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Blood flow restriction maintains blood pressure upon head-up tilt

VICKIE WONG[1], ZACHARY W. BELL[1], ROBERT W. SPTIZ[1], JUN SEOB SONG[1], YUJIRO YAMADA[1], TAKASHI ABE[2] and JEREMY P. LOENNEKE[1]*

[1] Department of Health, Exercise Science, and Recreation Management, Kevser Ermin Applied Physiology Laboratory, The University of Mississippi, University, MS, USA

[2] Institute of Health and Sports Science and Medicine, Juntendo University, Inzai, Chiba 270-1695, Japan

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ABSTRACT

Background: Orthostatic intolerance occurs in some astronauts following space flight. Although orthostatic blood pressure responses should normalize in the weeks following the return to Earth, there may be situations where an immediate short-term solution is necessary (e.g., emergency evacuation). *Purpose:* The purpose of this study was to examine different levels of blood flow restriction on changes in blood pressure and heart rate when transitioning from supine to a head-up tilt and determine whether this change differs based on sex. *Methods:* Eighty-nine participants (45 men, 44 women) completed the three visits with different pressures (Sham, Moderate, and High) in a randomized order. Cuffs were placed on the most proximal area of the thighs. Brachial blood pressure was measured at baseline, upon inflation of the cuffs in a supine position, immediately after tilt (70°), and eight more times separated by 45 seconds. *Results:* Data are presented as mean (SD). The change in systolic (High > Moderate > Sham) [High vs Sham: 5.5 (7.4) mmHg, High vs Moderate: 3 (7.4) mmHg, and Moderate vs Sham: 2.4 (8.4) mmHg] and diastolic pressure (High > Moderate = Sham) [High vs Sham: 2.4 (5.3) mmHg, High vs Moderate: 1.9 (6.3) mmHg] differed across applied pressures. The change in heart rate was initially greatest in the sham-pressure but increased the greatest in the high-pressure condition by the end of the head-up tilt period. Additionally, there was no influence of sex. *Conclusion:* Blood flow restriction applied in this study increased blood pressure in a pressure-dependent manner upon head-up tilt.

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* Corresponding author. P.O. Box 1848, University, MS 38677, USA. Tel.: +(662) 915-5567; fax: +(662) 915-5525. E-mail: jploenne@olemiss.edu

KEYWORDS

orthostatic intolerance, orthostatic hypotension, gender influence, no sex differences, external compression, systolic blood pressure, diastolic blood pressure

INTRODUCTION

When an individual goes from a supine to a head-up tilt position, there is typically an immediate drop in blood pressure followed by maintenance or recovery. However, there are some individuals that present a large drop in blood pressure (20 mmHg drop in systolic pressure and/or a 10 mm Hg drop in diastolic pressure) that does not recover [1]. This is termed orthostatic intolerance and refers to the inability to mount a sufficient physiologic response in order to sustain a standing position. This large drop in blood pressure can result in light-headedness, nausea, and potentially fainting [2]. Considering that women may have less responsiveness in autonomic functions associated with blood pressure regulation, orthostatic intolerance has been suggested to be more prevalent in women than in men [3, 4] and has also been reported to occur in many astronauts following space travel [5]. Although not all astronauts develop orthostatic intolerance from a mission, it has been determined that orthostatic intolerance has been observed in 25% of astronauts that return from short-duration travels and this increases to around 83% of cases for astronauts that return from long-duration travels of 129–190 days [6]. Although the blood pressure response to standing should normalize in the weeks following the return to Earth, there may be situations where an immediate short-term solution is necessary. For example, if there is an emergency whereby the astronauts are required to exit the spacecraft quickly upon landing, a failure to maintain blood pressure when attempting to stand and walk could be fatal (i.e., pass out while trying to escape).

We hypothesized that the application of blood flow restriction might be able to prevent this initial drop in blood pressure based on the following two ideas. First, a rapid drop in blood pressure cues the baroreceptors to send a signal to the medulla to increase the sympathetic signal and decrease the parasympathetic signal [7]. Blood flow restriction, which is the application of a cuff on a limb to reduce (not occlude) arterial inflow, has been shown to increase sympathetic responses, as measured by the ratio of low-frequency R-R/high-frequency R-R [8, 9]. Further, there is some suggestion that this change might be pressure dependent [8]. Secondarily, there is the idea that blood flow restriction might be able to augment cardiac output immediately following the change from the supine to head-up tilt position [10]. The application of blood flow restriction via cuffs slows the flow of blood towards the lower body [11] and that may allow for augmentation in cardiac output (at least initially). A previous paper using abdominal pressure supports this idea. This effect could also be dependent upon blood flow restriction pressure since postural changes have been previously shown to influence arterial occlusion pressure [12]. Therefore, the purpose of this study is to examine different levels of blood flow restriction on changes in blood pressure and heart rate when transitioning from a supine to an upright position in healthy individuals.

MATERIAL AND METHODS

Participants

Overtly healthy men and women between the ages of 18 and 35 years were recruited to participate in this study. A total of 98 participants were recruited for this study. Eight participants were unable to be rescheduled within the one to ten-day period and one participant did not meet the age requirement. Thus, 45 men [mean (SD): age of 23.5 (3.9) years; height of 176.5 (7.1) cm; body mass of 79.1 (11.0) kg; arterial occlusion pressure of 149.7 (21.5) mmHg] and 44 women [mean (SD): age of 22.0 (3.2) years; height of 164.8 (7.4) cm; body mass of 66.1 (14.5) kg; arterial occlusion pressure of 151.4 (21.7) mmHg] were included for the current study. All participants were asked to abstain from food consumption 2 h, caffeine 8 h, alcohol consumption and exercise 24 h prior to each visit. Participants were excluded if they used hypertensive medications or met 2 or more risk factors for thromboembolism [13]. Participants provided informed consent and followed COVID-19 protocols. These COVID-19 protocols required the use of a face mask that covered both the nose and mouth and implemented hand washing and sanitizing. The study received approval from the University's institutional review board and the ethical approval number was Protocol # 21-021.

Each participant completed each of his/her visits around the same time of day (plus/minus 1–2 h) to control for any circadian influence on the measured variables with visits generally separated by a period of one to 10 days. However, due to an unforeseeable weather event, the University was closed for a week and 11 participants who exceeded 10 days only once between visits were still included. In addition, as noted in Figs 1–3, we had missing data from specific time points within some of the comparisons. This was primarily due to equipment error (unable to read blood pressure at that time point) outside of a single case where a male participant within the high-pressure condition had his visit terminated prior to finishing all the blood pressure and heart rate measurements because he felt unwell towards the end of the visit. For missing data, we excluded cases per dependent variable within each comparison to maximize use of the available data. Of note, when we excluded cases listwise, the available sample was reduced, but the results were not appreciably changed (data not shown).

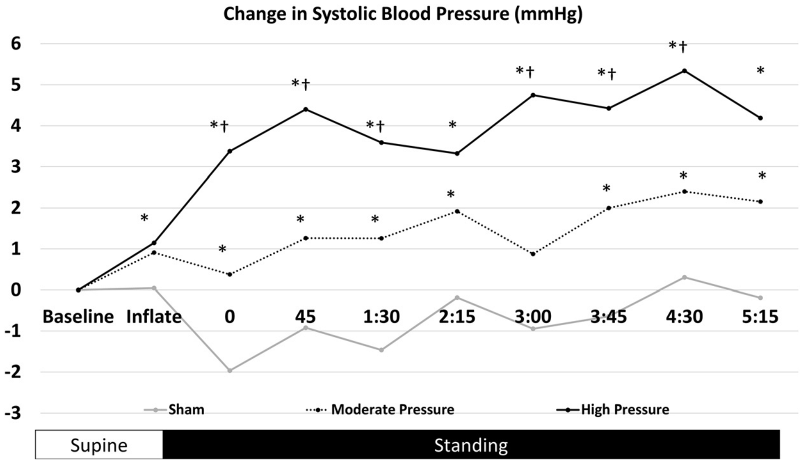

Fig. 1. The change in systolic blood pressure from baseline for the sham (grey), moderate pressure (dotted black), and the high pressure (solid black) conditions.

The median difference between conditions and the variability (2.5%, 97.5%) of those differences is noted in Table 1. * denotes a difference from the sham and †denotes a difference from the moderate pressure condition.

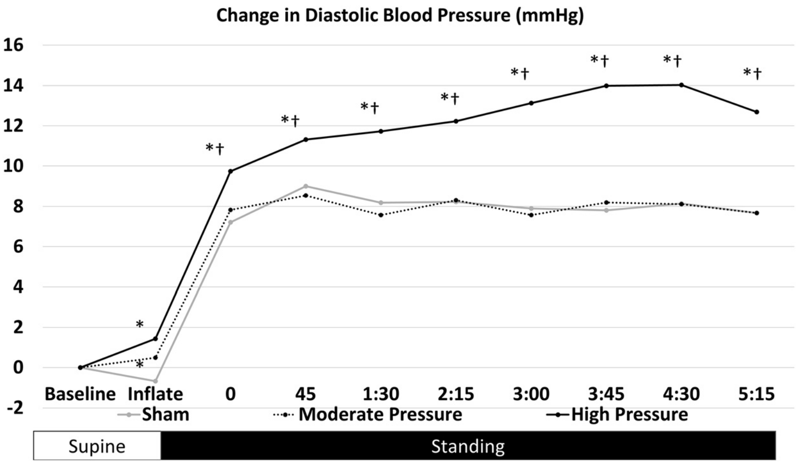

Fig. 2. The change in diastolic blood pressure from baseline for the sham (grey), moderate pressure (dotted black), and the high pressure (solid black) conditions.

The median difference between conditions and the variability (2.5%, 97.5%) of those differences is noted in Table 2. * denotes a difference from the sham and †denotes a difference from the moderate pressure condition.

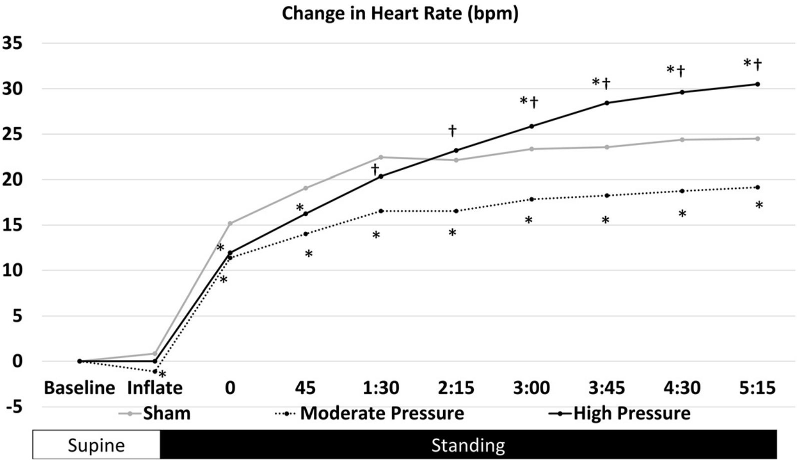

Fig. 3. The change in heart rate from baseline for the sham (grey), moderate pressure (dotted black), and the high pressure (solid black) conditions.

The median difference between conditions and the variability (2.5%, 97.5%) of those differences is noted in Table 3. * denotes a difference from the sham and †denotes a difference from the moderate pressure condition.

Experimental approach

In order to examine the influence of blood flow restriction on changes in blood pressure and heart rate when transitioning from a supine to a head-up tilt position, blood flow restriction was implemented in the lower body, whilst blood pressure and heart rate were measured at the participant's left arm. Head-up tilt was used as this represents a standardized and safe method for testing a positional perturbation. Along with the implementation of blood flow restriction, the pressures applied were also of interest. Therefore, the changes in blood pressure and heart rate following a sham, moderate pressure (40% of arterial occlusion), and high pressure (80% of arterial occlusion pressure) were also compared within the same participants. Each condition was completed on a separate day with at least 24 h between visits. Randomization was structured in a blocking method (men and women) whilst counterbalancing the three different pressures in each block.

Familiarization and blood flow restriction protocols

The first laboratory visit included measurements of height (cm) using a stadiometer, body mass (kg) using a digital weight scale (Seca, Chino, Estonia), arm circumference using a tape measure (to assign correct blood pressure cuff), and arterial occlusion pressure (mmHg). More specifically, a 12-cm nylon cuff was placed on the most proximal portion of the participants' right and left thigh, but the arterial occlusion pressure was determined in the right leg. A hand-held Doppler probe (MD6, Hokanson, Bellevue, WA) was placed near the posterior tibial artery to detect a pronounced auditory signal of blood flow. The cuff was inflated using an E20 Rapid Cuff Inflator (Hokanson, Bellevue, WA) until there was no audible recording of blood flow from the Doppler probe. The lowest cuff inflation pressure at which the blood flow distal to the cuff was no longer detectable was defined as arterial occlusion pressure. Once the arterial occlusion pressure was determined, the cuff was deflated. This pressure was used to set the relative pressures for the blood flow restriction protocols. For the familiarization session, in a randomized order, all three pressures were blindly presented to the participant for two minutes each to mimic the estimated six minutes of upright position on the tilt table (custom-built table by R.W.S) for the intervention days. Participants were also instructed to stay quiet and relaxed whilst on the tilt table to practice the procedure for the intervention sessions.

The three separate blood flow restriction conditions were: 1) a sham pressure inflated to 0 mmHg; 2) a moderate pressure condition inflated to 40% of the participants' supine arterial occlusion pressure; and 3) a high-pressure condition inflated to 80% of the participants' supine arterial occlusion pressure. Of note, both cuffs were inflated and remained inflated until the session was over. Each visit began with 10 min of supine rest. Baseline brachial blood pressure and heart rate were then acquired from the left arm which remained relaxed against the side of the participant's body using the Omron digital blood pressure monitor (HEM-907XL). Two baseline measurements were taken with one minute between measurements. If the two measurements differed by 5 mmHg in the systolic blood pressure, a third measurement was taken. Next, the cuffs were inflated on each leg while still in the supine position (either 0%, 40%, or 80% of arterial occlusion pressure). Blood pressure and heart rate were measured three seconds after cuff inflation on the legs. After that measurement was recorded, the participant was tilted up to 70° of head upright tilt from 0° of head upright tilt. Tilting took 3–5 s to complete. Blood pressure and heart rate were immediately measured upon tilt followed by measurements every

45 s in that same upright position (total of 8 measurements). Each blood pressure and heart rate measurement took around 35–40 s each. The cuffs on both legs remained inflated until the last measurement of blood pressure and heart rate was recorded, at which point the cuffs were deflated and participants were slowly tilted backwards to a supine position. This would conclude each visit, and participants would return to the lab twice more to complete the remaining blood flow restriction conditions.

Statistical analysis

To determine whether the change in blood pressure and heart rate from baseline differed between conditions (Sham, Moderate, and High), change scores were compared across conditions within each time point. The non-parametric version (Wilcoxon signed-rank) of the Bayesian paired sample *t*-test was used since assumptions of normality were not met for any of the dependent variables (visually determined from Q-Q plots). To determine if the difference in change scores between conditions differed by sex, the non-parametric version (Mann-Whitney) of the Bayesian independent samples *t*-test was computed. Uninformed Cauchy priors of 0.707 (centered on zero) were used for each of the tests as recommended by Wagenmakers and colleagues [14]. Bayes factors (BF_{10}) were used to provide evidence for (BF_{10} of ≤ 0.33) or against (BF_{10} of ≥ 3.0) the null hypothesis. A BF_{10} of "3" indicates that the observed data are 3 times more likely under the alternative than the null hypothesis. Likewise, a BF_{10} of 0.33 indicates that the observed data are 3 times more likely under the null than the alternative hypothesis. Some have suggested that a Bayes factor from 1 to 3 indicates anecdotal evidence for the alternative hypothesis, a Bayes factor from 3–10 indicates moderate evidence for the alternative, and a Bayes factor over 100 has been used to indicate extreme evidence for the alternative hypothesis [14]. Data are presented as mean (standard deviation) unless otherwise stated. Data was analyzed using JASP Version 0.14.1.0 (Netherlands). The theoretical advantages of Bayesian inference is described by Wagenmaker and colleagues [15]. Post-hoc Friedman tests (frequentist approach) were requested and completed during the review process in order to provide an overall test prior to comparing each condition. Statistical significance was set at $P < 0.05$.

RESULTS

Systolic blood pressure

There were differences between conditions for the change from baseline [115 (8) mmHg] in systolic blood pressure (Fig. 1). The median effect size of the differences in systolic blood pressure and the variability of those differences is found in Table 1. The change was generally pressure dependent (High Pressure > Moderate Pressure > Sham Pressure). Notably, the application of blood flow restriction was able to prevent the drop in systolic blood pressure when moving from a supine to the head-up tilt position [High vs Sham: 5.5 (7.4) mmHg, High vs Moderate: 3 (7.4) mmHg and Moderate vs Sham: 2.4 (8.4) mmHg]. In addition, Friedman non-parametric tests support that there were differences between conditions (Supplementary Table 1). We found no evidence (Supplementary Table 2) that results differed based on biological sex in any time points of the measurements (i.e., the mean differences were similar for men and women).

Table 1. The standardized effect size for differences in systolic blood pressure. Evidence is quantified with Bayes Factors (BF_{10}). The sample size for each comparison is in parentheses to the right of the BF_{10}. The effect size is noted as the median standardized effect with variability represented by 95% credible intervals.

Systolic Blood Pressure (mmHg)	High vs. Sham	Moderate vs. Sham	High vs. Moderate
Baseline to Inflate δ (95% CI)	0.33 (0.11, 0.54)	0.21 (0.009, 0.42)	0.04 (-0.15, 0.25)
BF_{10} (n)	10.1 ($n = 88$)	1.0 ($n = 88$)	0.1 ($n = 89$)
Baseline to 0 Tilt δ (95% CI)	0.8 (0.55, 1.06)	0.29 (0.07, 0.51)	0.42 (0.20, 0.65)
BF_{10} (n)	7127.7 ($n = 85$)	4.8 ($n = 85$)	90.3 ($n = 83$)
Baseline to 45 Tilt δ (95% CI)	0.77 (0.53, 1.009)	0.307 (0.09, 0.51)	0.45 (0.22, 0.68)
BF_{10} (n)	7319.3 ($n = 89$)	5.2 ($n = 88$)	106.9 ($n = 88$)
Baseline to 1:30 Tilt δ (95% CI)	0.65 (0.41, 0.89)	0.33 (0.12, 0.54)	0.36 (0.15, 0.58)
BF_{10} (n)	4872.8 ($n = 88$)	12.0 ($n = 89$)	55.2 ($n = 88$)
Baseline to 2:15 Tilt δ (95% CI)	0.48 (0.26, 0.70)	0.306 (0.09, 0.51)	0.17 (-0.03, 0.38)
BF_{10} (n)	140.4 ($n = 88$)	6.6 ($n = 87$)	0.5 ($n = 88$)
Baseline to 3:00 Tilt δ (95% CI)	0.7 (0.44, 0.94)	0.22 (0.006, 0.43)	0.507 (0.27, 0.73)
BF_{10} (n)	3949.7 ($n = 87$)	1.1 ($n = 86$)	595.9 ($n = 86$)
Baseline to 3:45 Tilt δ (95% CI)	0.55 (0.32, 0.78)	0.36 (0.14, 0.56)	0.28 (0.07, 0.50)
BF_{10} (n)	1388.3 ($n = 87$)	32.7 ($n = 89$)	3.5 ($n = 87$)
Baseline to 4:30 Tilt δ (95% CI)	0.55 (0.32, 0.77)	0.27 (0.06, 0.48)	0.36 (0.14, 0.58)
BF_{10} (n)	1398.7 ($n = 86$)	3.5 ($n = 88$)	14.8 ($n = 87$)
Baseline to 5:15 Tilt δ (95% CI)	0.47 (0.24, 0.70)	0.31 (0.10, 0.52)	0.19 (0.01, 0.41)
BF_{10} (n)	105.0 ($n = 85$)	7.6 ($n = 86$)	0.8 ($n = 88$)

Diastolic blood pressure

There were differences between conditions for the change from baseline [63 (7) mmHg] in diastolic blood pressure (Fig. 2). The median effect size of the differences in diastolic blood pressure and the variability of those differences is found in Table 2. The change was dependent of the high-pressure condition where there was the greatest increase in diastolic blood pressure over the other two conditions (High Pressure > Moderate Pressure = Sham Pressure). Diastolic blood pressure increased following head-up tilt and changes were greatest with the High pressure with no differences between Moderate and Sham [High vs Sham: 2.4 (5.3) mmHg, High vs Moderate: 1.9 (6.3) mmHg and Moderate vs Sham: 0.6 (5.1) mmHg]. In addition, Friedman non-parametric tests support that there were differences between conditions (Supplementary Table 1). We found no evidence (Supplementary Table 2) that results differed based on biological sex in any time points of the measurements (i.e., the mean differences were similar for men and women).

Heart rate

There were differences between conditions for the change from baseline [64 (10) bpm] in heart rate between the conditions (Fig. 3). The median effect size of the differences in heart rate and the variability of those differences is found in Table 3. During the first two minutes of head-up tilt, heart rate was greatest for the sham condition (Sham > High > Moderate) [High vs Sham: −3.5 (9.1) bpm, High vs Moderate: 0.5 (9.1) bpm, and Moderate vs Sham: -3.6 (9.3) bpm]. For the final three minutes, the change in heart rate was greatest for the high

Table 2. The standardized effect size for differences in diastolic blood pressure. Evidence is quantified with Bayes Factors (BF_{10}). The sample size for each comparison is in parentheses to the right of the BF_{10}. The effect size is noted as the median standardized effect with variability represented by 95% credible intervals.

Diastolic Blood Pressure (mmHg)	High vs. Sham	Moderate vs. Sham	High vs. Moderate
Baseline to Inflate δ (95% CI)	0.45 (0.23, 0.68)	0.27 (0.05, 0.48)	0.19 (−0.007, 0.40)
BF_{10} (n)	143.4 ($n = 88$)	3.0 ($n = 88$)	0.7 ($n = 89$)
Baseline to 0 Tilt δ (95% CI)	0.52 (0.29, 0.75)	0.15 (−0.05, 0.37)	0.35 (0.13, 0.57)
BF_{10} (n)	787.5 ($n = 85$)	0.3 ($n = 85$)	23.1 ($n = 83$)
Baseline to 45 Tilt δ (95% CI)	0.38 (0.16, 0.59)	−0.07 (−0.28, 0.13)	0.52 (0.29, 0.75)
BF_{10} (n)	27.8 ($n = 89$)	0.1 ($n = 88$)	242.7 ($n = 88$)
Baseline to 1:30 Tilt δ (95% CI)	0.52 (0.30, 0.75)	−0.11 (−0.3, 0.09)	0.68 (0.42, 0.92)
BF_{10} (n)	945.7 ($n = 88$)	0.2 ($n = 89$)	54644.8 ($n = 88$)
Baseline to 2:15 Tilt δ (95% CI)	0.70 (0.47, 0.93)	0.03 (−0.16, 0.24)	0.66 (0.43, 0.89)
BF_{10} (n)	6700.9 ($n = 88$)	0.1 ($n = 87$)	4584.9 ($n = 88$)
Baseline to 3:00 Tilt δ (95% CI)	0.84 (0.59, 1.1)	−0.03 (−0.24, 0.16)	1.1 (0.79, 1.39)
BF_{10} (n)	44048.0 ($n = 87$)	0.1 ($n = 86$)	3.661 e +14 ($n = 86$)
Baseline to 3:45 Tilt δ (95% CI)	0.96 (0.62, 1.25)	0.12 (−0.07, 0.32)	0.86 (0.61, 1.11)
BF_{10} (n)	13779.5 ($n = 87$)	0.2 ($n = 89$)	226131.7 ($n = 87$)
Baseline to 4:30 Tilt δ (95% CI)	0.75 (0.50, 0.99)	−0.001 (−0.2, 0.20)	0.87 (0.62, 1.12)
BF_{10} (n)	1.333e +7 ($n = 86$)	0.1 ($n = 88$)	8572.0 ($n = 87$)
Baseline to 5:15 Tilt δ (95% CI)	0.74 (0.49, 0.98)	−0.003 (−0.21, 0.20)	0.85 (0.58, 1.11)
BF_{10} (n)	14730.0 ($n = 85$)	0.1 ($n = 86$)	16059.8 ($n = 88$)

Table 3. The standardized effect size for differences in heart rate. Evidence is quantified with Bayes Factors (BF_{10}). The sample size for each comparison is in parentheses to the right of the BF_{10}. The effect size is noted as the median standardized effect with variability represented by 95% credible intervals.

Heart Rate (bpm)	High vs. Sham	Moderate vs. Sham	High vs. Moderate
Baseline to Inflate δ (95% CI)	−0.13 (−0.34, 0.07)	−0.37 (−0.58, −0.16)	0.2 (−0.01, 0.40)
BF_{10} (n)	0.2 ($n = 88$)	21.9 ($n = 88$)	0.7 ($n = 89$)
Baseline to 0 Tilt δ (95% CI)	−0.48 (−0.71, −0.26)	−0.44 (−0.67, −0.22)	0.05 (−0.15, 0.27)
BF_{10} (n)	242.0 ($n = 85$)	56.9 ($n = 85$)	0.1 ($n = 83$)
Baseline to 45 Tilt δ (95% CI)	−0.31 (−0.52, −0.10)	−0.69 (−0.92, −0.44)	0.24 (0.04, 0.45)
BF_{10} (n)	8.2 ($n = 89$)	43674.1 ($n = 88$)	1.9 ($n = 88$)
Baseline to 1:30 Tilt δ (95% CI)	−0.21 (−0.42, −0.003)	−0.69 (−0.92, −0.44)	0.47 (0.25, 0.69)
BF_{10} (n)	1.0 ($n = 88$)	2841.8 ($n = 89$)	129.8 ($n = 88$)
Baseline to 2:15 Tilt δ (95% CI)	0.17 (−0.033, 0.37)	−0.69 (−0.93, −0.43)	0.83 (0.56, 1.09)
BF_{10} (n)	0.37 ($n = 87$)	23514.5 ($n = 87$)	46355.8 ($n = 87$)
Baseline to 3:00 Tilt δ (95% CI)	0.3 (0.09, 0.50)	−0.63 (−0.85, −0.38)	1.14 (0.66, 1.41)
BF_{10} (n)	6.7 ($n = 87$)	2745.7 ($n = 86$)	60343.9 ($n = 86$)
Baseline to 3:45 Tilt δ (95% CI)	0.5 (0.29, 0.72)	−0.67 (−0.89, −0.43)	1.08 (0.73, 1.42)
BF_{10} (n)	1340.3 ($n = 87$)	3927.0 ($n = 89$)	12181.6 ($n = 87$)
Baseline to 4:30 Tilt δ (95% CI)	0.55 (0.32, 0.77)	−0.60 (−0.85, −0.35)	1.1 (0.89, 1.46)
BF_{10} (n)	771.4 ($n = 86$)	1383.5 ($n = 88$)	5.296 e + 6 ($n = 87$)
Baseline to 5:15 Tilt δ (95% CI)	0.58 (0.36, 0.80)	−0.58 (−0.80, −0.34)	1.22 (0.83, 1.53)
BF_{10} (n)	2928.8 ($n = 85$)	734.2 ($n = 86$)	10405.8 ($n = 88$)

pressure condition (High > Sham > Moderate) [High vs Moderate: 8.3 (10) bpm, Moderate vs Sham: −5.6 (9.8) bpm, and High vs Sham: 2.7 (10.2) bpm]. In addition, Friedman non-parametric tests support that there were differences between conditions (Supplementary Table 1). We found no evidence (Supplementary Table 2) that results differed based on biological sex in any time points of the measurements (i.e., the mean differences were similar for men and women).

DISCUSSION

The transition from a supine to upright position resulted in a small transient drop in systolic blood pressure. However, the application of blood flow restriction was able to maintain/increase this pressure. The findings are similar to that of early research studies [10, 16] that incorporated external compressions to prevent orthostatic systolic blood pressure declines. In line with the rationale of previous studies [10, 16], the application of blood flow restriction was used as a form of external pressure to improve venous return to the heart. Although this study did not include individuals with orthostatic hypotension, it has been noted that there is an impaired compensatory reflex in those with orthostatic hypotension that results in an increased pooling of the venous blood along with a reduction in both stroke volume and cardiac output that exaggerates a decrease in blood pressure with positional changes [17].

The change in blood pressure and heart rate for this study appeared to be pressure dependent, where the high pressure increased blood pressure and heart rate differently when compared to the moderate pressure. The moderate pressure appeared to produce a more favorable response, in that there was a slight increase in systolic blood pressure, but this condition had the lowest heart rate response throughout. This is in line with previous research where compressions of 40–60 mmHg have been applied to the lower extremities as a method to combat orthostatic hypotension [16]. Although we did not measure cardiac output, it is possible that a moderate pressure might have been able to augment cardiac output in the early phase while largely reducing the overall cardiovascular stress response to sustained inflation. However, it is not clear why the heart rate response was overall lower in the moderate pressure condition.

The cardiovascular response to head-up tilt has been found to differ by sex in some [4, 18, 19] but not all previous studies [20, 21]. There is some work that suggested that women respond to orthostatic challenges predominantly with vagal withdrawal whereas men respond with a greater sympathetic stimulation to the peripheral vasculature [18]. There have also been suggestions where lower orthostatic tolerance in women is associated with greater reductions in stroke volume [18], and women have greater elevations of heart rate following head-up tilt [4]. We found no difference in how men or women responded to head-up tilt with blood flow restriction. No other studies to our knowledge have investigated this research question. However, we also observed no sex difference in any of our outcomes when performing post-hoc analysis only in the sham condition (i.e. sex differences in the change relative to pre rather than in the difference in differences, data not shown) which agrees with some but not all of the previous literature [20, 21]. However, based on the sample included in the current study, there is no evidence to suggest the cardiovascular responses from the blood flow restriction differ on the basis of biological sex.

This study is not without limitations as our three main measurements (systolic and diastolic pressure, and heart rate) all came from a single device. Future work could include a heart rate assessment that is independently measured. In addition, although this study included a sham-control, there was no true control where the participants did nothing but lie down. However, the current study did not require a true control because the purpose was to determine if there are differences in blood pressure and heart rate with blood flow restriction during a head-up tilt protocol. We did not control for the phase of the menstrual cycle, however, a previous report found that the cardiovascular response to positional changes does not differ across the phases of the menstrual cycle [22]. Lastly, we did not investigate the mechanisms behind the observed response. This was the first study investigating this, so we sought to first establish whether there is an effect before adding additional measurements. Future work can investigate the question of "how".

CONCLUSION

Blood flow restriction did increase blood pressure among healthy participants that were brought to a head-up tilt position. This provides suggestive evidence that the application of blood flow restriction could be used to maintain pressure in response to standing, exemplified in this study with the head-up tilt test. Although this study cannot determine if blood flow restriction is an effective method in astronauts during an emergency evacuation, it does serve as an initial step moving forward. A next step might be implementing this method on those who have known orthostatic hypotension or intolerance. If this method produces favorable outcomes in this population, then there would be strong rationale to test this in astronauts.

Conflict of interest: The authors report no relationships that could be construed as a conflict of interest.

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SUPPLEMENTARY MATERIAL

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