Left ventricular systolic and diastolic function during tilt table positioning and passive heat stress in humans

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Running Head: Posture, heat stress and left ventricular function

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Abstract

The ventricular response to passive heat stress has predominately been studied in the supine position. It is presently unclear how acute changes in venous return influence ventricular function during heat stress. To address this question, left ventricular (LV) systolic and diastolic function were studied in seventeen healthy men (24.3 ± 4.0 yrs; mean ± SD), using two-dimensional transthoracic echocardiography with Doppler ultrasound, during tilt table positioning (supine, 30° head-up tilt, HUT; and 30° head-down tilt, HDT), under normothermic and passive heat stress (core temperature 0.8 ± 0.1°C above baseline) conditions. The supine heat stress LV volumetric and functional response was consistent with previous reports. Combining HUT with heat stress reduced end-diastolic (25.2 ± 4.1%) and end-systolic (65.4 ± 10.5%) volume from baseline, while heart rate (37.7 ± 2.0%), ejection fraction (9.4 ± 2.4%), and LV elastance (37.7 ± 3.6%) increased, and stroke volume (-28.6 ± 9.4%) and early diastolic inflow (-17.5 ± 6.5%) and annular tissue (-35.6 ± 7.0%) velocities were reduced. Combining HDT with heat stress restored end-diastolic volume, while LV elastance (16.8 ± 3.2%), ejection fraction (7.2 ± 2.1%), and systolic annular tissue velocities (22.4± 5.0%) remained elevated above baseline, and end-systolic volume was reduced (-15.3 ± 3.9%). Stroke volume, and the early and late diastolic inflow and annular tissue velocities were unchanged from baseline. This investigation extends previous work by demonstrating increased LV systolic function with heat stress, under varied levels of venous return, and highlights the preload dependency of early diastolic function during passive heat stress.

Key words: passive heat stress, tilt table, systolic function, diastolic function, left ventricle
Introduction

Whole-body passive heat stress results in multiple cardiovascular and neural adjustments, including increases in cardiac output (14, 17, 29), cutaneous vascular conductance (2, 5), splanchnic and renal sympathetic vasoconstriction (15, 26, 28), and muscle sympathetic nerve activity (6, 19). These responses occur in a coordinated effort to redistribute cardiac output to the cutaneous circulation, limit the reduction in blood pressure and protect against syncope.

In the supine heat stressed individual, left ventricular (LV) end-diastolic volume is significantly reduced compared to normothermic conditions (17-18, 34), along with reductions in central blood volume (5) and cardiac filling pressures (3, 27, 34, 37). Despite this significant reduction in preload, stroke volume (SV) is maintained during passive heating (14-15, 17-18, 23, 37) secondary to increased ventricular contractility (2, 5, 17-18) and ventricular diastolic suction (17-18). While supine measures are helpful, an important and understudied issue is what happens when blood pressure control mechanisms are challenged during orthostasis. Likewise, because supine heat stress significantly reduces cardiac preload, an equally important issue is what happens to cardiac function when preload is restored.

Passive postural changes by tilt table positioning can non-invasively produce a significant increase or decrease in venous return and allow the ventricular response to acute volume changes to be investigated (9). We therefore evaluated LV function in response to acute increases (head down tilt, HDT) and decreases (head up tilt, HUT) in preload during whole-body passive heat stress. We hypothesized that end-systolic reserve would be reduced during HUT heat stress, which would ultimately lead to a reduction in stroke volume. We further hypothesized that HDT heat stress would increase LV preload, and that diastolic functional parameters (e.g. LV twist and untwisting rate) would remain elevated above baseline, resulting in augmented early diastolic filling and stroke volume.

Methods

Subjects

Twenty-four healthy men volunteered to participate in the present study; all were free of any known cardiovascular, metabolic or neurological disease. Written informed consent was obtained from all subjects before participating in the study. The study procedures were approved by the University of Alberta Health Research Ethics Board. Three subjects were excluded from
the investigation prior to the experiment based on poor echocardiography image quality, 
determined during a pre-screening visit. An additional subject was excluded from the study, after 
presenting with abnormal resting electrophysiology during a familiarization trial.

**Instrumentation and Measurements**

Each subject wore a tube-lined water-perfusion suit (Allan VanGaurd Technologies, 
Ottawa, ON) and rested on an inversion table in a slight lateral decubitus position. The suit 
covered the entire body with the exception of the head, hands and feet. Four biomedical ceramic 
chip thermocouples (MA 100, 10K0 negative coefficient, Thermometrics, NJ) were affixed to 
each subject’s skin from which mean skin temperature was calculated (24). Core temperature 
was measured using an ingestible thermal capsule (VitalSense, Mini Mitter, Bend, OR). Beat-by-
beat heart rate was quantified from R-wave detection from a single lead ECG (lead II, Dual Bio 
Amp, ADInstruments, New South Wales, Australia), and arterial blood pressure was monitored 
using finger photoplethysmography (Finometer model 2; Finapres, Amsterdam, The 
Netherlands). Brachial artery blood pressure was also measured, from the opposite arm, every 
two minutes, using an automated blood pressure cuff (BPM-100, BpTRU Medical Devices, 
Coquitlam, BC), and used to calibrate the finger photoplethysmography.

Using a commercially available ultrasound machine (VividQ or Vivid7, GE Medical 
Systems, Milwaukee, Wisconsin), transthoracic two dimensional echocardiography with Doppler 
ultrasound was performed on each volunteer, following a modified functional protocol, based on 
the American Society of Echocardiography guidelines (12). Parasternal short axis images at the 
base (tips of mitral valve leaflets), papillary muscles (mid-ventricle) and apex (just proximal to 
LV luminal obliteration at end-systole, with no visible papillary muscle) were obtained to 
calculate ventricular volumes and for twisting and untwisting analysis; apical four chamber 
images were also acquired to measure left ventricular volumes. Pulsed Doppler was recorded at 
the tips of the mitral valve leaflets (apical 4-chamber view) to assess peak mitral inflow 
velocities. Peak lateral annular tissue velocity was assessed using tissue Doppler-ultrasound. All 
acquisitions were performed by the same experienced operator, and the data were recorded in the 
order listed above.
Protocol

Pre-screening/Familiarization: Upon enrollment into the study, subjects were screened for echocardiography image quality. Those subjects found to have good parasternal and apical acoustic windows returned to the laboratory on a separate day and were exposed to the heat stress and passive tilt table positioning (described below) in order to familiarize each subject with the experimental protocol.

Experimental Protocol: In order to establish a physiological baseline, thermoneutral water (34°C) was circulated throughout the suit during normothermic data collection. To elevate core temperature, 50°C water was circulated throughout the suit for 45 min. This heat stress protocol has previously been shown to elevate core temperature 0.8 – 1.0 °C above baseline (17-18). Following 45 min of heat stress, the water temperature perfusing the suit was lowered to 47°C in order to attenuate the rate of rise in core body temperature. Measurements were performed at baseline (thermoneutral) and during passive heat stress under the following conditions: 1) supine, 0° tilt; 2) 30° HDT; and 3) 30° HUT. The order of the HUT and HDT conditions was always randomized, and the tilt conditions were separated by five minutes of supine rest. Each position was held for 5 min prior to image acquisition, with the exception of the supine heat stress condition in which image acquisition commenced immediately (following 45 min of heat stress). Total imaging time was limited to 10 min.

Data Analysis

Heart rate and blood pressure data were sampled at a rate of 1,000 Hz, recorded with a data acquisition system (Powerlab 16/30, ADInstruments), and analyzed offline using associated software (LabChart 7.0 Pro, ADInstruments). Skin temperature was recorded using an 8-channel data logger (Smart-Reader 8 Plus, ACR Systems, Surrey, BC), and core temperature was recorded telemetrically using a VitalSense monitor (Bend, OR). Temperature data were recorded every five minutes. Echocardiography and Doppler data were analyzed off-line using commercially available software (EchoPAC 7.1, GE Medical Systems). Left ventricular volumes were calculated and averaged over three cardiac cycles, according to the area-length method (5/6 x LV cavity area (cm²) x LV length (cm)), in accordance with the current recommendations for quantification of LV volumes by two-dimensional echocardiography (12). Speckle-tracking analysis was applied to the basal and apical parasternal short axis images, in order to quantify
circumferential rotation as well as circumferential strain. Manual tracing of the endocardium and adjustment of the region of interest to fit and track the width of the myocardium was performed by the same observer. Left ventricular torsion was calculated as the difference between the apical and basal rotations from which the peak systolic torsion, peak twisting and peak untwisting rates were derived. Speckle-tracking data was averaged over three cardiac cycles, using in-house software in the MATLAB programming environment. Pulsed Doppler was used to quantify early and late diastolic inflow velocities. Tissue Doppler data was used to assess annular tissue velocities (lateral wall), during systole, early diastole and late diastole. All Doppler and two-dimensional data were analyzed and averaged over three cardiac cycles.

Left ventricular single point end-systolic elastance (a contractility index) was calculated as 0.9 x SBP (end-systolic blood pressure) divided by end-systolic volume (ESV) (1, 11). Mean arterial pressure was estimated as one-third pulse pressure plus diastolic blood pressure. Cardiac output was calculated as (LV end-diastolic volume minus LV end-systolic volume) multiplied by heart rate. Systemic vascular conductance was estimated as mean arterial pressure divided by cardiac output (1).

Intra-observer variability

The intra-rater variability for cardiac measures reported in this study was examined. Measurements were performed in a group of randomly selected subjects over a wide range of conditions by the same observer. Coefficient of variation (expressed as a percentage) was used to quantify the intra-rater variability of end-diastolic volume (4.23%), end-systolic volume (7.82%), early and late mitral inflow velocities (4.83% and 8.39%, respectfully), lateral annular peak early (5.30%), peak late (7.63%), and peak systolic (7.93%) tissue velocities, peak systolic torsion (9.54%), peak twisting rate (11.3%), peak untwisting rate (14.1%), and peak circumferential strain (4.56%).

Statistical Analysis

Data were analyzed using a two-way repeated measures analysis of variance. Where main effects were found, Tukey post hoc tests were used to define discrete differences. To differentiate the effects of tilt-table positioning from the effects of passive heat stress, data were compared between the largest volume changes (supine to HUT, and HUT to HDT), using paired sample t-
tests. Data are reported as mean ± standard error (SE), unless otherwise specified. The α-level for all statistical analyses was set at 0.05.

Results

Two subjects experienced pre-syncopal symptoms (severe hypotension, systolic blood pressure < 80 mmHg; nausea; lightheadedness) during HUT heat stress, while a third subject reported extreme discomfort during heat stress, requiring the experiment to be prematurely discontinued. Data is therefore reported on the 17 subjects who completed the entire experimental protocol (height, 177.0 ± 6.2 cm; weight 77.8 ± 9.6 kg; age 24 ± 4 yrs; mean ± SD). The three subjects removed from the data set did not exhibit different responses during the other conditions compared to the 17 other subjects (data not reported), therefore removing this data does not change the results in anyway.

Thermal and Hemodynamic Data

Before heating, mean skin temperature and core temperature were 33.6 ± 0.13 and 37.1 ± 0.05°C, respectively. HUT and HDT did not change mean skin temperature or core body temperature. Whole-body heating increased mean skin temperature by 3.6 ± 0.2°C (P < 0.05) and core temperature by 0.8 ± 0.1°C (P < 0.05), with no significant change in mean skin temperature or core temperature when postural changes were combined with heat stress (Table 1). Likewise, arterial blood pressure was also maintained throughout the experimental protocol (Table 1).

Heart rate significantly increased from normothermic baseline by 7 ± 2 beats·min⁻¹ with HUT, but did not significantly change with HDT (Figure 1). Supine heat stress and HDT heat stress significantly increased heart rate from normothermic baseline (supine +22± 3 beats·min⁻¹, HDT +20± 3 beats·min⁻¹; P < 0.05), with HUT heat stress elevating heart rate an additional 15± 2 beats·min⁻¹ above supine heat stress (P < 0.05). The percent change in heart rate was greater during heat stress than during normothermia, when comparing the extremes of volume unloading (supine to HUT) and volume loading (HUT to HDT) (Figure 2).

End-diastolic volume was significantly reduced from normothermic baseline with HUT (24.1 ± 5.8 mL), supine heat stress (22.8± 4.9 mL), and HUT heat stress (46.9± 8.6 mL; Figure 1). HDT did not change end-diastolic volume from normothermic baseline, while end-diastolic volume increased from supine heat stress (17.3 ± 3.5 mL) during HDT heat stress, returning to
baseline values (Figure 1). Interestingly, end-diastolic volume was changed by the same
magnitude, regardless of thermal condition, when comparing changes between supine and HUT
and HUT from HDT (Figure 2).

End-systolic volume did not change with HUT or HDT, nor was there a difference found
with HDT heat stress (Figure 1). Supine heat stress and HUT heat stress significantly reduced
end-systolic volume from normothermic baseline by 16.3 ± 3.4 mL and 28.1 ± 4.0 mL,
respectively (Figure 1). As a result, the percent change in end-systolic volume during volume
unloading (supine to HUT) and volume loading (HUT to HDT) was greater during heat stress
than during normothermia (Figure 2).

Stroke volume was maintained with supine heat stress, HDT, and HDT heat stress, while
HUT significantly reduced stroke volume in both thermal conditions (main condition effect for
posture, Figure 1). Stroke volume was similarly affected by volume unloading (supine to HUT)
and volume loading (HUT to HDT) in both thermal conditions (Figure 2). Ejection fraction and
LV end-systolic single point elastance increased with heat stress in all three postures (Figure 3).
Cardiac output significantly increased with heat stress, while systemic vascular resistance was
significantly reduced (Table 1).

Mitral inflow velocities

Early diastolic filling velocity was reduced by HUT and HUT heat stress (main effect for
posture), but remained unchanged from normothermic baseline during HDT, supine heat stress,
and HDT heat stress (Table 2). The change in early diastolic filling velocity during tilt table
positioning therefore occurred independent of heat stress, with no change between thermal
conditions observed during volume loading (HUT to HDT) or volume unloading (supine to
HUT) (Figure 4A).

Normothermic postural change did not alter the late diastolic filling velocities; however,
heat stress significantly increased late diastolic filling velocities in all three postures (P < 0.05,
Table 2).

Lateral annular tissue velocities

Peak early diastolic annular tissue velocity (lateral wall) remained unchanged from
normothermic baseline with HDT, supine heat stress, and HDT heat stress, while HUT
(normothermic and heat stress) significantly decreased early diastolic annular tissue velocities by $3.6 \pm 0.9 \text{ cm/s}^{-1}$ and $5.6 \pm 1.3 \text{ cm/s}^{-1}$, respectively (Table 2). Therefore, similar to early mitral inflow velocity, early diastolic tissue velocity changed independent of heat stress, with no difference found between thermal conditions when comparing volume loading (HUT to HDT) or volume unloading (supine to HUT) (Figure 4B).

Late diastolic annular tissue velocity (lateral wall) significantly increased during supine heat stress, but was unchanged from normothermic baseline during HUT heat stress or HDT tilt heat stress (Table 2).

Peak systolic annular tissues velocity (lateral wall) was significantly increased above normothermic values with heat stress in all three postures (Figure 3C). HUT significantly elevated systolic annular tissue velocity above normothermic baseline and HDT; whereas, HDT heat stress significantly decreased peak annular systolic tissue velocities from supine heat stress and HUT heat stress.

**Left ventricular twist, untwisting rate and circumferential strain**

Two-dimensional speckle tracking was performed on 11 subjects, based on echocardiography image quality. Head-up tilt and HDT did not significantly alter LV peak systolic torsion, twisting rate, untwisting rate, or circumferential strain (Figure 5). Supine heat stress and HUT heat stress significantly increased LV peak systolic torsion, peak twisting rate, peak untwisting rate, and circumferential strain above baseline, while HDT heat stress returned LV peak systolic torsion, twisting rate, untwisting rate and circumferential strain to baseline (Figure 5).

Volume unloading (supine to HUT) did not significantly change peak systolic torsion, peak twisting rate, peak untwisting rate or circumferential strain; however, volume loading (HUT to HDT) increased the percent change in peak systolic torsion ($P = 0.07$), peak twisting rate ($P = 0.08$), peak untwisting rate ($P < 0.05$), and circumferential strain ($P < 0.05$) during heat stress compared to normothermia (Figure 6).
The ventricular response to supine passive heat stress has received considerable attention in recent years (2, 17-18, 35); however, the ventricular response to acute postural changes during passive heat stress has not previously been reported. During supine heat stress, stroke volume is maintained despite significant reductions in central blood volume (5), cardiac filling pressures (3, 34, 37), and cardiac filling time (27). This response has been attributed to augmented cardiac contractility and improved diastolic function (2, 17-18). Supine positioning however offers augmented central blood volumes as compared to upright positioning. The present results extend previous work by modulating these positional loading effects. The major novel findings from this study were: 1) during HUT heat stress, LV stroke volume is preserved at normothermic HUT levels, secondary to a significant increase in LV contractility; 2) LV suction is important to the maintenance of early diastolic filling, as demonstrated by a reduction in early diastolic filling when LV twist and untwisting rates are not increased in the face of a further reduction in preload (HUT heat stress); and 3) HDT combined with heat stress restored LV preload, unmasking a preload-independent increase in LV contractility, evidenced by a reduced LV end-systolic volume and increased LV end-systolic elastance, ejection fraction, and systolic annular tissue velocity.

Since the seminal work of Rowell et al. (27), it has long been hypothesized that heat stress increases the contractile function of the LV, however experimental evidence to support this supposition has been lacking. Recently, Crandall et al. (5) demonstrated a 13% increase in LV ejection fraction during supine passive heat stress. Consistent with this global measure of contractility, increases in systolic annular tissue velocities, isovolumic acceleration, single point LV end-systolic elastance, LV torsion and circumferential and radial strain have also been reported in response to passive heat stress (2, 17-18). Indeed, the present results confirm these original investigations. A major novel finding of this investigation however, is that passive heat stress produces a preload-independent increase in contractile function. To our knowledge we are the first to demonstrate this finding. Bundgaard-Nielsen et al. (3) have demonstrated a leftward shift in the Frank-Starling relation after colloid volume loading (12 mL·kg⁻¹ Voluven) during heat stress. However, LV end-diastolic volume was not reported, and LV filling pressure (i.e.
pulmonary capillary wedge pressure) was 20% higher than baseline after colloid infusion. Therefore, it remains possible that colloid infusion increased preload above baseline values in this study. In the present investigation, 30° head-down tilt restored end-diastolic volume during heat stress compared to normothermic baseline values (Figure 1A). Despite this restoration of preload, end-systolic volume remained significantly reduced (-17.5 ± 3.6%, Figure 1B), and systolic annular tissue velocity (28.8 ± 4.5%), ejection fraction (5.9 ± 1.6%) and LV end-systolic single point elastance (11.3 ± 3.3%) remained significantly higher than normothermia (Figure 3). Together, these data provide the first preload-independent measure of increased contractility during passive heat stress, and support the original hypothesis of Rowell et al (27).

The magnitude of change in systolic function during passive heating, combined with reports of frequent orthostatic intolerance during heat stress (10, 13, 36), led to the hypothesis that end-systolic reserve would be reduced when heat stress was combined with an orthostatic challenge. This was supported with recent data demonstrating large reductions in LV end-diastolic volume during orthostatic heat stress, with a concomitant reduction in stroke volume (34). Contrary to our hypothesis however, the present data suggest that systolic function continues to improve during orthostatic heat stress. For example, similar to previous reports (34), end-diastolic volume was significantly reduced with heat stress (12.4 ± 2.5%), and continued to decline an additional 12.5 ± 5.0% when combined with HUT (Figure 1A). However, in the face of this significant reduction in preload, the change in stroke volume did not differ between thermal conditions when comparing the volume change from supine to HUT. This was associated with a 65.4 ± 10.5% reduction in end-systolic volume from baseline (28.6 ± 6.0% from supine heat stress). Interestingly, in the absence of heat stress, HUT does not significantly change end-systolic volume, despite an 18.1 ± 4.3% reduction in end-diastolic volume (Figure 1). Therefore, the similar stroke volume found between HUT and HUT heat stress, suggests that systolic function was markedly improved in order to compensate for the much larger reduction in end-diastolic volume during the combined stress of heat and orthostasis. This conclusion is supported with additional indices of contractility (e.g. LV elastance, ejection fraction, and circumferential strain) increasing during heat stress from the supine position to the HUT position.
In contrast to the present results, stroke volume has previously been found to decrease to a greater extent during orthostatic heat stress compared to orthostasis alone (34). It has been reasoned that because heat stress shifts ones operating point along the Frank-Starling curve to the left (along the steep portion of the Starling curve), any further reduction in cardiac filling pressure (as occurs during orthostasis) results in a much greater reduction in stroke volume (34). Aside from possible measurement differences (i.e. thermodilution vs. echocardiography) and/or differing magnitudes of orthostatic stress, an explanation for these differing results remains unknown. Our findings however, are consistent with a previous report (36) showing a similar change in stroke volume during heat stress combined with 60° HUT compared to normothermic 60° HUT. Furthermore, we are confident this difference cannot simply be explained by measurement error, as we also measured stroke volume according to the velocity time integral method (data not reported), which produced similar results.

Diastolic function

Early mitral inflow velocity and early annular tissue velocity are preload dependent, with significant decreases in early mitral inflow velocity (4, 30) and early annular tissue velocity (7, 16, 22) accompanying reductions in preload. In the present study, HUT and HUT heat stress reduced early inflow and annular tissue velocities. Given the preload dependence of these measures, our findings likely reflect a large reduction in preload (driving pressure), without a compensatory change in ventricular suction.

In support of this argument, early mitral inflow and annular tissue velocities remain unchanged during whole-body passive heat stress (2, 17-18), despite reductions in central blood volume (5), cardiac filling pressures (3, 34, 37), and left atrial volume at the time of mitral valve opening (17-18). This has been associated with increased ventricular suction, manifest as a significant increase in peak LV twist and untwisting rate, and lower end-systolic volume (17-18). Whether a further reduction in preload would affect early diastolic filling has, until now, remained unknown. While the present results support our hypothesis that orthostatic heat stress would reduce indices of early diastolic function, the mechanism for this response appears to be slightly different than originally assumed. As mentioned above, preload was significantly reduced with HUT, resulting in a reduction in the atrial driving pressure facilitating early diastolic filling. In the absence of heat stress, LV twist and untwisting rates remained unchanged.
with HUT, resulting in a significant reduction in early diastolic inflow and annular tissue velocities. However, in the presence of heat stress (considered to be a hyperadrenergic state (25)), LV twist and untwisting rates increased above baseline, facilitating the maintenance of early diastolic function. In the face of a further reduction in preload however (HUT heat stress), early mitral inflow and annular tissue velocities were significantly reduced, possibly suggesting a critical threshold for which ventricular suction cannot compensate for large changes in preload. Indeed, the rate of twist and untwist did not significantly increase with HUT heat stress from supine heat stress, yet preload was reduced by 18.1 ± 4.1%. As a result of a mismatch between driving pressure (preload) and ventricular suction, early diastolic filling was significantly reduced. Presumably, if LV twist and untwisting rates were increased during HUT heat stress, above supine heat stress, early diastolic filling would have been maintained.

Head-down tilt redistributes blood to the thoracic region, increasing central blood volume and cardiac filling pressures (8, 31-32). In the present investigation early mitral inflow and annular tissue velocities remained unchanged from the supine position with HDT, regardless of thermal condition. We originally hypothesized that HDT heat stress would not only increase preload, due to blood volume shifts, but that LV recoil would remain elevated, contributing to an increase in early diastolic function. Contrary to this hypothesis, early diastolic filling was not improved beyond normothermic baseline, possibly explained by the reduction in LV torsion, twisting rate, and untwisting rate during HDT heat stress, which appeared to be preload dependent. This result is in direct contrast with a recent report (33) which found that increasing preload (saline infusion) augmented peak systolic LV torsion and peak early diastolic untwisting rate. Two important differences exist between the present investigation and the aforementioned study (33) however which likely contributes to this discrepancy. First, supine heat stress significantly alters heart rate, afterload (LV end-systolic wall stress (17)), preload, and contractility, while saline infusion appeared only to alter preload and systolic function (longitudinal, circumferential and radial strain). Second, preload was simply returned to baseline values in the present investigation during head-down tilt heat stress, while saline infusion significantly augmented preload above baseline. Therefore, while posture appears to have altered LV torsion in the present investigation, other factors other than preload may have contributed to this response.
Late diastolic inflow velocity was increased in all three conditions with heat stress. While others have previously suggested that this may reflect increased atrial contractile function during heat stress (2), we maintain that this finding is likely a heart rate phenomenon (17). Interestingly, late diastolic tissue velocity did not share a similar response with its corresponding inflow velocity. For example, HUT heat stress reduced the late diastolic tissue velocity compared to supine heat stress. Similar to ventricular function, the left atrium is believed to operate in accordance with Frank-Starling mechanism (21). Because HUT heat stress significantly reduces preload, the reduced atrial systolic tissue velocity may reflect a shift in the optimum left atrial volume.

**Experimental Considerations**

The present investigation used two-dimensional speckle tracking echocardiography (STE) to assess LV basal and apical rotation and resulting LV torsion dynamics. Ultrasound imaging produces speckle patterns within the tissue, as a result of constructive and destructive interference of ultrasound. Speckle tracking echocardiography is a reproducible, non-invasive technique to quantify speckle motion and therefore LV torsion and strain (20). Indeed, Notomi et al. (20) have compared STE with tagged MRI, which produced a strong correlation ($r = 0.93$, $P < 0.0001$). Our group has previously published two reports (17-18) evaluating LV torsion during passive heat stress using tagged MRI. While we have not directly compared STE with tagged MRI, the striking similarity between the present data (normothermic supine vs. supine heat stress) and our previous work (under similar conditions) reinforces our confidence in the present findings.

**Limitations**

The present study used a single, mild level ($\pm 30^\circ$) of tilt table positioning to study the influence of venous return on ventricular function during passive heat stress. These results therefore cannot be extended to more extreme tilt angles, which would be particularly advantageous in understanding the increased incidence of orthostatic intolerance during heat stress. Nonetheless, the current level of tilt table positioning produced marked changes in preload during HUT, and successfully restored preload during the HDT heat stress condition, thus accomplishing the purpose of the present study.
An additional limitation of the present study was that the interventions (i.e. tilt table positioning) were not performed in a true randomized order. For practical reasons, the supine position preceded the two other conditions, which were randomized. Given the maintenance of core temperature and mean skin temperature between positions, as well as the time allotted in each position for equilibration, it is unlikely that the absence of a true randomized order adversely affected the interpretation of the present results.

Finally, the interpretation of the present results regarding LV systolic function, has focused on contractility. However, heat stress significantly reduces systemic vascular resistance (Table 1), and LV end-systolic wall stress (17-18), making it possible for improvements in systolic function to at least be partially attributable to a reduction in afterload. While we have attempted to account for this potential limitation by using load independent indexes of systolic function (i.e. LV end-systolic elastance), the potential for this variable to influence our interpretation of the results must be acknowledged.

Conclusion

In summary, these data extend previous investigations of LV systolic and diastolic function during whole-body passive heat stress. From this investigation, it is evident that heat stress produces a preload independent increase in LV contractility, and that LV end-systolic reserve is preserved during HUT heat stress, resulting in a similar reduction in stroke volume during HUT heat stress than when HUT is performed independent of heat stress. Furthermore, the reduction in early diastolic filling with HUT heat stress supports the role of LV twist, untwist and suction in maintaining early diastolic filling during passive heat stress.


Acknowledgments

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Table 1. Thermal and hemodynamic response to passive tilt-table positioning and passive heat stress

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normothermia</th>
<th>Heat stress</th>
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<tbody>
<tr>
<td>Skin temperature, °C</td>
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<tr>
<td>Supine</td>
<td>33.6 ± 0.1</td>
<td>37.2 ± 0.2*</td>
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<td>Head-up tilt</td>
<td>33.7 ± 0.1</td>
<td>37.0 ± 0.2*</td>
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<tr>
<td>Head-down tilt</td>
<td>33.5 ± 0.2</td>
<td>37.0 ± 0.2*</td>
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<td>Core temperature, °C</td>
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<td>Supine</td>
<td>37.1 ± 0.05</td>
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<td>Head-up tilt</td>
<td>37.0 ± 0.04</td>
<td>37.9 ± 0.08*</td>
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<td>Head-down tilt</td>
<td>37.0 ± 0.06</td>
<td>37.9 ± 0.08*</td>
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<td>Systolic blood pressure, mmHg</td>
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<td>Supine</td>
<td>99 ± 2</td>
<td>103 ± 2</td>
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<td>Head-up tilt</td>
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<td>Diastolic blood pressure, mmHg</td>
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<tr>
<td>Supine</td>
<td>55 ± 2</td>
<td>55 ± 2</td>
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<tr>
<td>Head-up tilt</td>
<td>62 ± 2</td>
<td>6 ± 2</td>
</tr>
<tr>
<td>Head-down tilt</td>
<td>62 ± 2</td>
<td>58 ± 3</td>
</tr>
<tr>
<td>Mean arterial blood pressure, mmHg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>70 ± 2</td>
<td>71 ± 2</td>
</tr>
<tr>
<td>Head-up tilt</td>
<td>77 ± 2</td>
<td>75 ± 2</td>
</tr>
<tr>
<td>Head-down tilt</td>
<td>78 ± 2</td>
<td>74 ± 3</td>
</tr>
<tr>
<td>Cardiac output, L·min⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>6.0 ± 0.4</td>
<td>7.6 ± 0.4*</td>
</tr>
<tr>
<td>Head-up tilt</td>
<td>5.3 ± 0.3</td>
<td>7.9 ± 0.6*</td>
</tr>
<tr>
<td>Head-down tilt</td>
<td>6.1 ± 0.3</td>
<td>8.2 ± 0.4*</td>
</tr>
<tr>
<td>Systemic vascular resistance, mmHg·L⁻¹·min⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>12.3 ± 0.7</td>
<td>9.8 ± 0.7*</td>
</tr>
<tr>
<td>Head-up tilt</td>
<td>15.1 ± 0.8*</td>
<td>10.2 ± 0.7*</td>
</tr>
<tr>
<td>Head-down tilt</td>
<td>13.1 ± 0.7</td>
<td>9.2 ± 0.5*</td>
</tr>
</tbody>
</table>

Data reported as mean ± SE. * indicates a significant difference between thermal conditions. # indicates a significant difference from supine (within a thermal condition).
Table 2  Mitral inflow and lateral annular tissue velocities during heat stress and passive postural change

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normothermia</th>
<th>Heat Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early diastolic filling velocity, cm·s⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>72.6 ± 3.4</td>
<td>72.4 ± 2.7</td>
</tr>
<tr>
<td>Head-up tilt</td>
<td>59.4 ± 2.7*</td>
<td>63.1 ± 2.8*</td>
</tr>
<tr>
<td>Head-down tilt</td>
<td>77.4 ± 2.9</td>
<td>72.4 ± 3.6</td>
</tr>
<tr>
<td>Late diastolic filling velocity, cm·s⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>37.4 ± 2.2</td>
<td>55.3 ± 3.5*</td>
</tr>
<tr>
<td>Head-up tilt</td>
<td>37.8 ± 2.1</td>
<td>70.7 ± 4.0*#</td>
</tr>
<tr>
<td>Head-down tilt</td>
<td>42.3 ± 2.5</td>
<td>56.4 ± 3.0*</td>
</tr>
<tr>
<td>Early diastolic tissue velocity, cm·s⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>19.0 ± 0.73</td>
<td>18.5 ± 0.68</td>
</tr>
<tr>
<td>Head-up tilt</td>
<td>15.4 ± 0.76*</td>
<td>14.1 ± 0.58*</td>
</tr>
<tr>
<td>Head-down tilt</td>
<td>18.5 ± 0.55</td>
<td>17.6 ± 0.70</td>
</tr>
<tr>
<td>Late diastolic tissue velocity, cm·s⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>6.1 ± 0.34</td>
<td>7.9 ± 0.36*</td>
</tr>
<tr>
<td>Head-up tilt</td>
<td>5.8 ± 0.31</td>
<td>6.0 ± 0.43#</td>
</tr>
<tr>
<td>Head-down tilt</td>
<td>6.5 ± 0.34</td>
<td>7.1 ± 0.39</td>
</tr>
</tbody>
</table>

Data reported as mean ± SE. * indicates a significant difference between thermal conditions. # indicates a significant difference from supine (within thermal condition). ♦ indicates a significant main effect for posture.
**Figure Legend**

**Figure 1** Left ventricular end-diastolic volume (A), end-systolic volume (B), stroke volume (C), and heart rate (D) during normothermia (black bars) and whole-body passive heat stress (grey bars), in the supine position, and during 30° head-up tilt (HUT), and 30° head-down tilt (HDT). Data presented as mean ± SE. * indicates a significant difference between thermal conditions. Black brackets indicate differences between tilt conditions during normothermia, red brackets indicate differences between tilt conditions during heat stress, and green brackets indicate a significant main effect for posture.

**Figure 2** Percent change in left ventricular end-diastolic volume (A), end-systolic volume (B), stroke volume (C), and heart rate (D) in response to a postural change from supine to head-up tilt (HUT), and from HUT to head-down tilt (HDT) during normothermia (black bars) and whole-body passive heat stress (grey bars). Data presented as mean ± SE. * indicates a significant difference between thermal conditions.

**Figure 3** Left ventricular ejection fraction (A), single point end-systolic elastance (B), and peak lateral annular systolic tissue velocity (C) during normothermia (black bars) and whole-body passive heat stress (grey bars), in the supine position, and during 30° head-up tilt (HUT), and 30° head-down tilt (HDT). Data presented as mean ± SE. * indicates a significant difference between thermal conditions. Black brackets indicate differences between tilt conditions during normothermia, and red brackets indicate differences between tilt conditions during heat stress.

**Figure 4** Percent change in left ventricular early diastolic peak inflow velocity (A) and early diastolic peak lateral annular tissue velocity (B) in response to a postural change from supine to head-up tilt (HUT), and from HUT to head-down tilt (HDT) during normothermia and whole-body passive heat stress. Data presented as mean ± SE. * indicates a significant difference between thermal conditions.

**Figure 5** Left ventricular peak systolic torsion (A), circumferential strain (B), twisting rate (C) and untwisting rate (D) during normothermia and whole-body passive heat stress in the supine position, and during 30° head-up tilt (HUT), and 30° head-down tilt (HDT). Data presented as mean ± SE. * indicates a significant difference between thermal conditions. The red brackets indicate differences between tilt conditions during heat stress.
Figure 6  Percent change in left ventricular peak systolic torsion (A), peak twisting rate (B), peak untwisting rate (C) and circumferential strain (D) in response to a postural change from supine to head-up tilt (HUT), and from HUT to head-down tilt (HDT) during normothermia and whole-body passive heat stress. Data presented as mean ± SE. * indicates a significant difference between thermal conditions.
Figure 2
Figure 3
Figure 4

(A) Early diastolic filling velocity

(B) Early diastolic tissue velocity
Figure 5
Figure 6