition at rest.
While strain and strain rates were maintained with dehydration during exercise (indicating a similar contractile state to that seen at rest), peak systolic basal rotation and twist did not increase from control exercise to 3.5% dehydration exercise. Given that MAP was significantly higher during 2% and 3.5% dehydration exercise compared with 2% and 3.5% dehydration at rest, a maintained LV circumferential and radial strain and LV twist may be reflective of an important compensatory mechanism for a reduction in MAP. However, the significant decline in MAP with progressive dehydration during exercise could be expected to increase LV twist (5). Thus the present data suggest that dehydration prevented a further increase in LV twist during one-legged knee-extensor exercise. Considering that the magnitude of dehydration and the response in EDV were identical at rest and during exercise, the difference in MAP may have caused the variation in the LV twist response seen between rest and exercise.

**Diastolic LV mechanics.** LV untwisting velocity is related to diastolic “suction” (7, 23, 25). In this study, LV untwisting was maintained with dehydration and rehydration at rest and during small muscle mass exercise, and hence, it is assumed that LV suction was also maintained. Maintained suction concomitant with a reduced venous return (17), however, will result in reduced LV filling, as evidenced by the significant decline in EDV in this study. While maintained LV untwisting indicates that the reduction in EDV and the resulting decline in SV with dehydration are probably not caused by reduced LV function per se, it remains unknown why LV untwisting was unaltered at rest. Given that systolic twist increased at rest, and the kinetic energy required for diastolic untwisting is thought to be stored in systole (13, 16, 24), it may seem surprising that LV untwisting did not also increase. However, it is important to note that the increase in systolic twist and twist velocity at rest was caused solely by enhanced basal rotation/rotation velocity. Conversely, previous studies have shown that LV untwisting is largely determined by diastolic apical function (15, 24, 27). In this study, neither diastolic basal rotation velocity nor diastolic apical rotation velocity increased with dehydration at rest. Although the overall maintenance of twist mechanics is reflective of a compensatory reserve, the present findings also indicate that dehydration inhibits an increase in diastolic basal and apical function at rest and during small muscle mass exercise, as changes in systolic function did not result in concomitant improvements in diastolic mechanics.

A central characteristic of dehydration, which may possibly explain the absence of an increase in LV untwisting, was the pronounced decline in EDV of ~30 ml. Smaller reductions in EDV of 15 and 17 ml caused by heat stress with maintained hydration (23, 32) and lower body-negative pressure (6) are accompanied by significantly enhanced LV untwisting velocities, whereas larger reductions in EDV caused by head-up tilt during heat stress do not result in further augmentation of LV untwisting velocity (22). Thus it is possible that the reduction in blood volume consequent to dehydration, as opposed to a mere redistribution of blood induced by heat stress or lower body-negative pressure, prevented an increase in LV untwisting velocity.

Similar to the response in diastolic LV mechanics at rest, diastolic LV mechanics during one-legged knee-extensor exercise were maintained at control levels throughout all conditions of dehydration and rehydration. Together, these responses differ from that of systolic LV mechanics, which showed an increase with dehydration at rest and maintenance during exercise. The difference between resting and exercising systolic LV mechanics may be explained by the altered MAP response during exercise. In contrast, the similar diastolic LV mechanics during rest and exercise may be caused by the prevailing preload, as EDV was identical at rest and during exercise. The present study thereby provides novel insight into LV mechanics by demonstrating that systolic and diastolic LV mechanics can be uncoupled as a consequence of concurrent changes in preload and afterload. This finding warrants further investigation, as it could also have important clinical implications for the understanding of cardiac dysfunction.

**Experimental limitations.** While the methods used in this study have been chosen carefully, some inherent limitations deserve brief discussion. Firstly, the authors acknowledge that the 1D method of calculating LV SV (34) is imperfect, owing to geometrical assumptions. However, this method has been shown to be valid in healthy, symmetrically contracting hearts (18), and in the present study, the reported changes in LV volumes caused by dehydration and rehydration were similar to previous investigations (10, 11). The second potential limitation is the use of one-legged knee-extensor exercise, making it difficult to relate the findings directly to whole-body exercise. However, in the present study, the decline in SV with dehydration during knee-extensor exercise was comparable with that previously reported during whole-body exercise at similar levels of dehydration (20 ml vs. 27 ml, respectively) (8, 11). This suggests that the impact of dehydration upon LV mechanics may be greater than that of exercise modality.

**Conclusion.** The present study shows that the marked reduction in SV caused by progressive dehydration at rest and during small muscle mass exercise is the result of reduced LV filling, as indicated by the decline in EDV. Despite the large reduction in EDV, systolic and diastolic LV twist mechanics were maintained or even slightly enhanced. The authors conclude that the reduction in SV with dehydration at rest and during small muscle mass exercise is not the result of reduced intrinsic LV function but likely caused by other factors such as a lower venous return and reduced filling time.

**ACKNOWLEDGMENTS**

The authors thank all participants for their dedicated commitment throughout the experiments. Present addresses: D. A. Low, Autonomic and Neurovascular Medicine Unit, St. Mary’s Hospital, Clinical Neurosciences, Faculty of Medicine, Imperial College, London, UK; J. Pearson, Institute for Exercise and Environmental Medicine, Texas Health Presbyterian Hospital, 8200 Walnut Hill Lane, Dallas, TX 75231-4402; E. J. Stöhr, Cardiff School of Sport, University of Wales Institute Cardiff, Cardiff, UK.

**GRANTS**

This study was partially funded by the Gatorade Sports Science Institute (Barrington, IL).

**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the author(s).

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