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Knee-high compression socks minimize head-up tilt-induced cerebral and cardiovascular responses following dynamic exercise

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In healthy individuals during a non-exercised state, knee-high compression socks (CS) may reduce the magnitude of lower limb venous pooling during orthostasis but are not effective at minimizing the incidence of pre-syncopal symptoms. However, exaggerated reductions in cerebral blood flow velocity (CBV) and cardiac stroke volume (SV) occur during passive head-up tilt (HUT) testing following dynamic exercise. It is unknown if CS can minimize post-exercise HUT-induced decrements in CBV and SV in this population. To test the hypothesis that CS will attenuate the reductions in SV and CBV during 60° HUT following 60 minutes of moderate-intensity (60% VO_2peak) cycling exercise. Ten healthy volunteers (22.6 ± 2.1 years, 24.1 ± 2.5 kg/m^2) completed pre- and post-exercise 15-minute HUT tests during randomized CS and Control (no CS) conditions. Changes in blood pressure (finger plethysmography), SV (Modelflow® method), and CBV (Transcranial Doppler) were measured during HUT and preceding supine rest periods. Pre-exercise HUT-induced similar (all, $P > .47$) reductions in SV (Control; −23.1 ± 11.5%, CS; −20.5 ± 10.9%) and CBV (Control; −18.1 ± 6.3%, CS; −15.3 ± 9.0%). However, larger post-exercise decreases in SV and CBV during HUT were observed in the Control versus CS condition. Specifically, CS attenuated the drop in SV (Control: −32.9 ± 5.6%, CS: −24.3 ± 11.6%; $P = .01$) and CBV (Control: −25.1 ± 5.8%, CS: −17.6 ± 7.8%; $P = .02$) during the post-exercise HUT test. These results indicate that CS attenuated HUT-induced reductions in SV and CBV following moderate-intensity cycling exercise and suggest that CS may be an effective countermeasure to reduce the incidence of post-exercise syncope in vulnerable populations.

KEYWORDS
dynamic exercise, orthostasis, transcranial doppler, venous compression

1 | INTRODUCTION

During a postural stress, blood translocates to the capacitance vessels of the lower limb. Despite one way valves located within veins to counteract the backflow of blood away from the heart, blood volumes of about 500-600 mL move into the legs during standing causing a significant decrease in cardiac preload, stroke volume (SV), and cardiac output (Q).[1-3] Orthostatic intolerance is characterized by the development of pre-syncopal symptoms such as lightheadedness and dizziness due to cerebral hypoperfusion.

Aerobic exercise has been shown to exacerbate orthostatic intolerance and is a commonly reported phenomenon after prolonged endurance exercises such as marathon and ultramarathon races.[4,5] During the exercise recovery period, a combination of deceased central sympathetic drive to the vasculature,[6] reduced signal transduction from sympathetic nerve activity into vasoconstriction,[6] and local vasodilator mechanisms[7] contribute to a large increase in total vascular conductance (TVC), that is, not completely offset by a corresponding rise in cardiac output (Q) leading to post-exercise hypotension. A sustained

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(~2 hours) post-exercise vasodilation that peaks within the first 30 minutes following moderate-intensity aerobic exercise[7] contributes to exacerbated venous pooling during orthostasis[8,9] eliciting larger reductions in SV and cerebral blood flow velocity (CBV), as well as, an increased prevalence of syncope compared to the non-exercised state.[8-10]

Compression socks (CS) have been used to reduce venous pooling in a number of clinical settings including lymphedema[11] and deep vein thrombosis.[12] Compression socks exert external pressure onto the lower leg that reduces venous cross-sectional area and increases venous pressure.[12] Previous studies have demonstrated that knee-high CS are ineffective at reducing orthostatically mediated cerebral and cardiovascular responses to head-up tilt (HUT) in healthy untrained populations before exercise.[13-15] Conversely, lower limb compression stockings have been shown to reduce the incidence of pre-syncopal symptoms in orthostatically intolerant athletes following maximal exercise partially via an attenuated drop is SV and Q.[16]

However, it is unknown if CS can help attenuate the exaggerated post-exercise HUT-induced decreases in SV, Q, and CBV in normotensive individuals without a history of orthostatic intolerance. As such, the objective of this study was to test the hypothesis that knee-high CS (30-40 mm Hg compression rating) are effective at minimizing post-exercise reductions in SV, Q, and CBV during a 15-minute passive 60° HUT in a group of young, healthy, normotensive adults.

2 | METHODS

2.1 | Participants

This study complied with the Declaration of Helsinki and was approved by the Health Science Research Ethics Board at Dalhousie University. Ten young, healthy participants (4♀) provided written informed consent (Table 1). A health history questionnaire documented that participants were free of cardiovascular, metabolic, pulmonary, or neurological disorders. Additionally, none of the participants were taking prescription medications known to effect cardiovascular function and were all non-smokers. To avoid any potential confounding hormonal influences, women were assessed on days 1-7 of their menstrual cycle.

2.2 | Experimental protocol

This study involved 3 days of testing in a randomized condition crossover design. Participants abstained from alcohol, caffeine, and nicotine consumption, as well as, engagement in vigorous physical activity 24 hours prior to testing. Participants were well rested (~8 hours of sleep), well hydrated, and consumed their last meal at least 3 hours before each test session. All experimental sessions were scheduled at the same time of day for each participant and conducted in a thermoneutral room (~21°C). All sessions were separated by at least 48 hours to negate any after-effects from previous exercise sessions on cardiovascular function and were all conducted within a 2-week period.

TABLE 1 Participant characteristics

Age (years)	23 ± 2 (19-26)
Height (cm)	177 ± 8 (168-193)
Weight (kg)	75 ± 9 (65-93)
BMI ($kg \bullet m^{-2}$)	24.1 ± 2.5 (20.6-28.2)
VO_{2peak} ($mL \bullet kg^{-1} \bullet min^{-1}$)	50.5 ± 10.5 (33.5-67.4)
Peak Workload (W)	264 ± 57 (190-350)
Ankle Circumference (cm)	22.4 ± 1.2 (21.0-24.5)
Lower Leg Circumference (cm)	36.6 ± 2.1 (33.5-40.0)

Values are means ± SD (range) from 10 participants (4 females). BMI, body mass index; VO_{2peak}, peak oxygen consumption.

2.2.1 | Day 1

Participants underwent a graded cycle exercise protocol to determine peak oxygen consumption (VO_{2peak}). Measurements of VO_{2peak} were determined by having the participant wear a face mask connected in series with a mixing chamber-based metabolic system (TrueOne 2400, Parvomedics Inc. Utah, USA). The graded cycle exercise protocol involved an initial 5-minute warm-up at a comfortable self-selected workload (~25-50 Watts). Every minute thereafter, the exercise workload gradually increased by 20 Watts until volitional fatigue. VO_2 data were averaged every 15 seconds throughout the test. Peak workload was documented and used for the moderate-intensity cycling bouts in Days 2 and 3 (see below). Individuals were sized for CS by measuring their lower leg and ankle circumferences and following the manufacturer's (JOBST®) sizing specification guide.

2.2.2 | Days 2 and 3

Participants underwent a randomly assigned crossover of the CS and Control (CTL) conditions. In the CTL condition, participants wore traditional, non-compressive, ankle-high socks. Participants were positioned horizontally on the tilt table before being instrumented for measurements of HR, BP, and MCAv. Participants were secured by wide Velcro® straps around their mid-chest and hips to help support them during the tilt test in case of syncope. Once all signals were stable, supine baseline data were recorded before the motorized tilt table was raised to 60° above the horizontal level for 15 minutes. The above procedures were repeated again after a bout of dynamic exercise, which consisted of a 5-minute warm-up period (~25-50 W) prior to 60 minutes of cycling at 60% of their maximum workload. Participants were then immediately moved back to the tilt

table for post-exercise recordings. Approximately 15 minutes elapsed between the end of exercise and the start of the post-exercise HUT tests.

2.3 | Physiological measurements

Continuous heart rate (HR) was determined via cardiac intervals obtained from lead II of a bipolar electrocardiogram. Beat-by-beat systolic (SBP) and diastolic (DBP) blood pressures were measured using finger photoplethysmography (Portapres®; Finapres Medical Systems, Amsterdam, the Netherlands). Brachial measurements of SBP and DBP were also recorded by an automated patient vital signs monitor (Carescape v100®, General Electric Healthcare. Illinois, USA). These values were then used to calibrate corresponding SBP and DBP deflections of the raw Portapres® waveform recording. CBV was recorded from the right middle cerebral artery (MCAv) by non-invasive transcranial Doppler ultrasound (Multigon Industries Inc. New York, USA) using a 2 MHz probe positioned in the trans-temporal window. The Doppler probe was held in a fixed location using a custom headset. All data were sampled continuously at 400 Hz using a PowerLab (PL3508 PowerLab 8/53, ADInstruments, Sydney, Australia) data acquisition system with the exception of the electrocardiogram waveform, which was sampled at 1000 Hz. Recordings were displayed in real time and analyzed offline using LabChart data analysis software (ADInstruments, Sydney, Australia).

2.4 | Data analysis

Beat-by-beat SBP and DBP were determined from the raw Portapres® recording as the maximum and minimum deflections within each heartbeat, respectively. These pressures were then used to calculate MAP using the equation ⅓ SBP + ⅔ DBP. In addition, SV and Q were derived from the raw finger blood pressure waveforms using the previously used and validated[17-20] Modelflow® method incorporated into the proprietary Beatscope® software (version 1.1; TNO BMI, Amsterdam, the Netherlands). The finger used for recording blood pressure was maintained at heart level throughout both supine and HUT time points. Any minor deviations in height between the heart and finger were corrected using the Portapres® height correction unit. Cardiac output was calculated as the product of HR and SV and total vascular conductance (TVC) as Q/MAP. Baseline data were obtained over the last 5 minutes of supine rest. Inter-individual heterogeneity in cardiovascular and cerebrovascular responses, such as time to pre-syncope or maximal drop in SV, is well documented in response to HUT.[21] As such, we documented data for each participant at their lowest (eg, SV, CBV), or highest (eg, HR) responses following HUT, as well as, minute-by-minute averages for all variables during HUT. Minute-by-minute averages were expressed as percentage of completed HUT to account for any individuals who were not able to complete the entirety of the 15-minute test. Steady-state orthostasis analysis consisted of data averaged over the final 5 minutes of HUT.

The ratio of body height to lower leg circumference was determined from participant anthropometric measurements. We quantified individual MCAv responses to HUT while wearing the CS relative to the CTL condition. Simple regression analysis was performed on the relationship between the body height to lower leg circumference ratio and the change in post-exercise MCAv between conditions (ie, CS MCAv—CTL MCAv).

Previous work has demonstrated a significant linear relationship between reductions in Q and MCAv, where small reductions in Q have minimal effect on MCAv.[22] This is indicated by being closer to the positive end of the linear relationship between the two variables. Large reductions in Q result in exaggerated effects on MCAv and a shift toward the negative end of the linear relationship. To confirm the proposed mechanism for CS, we used a simple linear regression to statistically compare the relationship between changes in Q and MCAv during HUT.

2.5 | Statistical analysis

Three-way repeated-measures ANOVAs (Time × Body Position × Condition) were used to identify significant differences in absolute data where "Time" included the pre- versus post-exercise periods, "Body Position" represented supine versus HUT, and "Condition" as CS versus CTL. Similarly, two-way repeated-measures ANOVAs (Condition × Time) were used for all relative comparisons (HUT-Supine) between the CS and CTL conditions. A Bonferroni correction was used to adjust the *P*-value for multiple comparisons. The assumption of sphericity was tested using Mauchly's test and the Greenhouse-Geisser correction factor to the degrees of freedom used for all positive tests. Normality was determined by assessing the skewness and kurtosis of the distribution, as well as, performing a Kolmogorov-Smirnov test. All statistical analyses were conducted using SPSS software version 22 (IBM). Data are presented as means ± standard deviation (SD). Statistical significance was set at $P < .05$.

3 | RESULTS

3.1 | Pre-exercise responses

3.1.1 | Supine comparisons

The use of knee-high CS had no effect (all $P > .13$) on any dependent variable before a bout of moderate-intensity aerobic exercise during rest (Table S1).

3.1.2 | HUT comparisons

No differences were present between CS and CTL conditions when assessed minute-by-minute in any of the dependant variables before exercise (all, $P > .32$). HUT caused a significant increase in HR before exercise in the both CTL and CS conditions (Figure 1A, Table S1). Notable reductions in SV occurred in both CS and CTL conditions following HUT (Figure 1B, Table S1, Table 2). Irrespective of condition, Q, MAP, and TVC were all maintained during pre-exercise HUT (Figure 1C-E, Table S1). Absolute MCAv was significantly reduced after HUT in both conditions (Figure 1F, Table S1). Furthermore, the magnitude of the response to HUT, represented as a percent change (Δ%) from supine rest to the final 5 minutes of tilt (Figures 1A-F), was similar for all pre-exercise variables between conditions (all, $P > .47$). Additionally, the absolute change from baseline to the lowest value (ie, the nadir) showed no effect of condition on SV, Q, MAP, TVC, or MCAv (Table 2; all, $P > .34$). HUT produced a maximal increase (ie, the difference from baseline to peak response following tilt) in HR in CTL and CS conditions by 25 ± 8 bpm and 22 ± 7 bpm, respectively (Table 2; $P = .42$).

3.2 | Post-exercise responses

3.2.1 | Supine comparisons

No significant differences in any of the resting dependant variables were observed between CS and CTL conditions (Table 2). Following exercise, resting HR was significantly increased during both CTL and CS conditions (Table S1). Resting SV decreased post-exercise in both the CS and the CTL condition ($P < .05$). Post-exercise resting Q, MAP, and TVC was not different (all, $P \geq .34$) compared to pre-exercise rest in the both CTL and CS conditions.

3.2.2 | HUT response

One participant experienced pre-syncopal symptoms during the post-exercise HUT in the CTL condition only. This was accompanied by exaggerated reductions in MAP, SV, MCAv, and a paradoxical decrease in HR that resulted in early termination (~10 minutes) of the HUT test (Figure S1A-D). However, while wearing the CS, these variables were stable at the same time point during HUT and the participant

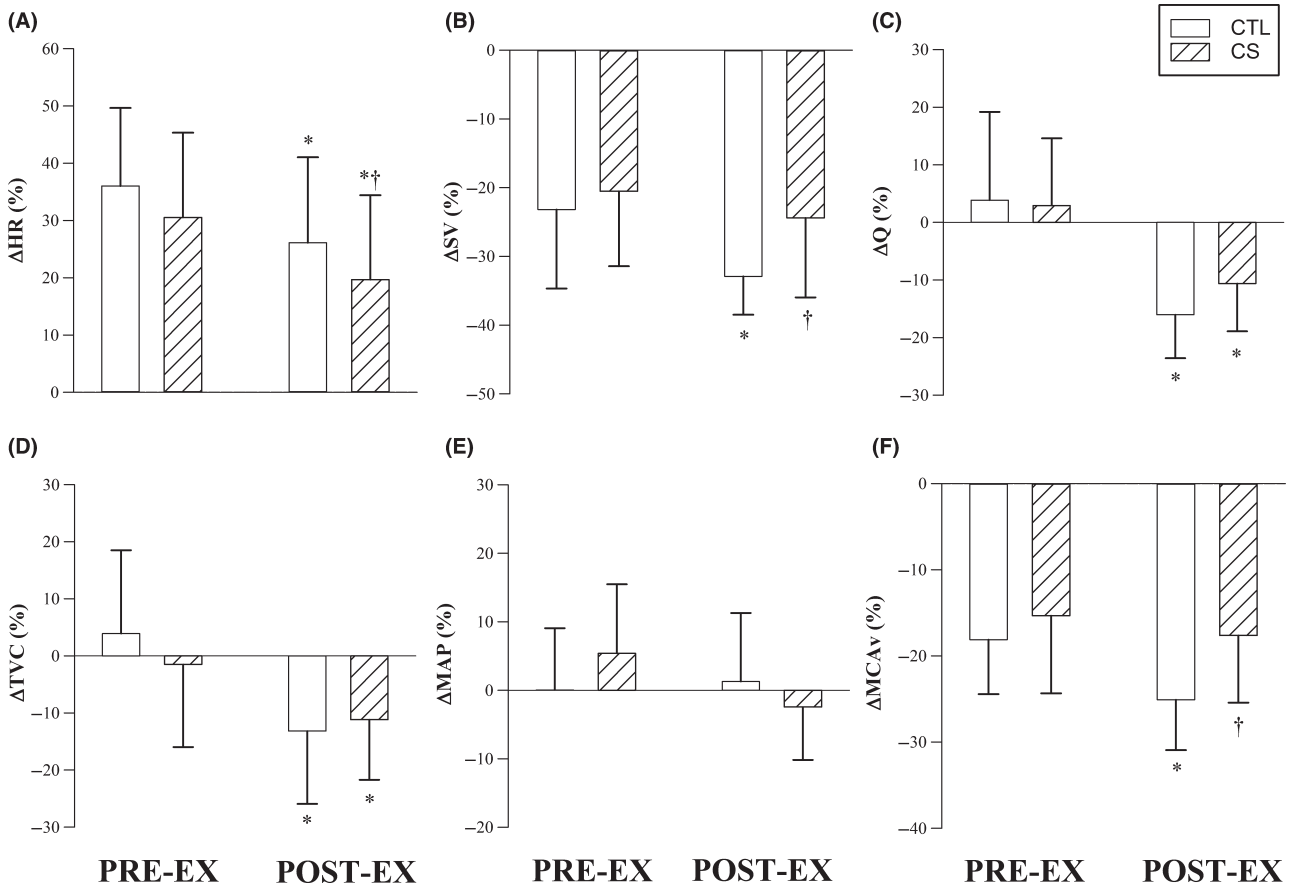

FIGURE 1 Percent change from supine rest to head-up tilt when wearing compression socks (CS) relative to control (CTL; no compression sock), pre- (PRE-EX) and post-exercise (POST-EX). A, Heart Rate (HR); (B) Stroke Volume (SV); (C) Cardiac Output (Q); (D) Mean Arterial Pressure (MAP); (E) Total Vascular Conductance (TVC); (F) Middle Cerebral Artery Velocity (MCAv). *$P < .05$ vs Pre-Ex CTL; † $P < .05$ vs Post-Ex CTL. Values represented as means ±SD

TABLE 2 Delta values measured from supine rest to peak/nadir between CS and CTL conditions following a HUT maneuver

	Pre-exercise		Post-exercise	
	CTL	CS	CTL	CS
ΔHR (bpm)	25 ± 8	22 ± 7	25 ± 10	18 ± 9†
ΔSV (mL)	−26 ± 11	−23 ± 9	−30 ± 9*	−23 ± 6†
ΔQ (L/min)	−0.5 ± 0.6	−0.3 ± 0.7	−2.1 ± 0.9*	−1.2 ± 0.4*†
ΔMAP (mmHg)	−7.5 ± 9.5	−3.7 ± 7.8	−7.3 ± 5.9	−8.4 ± 6.4
ΔTVC (L·min/mmHg)	−7.9 ± 13	−8.5 ± 18	−23 ± 18*	−15 ± 11*
ΔMCAv (cm/s)	−14 ± 7	−14 ± 5	−18 ± 5*	−12 ± 5†

Values are means ± SD.

HR, Heart Rate; MAP, Mean Arterial Pressure; SV, Stroke Volume; MCAv, Middle Cerebral Artery velocity; HUT, Head-Up Tilt; TVC, Total Vascular Conductance; Q, Cardiac Output; CTL, Control; CS, Compression Socks.

*$P < .05$ Compared to pre-exercise (same condition).

†$P < .05$ Compared to post-exercise CTL.

was able to complete the entire 15-minute HUT test (Figure S1E-H).

HUT following aerobic exercise elicited changes in HR, SV, Q, MCAv, and TVC during both conditions (Figure 1, Table S1). Compared to before exercise, the rise in HR elicited by HUT was diminished ($P < .05$) after exercise in both conditions (Figure 1A). Post-exercise HUT produced larger drops in SV ($P < .01$) and MCAv ($P < .05$) in the CTL condition (Figures 1B and F). Both conditions had larger HUT-mediated reductions in Q and TVC post-exercise versus pre-exercise (Figure 1C and E). Post-exercise MAP during HUT did not differ from pre-exercise for either condition ($P > .12$).

3.2.3 | Effect of post-exercise compression socks

There were no absolute differences between CS and CTL conditions during the last 5 minutes of rest or HUT for HR, SV, Q, MAP, TVC, or MCAv following exercise (Table S1). However, minute-by-minute average data demonstrated significantly higher absolute SV, Q, and MCAv values during CS in around the 80% completion time of the 15-minute HUT (Figure S2B-D). Additionally, the absolute change in SV, Q, and MCAv (from supine rest) to the nadir following HUT was attenuated with the use of CS (all $P < .03$; Table 2). Furthermore, the absolute change from baseline to the peak HR response following HUT was also reduced with CS (Table 2). There were no differences (all, $P > .09$) in the last 5 minutes of HUT-mediated Q, TVC, and MAP (Figure S2C-E) responses between conditions. Importantly, CS attenuated the percent drop in SV and MCAv during last 5 minutes of the post-exercise HUT period (Figure S2B and F).

Regression statistics were used to compare the relationship between HUT-induced changes in Q (ie, central blood volume) and MCAv (Figure 2). Individual data from both conditions were compared over a wide range of Q and MCAv. There was a significant correlation between the HUT-mediated percent change (from supine rest) in Q and MCAv ($r = 0.49$, $P = .003$).

3.3 | Anthropometric response

Considerable variability between individual responses to CS was apparent when examining the relationship between body height and lower leg circumference with the HUT-induced change in MCAv between CS and CTL conditions (Figure 3). Both pre- (Figure 3A) and post-exercise (Figure 3B) regressions showed that the magnitude of the MCAv response to CS was significantly associated with this ratio (both, $r > 0.82$ $P < .007$; Figure 3).

4 | DISCUSSION

This study aimed to assess whether knee-high CS can attenuate HUT-induced reductions in SV and CBV after a bout of moderate-intensity aerobic exercise. Our findings demonstrated that CS attenuated the reductions in SV, Q, CBV, as well as, minimized the increase in HR during HUT following exercise. Furthermore, CS permitted the completion of post-exercise HUT in one of our participants who suffered from pre-syncope following exercise in the Control condition. These results suggest that CS have the potential to reduce the physiological responses to HUT following exercise. As such, CS may be of benefit to individuals who are more susceptible to post-exercise syncope.

4.1 | Pre-exercise HUT

Consistent with previous research,[2,3,10] 60° HUT elicited reductions in SV and MCAv, as well as, a commensurate

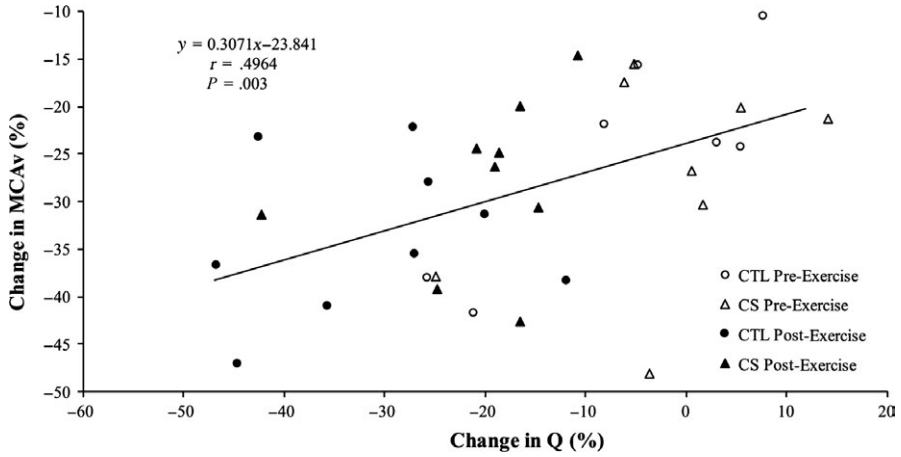

FIGURE 2 Correlation between changes (from supine rest) in Q and MCAv during HUT separated between both pre- (open symbols) and post-exercise (filled symbols), as well as, CTL (circles) and CS (triangles) conditions. Each percentage change in Q corresponds to a 0.30% change in MCAv. Larger reductions in Q, such as those provoked in the CTL group post-exercise corresponded with greater reductions in MCAv (negative end of the regression). Conversely, smaller reductions in Q, such as CTL and CS pre-exercise HUT corresponded with attenuated reductions in MCAv. Mean post-exercise CS values are situated between these two extremes providing evidence for the partial attenuation of central blood volume reductions and MCAv

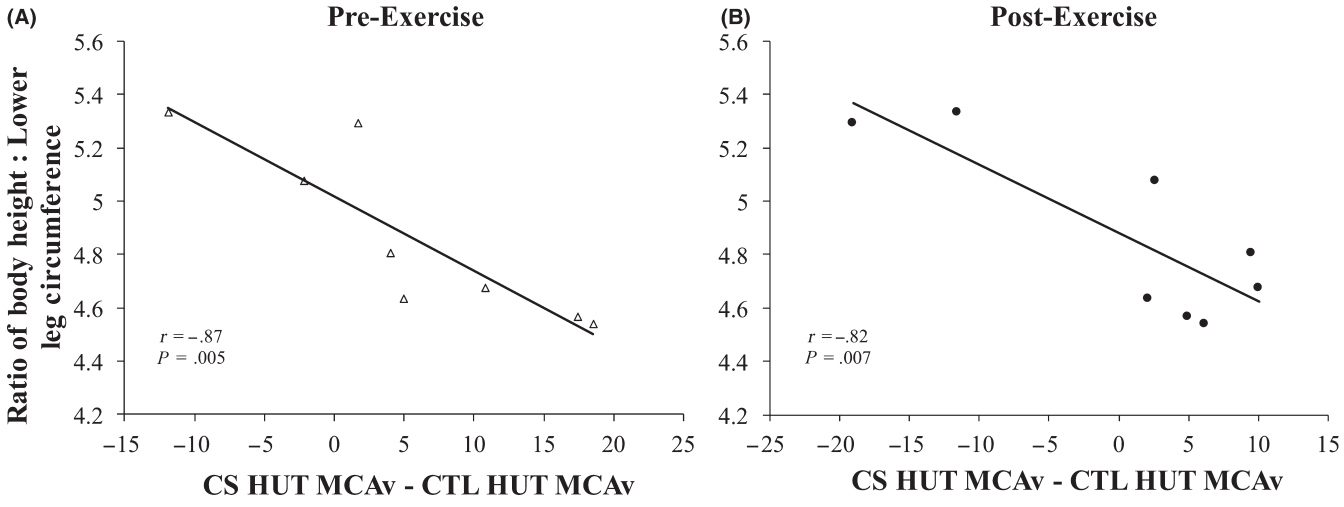

FIGURE 3 Relationship between the difference (CS-CTL) in pre- and post-exercise HUT MCAv (Zero denotes no change in MCAv with CS during HUT while positive numbers indicate the increase in MCAv in during HUT with CS.) and the ratio of body height to lower leg circumference. CS, Compression Socks; CTL, Control (ie, no CS); MCAv, Middle Cerebral Artery velocity

increase in HR that maintained Q. Additionally, participants demonstrated effective baroreflex-mediated control of MAP and a maintenance of TVC comparable to previous studies that performed HUT following 1 hour of cycling at 70% heart rate reserve in young healthy volunteers.[9,10]

The magnitude of the baroreflex-mediated cardio- and cerebrovascular responses between the CS and CTL conditions was similar during the pre-exercise HUT test. During orthostasis, the majority of venous blood moves into the splanchnic and gluteal regions rather than the lower leg.[1] The lower limbs only contribute to about one third of the orthostatic fluid shift during standing.[1] This may explain why the majority of studies, including the present study, have not observed a benefit of lower limb compression for the amelioration of orthostatic intolerance without a prior bout of aerobic exercise.[13-15,19]

4.2 | Post-exercise HUT

In the present study, we demonstrated that HUT following 60 minutes of moderate-intensity cycling exercise resulted in larger reductions in SV, Q, MCAv, and TVC compared to pre-exercise HUT similar to those found in previous studies.[6,8-10,23] This is the first known study to investigate the use of CS as a modality to attenuate cardio- and cerebrovascular responses to orthostasis following

exercise. Compared to CTL, CS attenuated HUT-mediated reductions in SV and MCAv following exercise (Figure 1). Additionally, CS minimized the maximal HUT-induced changes in HR, SV, Q, and MCAv (Table 2), as well as, increased SV, Q, and MCAv near the end of the post-exercise HUT test (Figure S2). We attribute the change in SV and Q to the mechanical compression of lower limb venous vascular beds. This in-turn reduces lower leg venous cross-sectional area and counteracts venous pooling by increasing central venous pressure and cardiac filling.[12] Following a bout of exercise, a greater volume of blood translocates into the lower leg during orthostasis compared to before exercise.[1,6] This may allow CS to have a greater net effect on blood volume and pooling in the lower extremities. A similar hypothesis has been proposed by Lucas et al[24] after examining the effect of compression leggings on young and elderly individuals subjected to combined heat and orthostatic stress. The authors found that under combined heat and orthostatic stress, compression leggings maintained MAP by passively reducing the venous pooling in the lower limbs and increasing TPR.

A positive linear association between CBV and acute changes in central blood volume has been demonstrated at rest and when central blood volume is decreased by orthostatic stress.[18,22] A review by Meng et al[22] found that there is about a 10% CBV decrease for a 30% Q reduction based on eight data pairs from five previous studies. All data from these studies were obtained from young healthy volunteers whose central blood volume was decreased by lower body negative pressure or HUT, and increased by saline or albumin infusion. Our correlation between HUT-mediated changes in Q and MCAv across conditions found a similar trend further supporting a proposed mechanism of increased Q through changes in venous return with CS (Figure 2). We demonstrated an attenuated reduction of MCAv during post-exercise HUT with the addition of CS, also indicated by a shift of the post-exercise CS group mean toward the positive end of this relationship (Figure 2). This shift was characterized by smaller reductions in Q and MCAv.

Furthermore, the rise in HR during HUT was also reduced with the addition of compression socks (Figure 1A, Table 2). Increased venous blood volume back to the heart, and subsequently an increase in SV (Figure S2B), would be expected to reduce the magnitude of the baroreflex-mediated rise in HR during HUT. Potential differences in SV could subsequently affect arterial baroreceptor responses through changes in pulse pressure. This may account for the observed difference in HR response to HUT with CS.[3] Alternatively, another explanation for the reduction in HR during HUT with the addition of CS may be due to a reduction in the unloading of low-pressure cardiopulmonary baroreceptors in the left atria.[3,25] The attenuated HUT-induced changes in HR and SV with CS also suggest that CS minimized reductions in central blood volume to better maintain MCAv.

4.3 | Anthropometric variability

As was the case before exercise, decreases in TVC during post-exercise HUT offset corresponding reductions in Q during both conditions resulting in the maintenance of MAP. However, considerable variability exists between individual physiologic responses to CS. Current sizing charts for compression socks are based on individual ankle and lower leg circumferences. Based on these guidelines, all of our participants were prescribed a "medium" size (Table 1). Upon subsequent analysis of our data, we found a significant inverse relationship ($r = -0.82$; $P = .007$) between the participant's body height to lower leg circumference ratio and the difference in both pre- and post-exercise HUT-induced MCAv values between the CS and CTL conditions (Figure 3).

Taller individuals have a longer distance for blood to travel from the lower legs to the heart. Therefore, these individuals would require larger external forces to generate sufficient pressure to translocate blood the extra distance back to the heart as characterized by the relationship between pressure and length of a tube in Poiseuille's equation.[26] This suggests that CS may provide insufficient external pressures to enhance venous return in taller individuals with smaller lower leg circumference. Previous findings by Protheroe et al[14] demonstrated a positive relationship between the body height:lower leg circumference ratio and changes in orthostatic tolerance after combined HUT and lower body negative pressure in young healthy volunteers. Their results, in conjunction with similar observations from the present study, highlight the need for individualized treatment procedures for optimizing the method used to effectively size individuals for CS to obtain the greatest physiological benefit.

4.4 | Implications and future directions

The use of compression garments, such as socks and pants, has become a growing modality used by athletes and exercise enthusiasts. Additionally, healthcare providers commonly prescribe CS for individuals who suffer from orthostatic syncope. Our results corroborate previous findings that suggest that individuals should be weary when adopting the use of knee-high CS as a method to prevent the physiological response to orthostasis during the non-exercised state in healthy individuals. However, there is potential, although relatively minor, that CS could be used as a countermeasure to protect against the physiological deficits associated with orthostasis in the post-exercise state. Future studies should compare differences in sizing recommendations and their impact on the physiologic responses to orthostatic responses and how they may differ between individuals. Although the

orthostatic protection offered by CS in the current study was relatively minor, CS may offer greater benefit to populations at a higher risk of experiencing syncopal events after exercises such as endurance athletes[27,28] or those with autonomic dysfunction.[29] However, this hypothesis requires further examination.

This study highlights the potential for CS to minimize cardiovascular and cerebrovascular deficits associated with orthostasis following exercise. We acknowledge that we did not induce syncope in our participants, which does not allow us to determine if CS are effective at preventing post-exercise orthostatic intolerance. Our study population consisted of healthy individuals, and therefore most participants had effective cardiovascular control to prevent any pre-syncopal symptoms. Combined with the fact that our participants were not stressed to syncope is most likely why our findings did not show any alterations of MAP between conditions and why only absolute and percent change data reveal differences between conditions. Furthermore, it was not an aim of the present study to assess the efficacy of compression socks on the time to pre-syncope but on the physiologic responses to HUT following exercise. The physiologic responses to orthostasis are similar, albeit exaggerated, during syncope[18] and are therefore possible that CS could reduce syncopal events in healthy individuals following exercise, however, this hypothesis requires further testing.

Additionally, approximately 15 minutes ensued before the start of our post-exercise HUT test. The hemodynamic responses measured immediately post-exercise would surely be greater, as well as, the susceptibility of orthostatic intolerance, than when our measurements were collected. It would therefore be of interest for future investigation to assess whether CS can mitigate the cardiovascular and cerebral perfusion responses to an orthostatic challenge during this more vulnerable period of time. Furthermore, this would also represent a more ecologically valid condition representative of a scenario that might occur following a sporting event or aerobic training session.

The inability to confirm the amount of pressure exerted on the lower leg by the compression socks is another potential limitation of this study. The socks used in this study were rated at 30-40 mm Hg and obtained by a medical grade manufacturer (JOBST®). Our participants were fit according to the manufacturer's specifications, and we therefore do not perceive our inability to confirm the external pressure exerted by them as a detriment to the study. However, the ability to directly measure the pressure exerted on the lower leg by the compression socks is an important measure to include in future research. Specifically, as this pressure may be less in taller individuals with thinner lower limbs thus minimizing the potential benefit of compression socks for minimizing post-exercise reductions in SV and cerebral blood flow during postural challenges.

In conclusion, the primary objective of this study was to assess the efficacy of knee-high compression socks at minimizing reductions in cerebral and cardiovascular responses to HUT after aerobic exercise. To examine this question, we assessed changes in cerebral and cardiovascular measures during HUT both before and after a one-hour bout of moderate-intensity aerobic exercise when using CS or ankle-high socks. We found that CS significantly reduced HUT-induced changes in HR, SV, Q, and CBV following a bout of aerobic exercise suggesting CS may provide a practical means of minimizing the physiologic response to post-exercise orthostasis.

5 | PERSPECTIVES

In the present study, we demonstrated that knee-high compression socks minimized head-up tilt-induced reductions in cardiac stroke volume and cerebral blood flow following, but not before, a 60-minute bout of moderate-intensity aerobic exercise. To our knowledge, this is the first study to assess the cerebral and cardiovascular effects of CS following a bout of moderate-intensity aerobic exercise and to demonstrate the potential of CS to minimize some of the physiological deficits associated with syncope. Previous work by Morrison et al[19] highlighted the effects of passive heating coupled with an orthostatic stress and the lack of efficacy for compression garments to counteract these postural changes. While exercise greatly increases core and skin temperature, passive heating does not accurately represent other vasodilatory phenomenon present after exercise that may contribute to the effects observed in the present study.[30] Regardless of their efficacy, the popularity of CS is evident at both amateur and professional levels of sport.[31] Athletes are at especially high risk for syncopal events due to abnormal peripheral vascular regulation.[6,27] Our results suggest that compression socks could have the potential clinical utility to reduce the incidence of post-exercise orthostatic syncope in such vulnerable populations.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

TWD and DSK contributed to conception and experimental design; TWD, MWO, and SAR performed the experiments; TWD analyzed the data, prepared the figures, and drafted the manuscript; TWD, MWO, and DSK interpreted the results of experiments; TWD, MWO, SAR, and DSK edited and revised the manuscript; TWD, MWO, SAR, and DSK approved the final version of manuscript.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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