Cardiovascular Effects From Venous Blood Pooling in the Lower Limbs During Prolonged Sitting

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Purpose To investigate whether venous blood pooling in the lower limbs from prolonged sitting induces harmful cardiovascular effects by reducing stroke volume (SV) and cardiac output (CO).

Methods A randomized crossover trial involving 16 participants (mean age = 24.8 years ± 6.0 years, 44% women, 1 dropout) was conducted. The trial consisted of 2 conditions: cuff and noncuff, both involving 2 hours of prolonged sitting with tourniquets placed proximal to each knee. In the cuff condition, the tourniquets were inflated to subdiastolic pressure, allowing arterial inflow but preventing venous outflow. Venous blood pooling was assessed by measuring calf circumference. Cardiac Doppler sonography was used to measure CO, SV, and heart rate (HR) before and after the sitting period.

Results Although the interaction effect between venous blood pooling and CO was not statistically significant ($P = .190$), there was a significant main effect for time (effect size [ES] = 0.36, $\beta = -0.238$, 5.42% decrease). A medium-sized time-by-condition interaction effect for SV was observed (ES = 0.37, $\beta = 6.165$), with a 5.87% decrease in the cuff condition and a 2.81% increase in the noncuff condition. Furthermore, there was a large interaction effect for venous blood pooling as measured by calf circumference (ES = 1.98, $\beta = -0.987$), with a 3.69% increase in the cuff condition and a 0.03% increase in the noncuff condition.

Discussion Understanding the physiological adaptations that occur during prolonged sitting can provide insight into how and how often to interrupt sitting to prevent deleterious cardiovascular effects. SV decreased during the sitting period of 120 minutes in the cuff condition and increased slightly during in the noncuff condition. However, the changes in CO and HR were more variable and were not perfectly in line with the authors' hypotheses.

Conclusion The findings indicate that as venous blood pooling increases during prolonged sitting, SV decreases, suggesting venous blood pooling influences certain hemodynamic changes associated with prolonged sitting.

Keywords | *venous blood pooling, hemodynamics, stroke volume, cardiac output, cardiac Doppler sonography*

Sedentary behavior has been associated strongly with an increased risk for cardiovascular disease,[1-5] which is responsible for more than 800 000 deaths annually in the United States.[6] Although the evidence relating sedentary behavior to cardiovascular disease is developing rapidly,[7-12] understanding of the underlying physiological mechanisms is still limited. Without comprehending how sedentary behavior affects cardiovascular disease risk at a physiological level, devising strategies to mitigate sedentary behavior-related cardiovascular disease risk is challenging.

Prolonged sitting, often defined as at least 1 hour of uninterrupted sitting,[13] is the most prevalent form of sedentary behavior in the United States and other western countries.[14] A hypothesis is that prolonged sitting affects the cardiovascular system by reducing stroke volume (SV), thereby diminishing the heart's efficiency and increasing mean arterial pressure,[12,15] the latter of which is related to cardiovascular disease risk.[16] In addition, during prolonged sitting, decreased venous return commonly is observed with a concomitant increase in venous blood pooling in the lower limbs.[7,11,17]

This phenomenon has been suggested as the primary contributing factor to central hemodynamic changes. The proposed physiological mechanism is depicted in **Figure 1**.

This study aimed to assess central hemodynamic changes, including SV, after an acute bout of prolonged sitting, with and without manipulation of venous blood pooling.

Methods

Ethical approval was obtained for this study from the University of North Carolina at Chapel Hill Institutional Review Board (20-3403). All participants provided written informed consent, and there was no monetary incentive to participate. In addition, this study was conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

Sample Size

A power analysis was performed to determine sample size using G*Power 3.1 (Heinrich Heine Universität Düsseldorf).[18] Using a type I error threshold of significance at .05, power of 0.80, and an estimated effect size (ES) of 0.25 (moderate ES), a required sample size of 12 participants was calculated. The number was inflated to 16 to account for loss to follow-up and potential data quality issues while retaining adequate power.

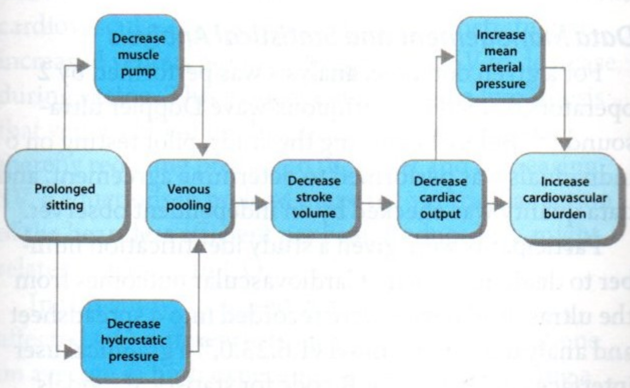

Figure 1. *Proposed mechanism illustrating how prolonged sitting leads to alterations in hemodynamics that increase cardiovascular burden. Image courtesy of the authors.*

Participants

Sixteen participants between the ages of 18 and 45 years were recruited via flyers, social media and Research for Me, a study recruitment service at the University of North Carolina at Chapel Hill. These participants were healthy (ie, no self-reported existing cardiometabolic diseases), nonsmoking, nonvaping, and not pregnant or planning to become pregnant. Those with known cardiometabolic disease were excluded, as well as persons prescribed medication known to alter blood pressure or the sympathetic response. These criteria were implemented to ensure no pathological or pharmaceutical effects would obscure arterial stiffness or hemodynamic changes during the study.

Experimental Design

A randomized crossover trial was conducted in a controlled laboratory environment, characterized by a quiet and climate-controlled setting. Trial visits started between 6:00 AM and 9:00 AM. Before each visit, participants followed specific guidelines, which included fasting from alcohol, caffeine, and food for 8 hours and refraining from intense exercise for 24 hours. Each participant made 3 visits to the laboratory (see **Figure 2**).

During visit 1, participants were familiarized with the laboratory surroundings, and anthropometric measurements were recorded. Visits 2 and 3 were experimental visits, occurring in a 7-day interval. For each experimental visit, a randomized condition was assigned: cuff or noncuff. The order of cuff or noncuff condition was randomized before the familiarization session using online randomization software (Research Randomizer). The cuff condition involved the application and inflation of bilateral occlusive cuffs on the participants' legs to induce venous blood pooling. The

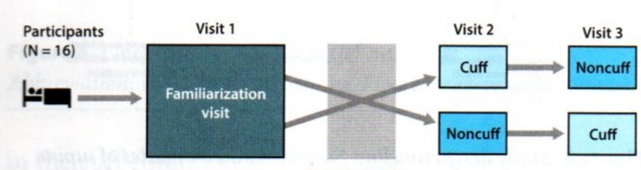

Figure 2. *Randomized crossover study design. Image courtesy of the authors.*

noncuff condition had cuffs applied, but they were not inflated, serving as a control condition.

During each experimental visit, the participant rested for 20 minutes supine on an AM-353 Power Adjustable Treatment Table (Armedica). After resting, measurements of cardiovascular function were collected in a supine posture. Participants were moved passively to a seated position and engaged in prolonged sitting for 2 hours with (cuff) or without (noncuff) venous blood pooling induction. In the cuff condition, the cuffs were inflated to a subdiastolic pressure for the entire 2-hour sitting period. During the sitting bout, participants watched a nonstimulatory home improvement documentary. Participants were not allowed to fidget their legs, and their movements were monitored by a research assistant for each duration of prolonged sitting. No restroom breaks were required by participants during any experimental conditions. After the prolonged sitting session, participants were returned to a supine position for postcondition cardiovascular measurements (see **Figure 3**).

Measurements and Outcomes

The primary aim of the study was to examine changes in SV, CO, and HR during a bout of prolonged sitting, with or without venous blood pooling induction. Measurements were obtained in triplicate, with the closest 2 data points averaged. Venous blood pooling was quantified using calf circumference assessed by a pressure-calibrated tape measure (Gulick tape measure) before and after each sitting bout. Calf circumference was recorded at the widest part of the calf; these measurements were taken immediately after shifting to a seated posture and immediately before shifting to a supine posture.

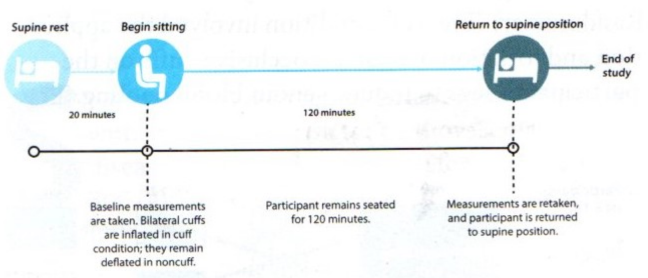

Figure 3. *Study design timeline. Subjects had 20 minutes of supine rest before baseline measurements were taken with participants in a seated position. Measurements were taken again at the end of the sitting period, before returning participants to supine position. Image courtesy of the authors.*

Cardiovascular measurements (before and after sitting) were taken with the participant in a supine position, as this has been shown to be the most precise posture for measurement.[19] Participant cardiovascular data were obtained using a continuous-wave Doppler ultrasound device (USCOM 1A; Uscom Ltd). The transducer was applied to the participant's chest at the level of the suprasternal notch and pointed at the aortic valve to measure SV. The transducer was adjusted until a minimum of 3 distinct waveforms were obtained. Three measurements were taken at each timepoint, and low-quality data affected by signal noise were removed from outcome calculations during data reduction. The device then applied a proprietary algorithm to estimate SV and used HR to calculate CO.

Quality Control

For a given outcome, all measurements and analyses were conducted by a single observer. The first 3 data sets were graded by an independent observer. At the conclusion of the study, a random selection of 18.8% of the datasets (ie, all data from 3 participants) were recorded by another independent observer and used to calculate interobserver reliability.

Data Management and Statistical Analysis

For a given outcome, analysis was performed by 2 operators trained in continuous-wave Doppler ultrasound.[20,21] Before beginning the study, pilot testing on 6 individuals was performed to determine agreement, and data quality was checked by an independent observer.

Participants were given a study identification number to deidentify them. Cardiovascular outcomes from the ultrasound device were recorded into a spreadsheet and analyzed using Jamovi v1.6.23.0,[22] a graphical user interface application for R code for statistical models. A random-effects linear mixed model was used to analyze the data. Linear mixed models can be adjusted for covariates and can incorporate fixed (ie, group) effects such as age or sex and random (ie, individual) effects, making it an ideal statistical analysis for this study.

Results

Use of the venous occlusion cuffs resulted in a large, significant interaction effect for venous blood pooling as measured by calf circumference (ES = 1.98, $\beta = -0.987$ cm, $P < .001$), with a larger increase in calf circumference in the cuff condition (3.69% increase) than in the noncuff condition (0.03% increase).

Stroke Volume, Cardiac Output, and Heart Rate

There also was a medium, significant interaction effect for SV (ES = 0.37, $\beta = 6.165$ cm^3, cuff: 5.87% decrease, noncuff: 2.81% increase). Although there was a nonsignificant interaction effect between venous blood pooling and CO (ES = 0.22, $\beta = 0.293$, $P = .190$), there was a significant main effect for time (ES = 0.36, $\beta = -0.238$, 5.42% decrease). No significant interaction effects or significant main effects were detected for HR. **Figures 4**, **5**, and **6** show the changes in SV, CO, and HR for the cuff and noncuff conditions after 120 minutes of prolonged sitting.

Discussion

This research sought to elucidate the role of venous blood pooling in the mechanism of cardiovascular changes during an acute bout of prolonged sitting. Understanding the physiological adaptations that occur during prolonged sitting can provide insight on how and how often to interrupt sitting to prevent deleterious cardiovascular effects. The results demonstrate that increased venous blood pooling caused SV to decrease during sitting. This evidence supports the hypothesis that venous blood pooling reduces venous return, thereby reducing preload to the heart and decreasing SV. Reductions in preload make the ventricular action of the heart less efficient per beat. Reduced SV might relate to changes in CO.

In this study, increased venous blood pooling affected CO differently from SV, showing reductions on average in both experimental conditions during a specific period. This effect differed from that for SV, which showed a time-by-condition interaction effect. SV decreased during the sitting period of 120 minutes in the cuff condition and increased slightly during the noncuff condition. However, SV is a multiplicand of CO with HR via the Fick equation (SV = CO/HR)[23] meaning that with no changes in HR approximately a

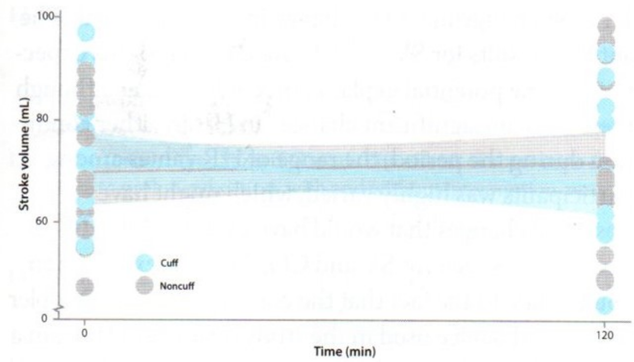

Figure 4. *Linear mixed model data for stroke volume. Figure courtesy of the authors.*

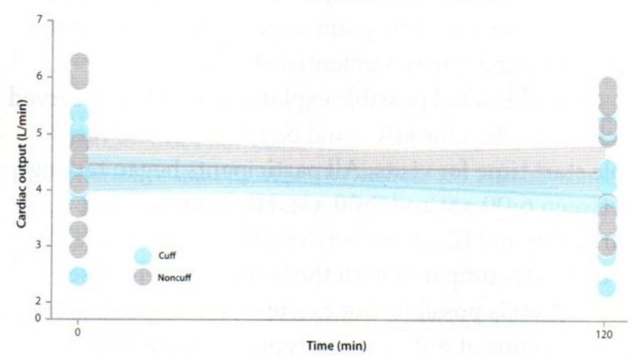

Figure 5. *Linear mixed model data for cardiac output. Figure courtesy of the authors.*

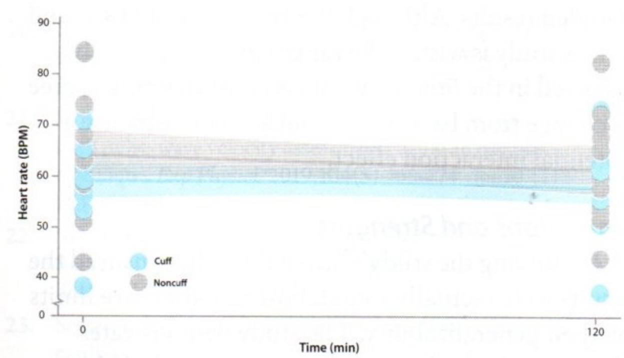

Figure 6. *Linear mixed model data for heart rate. Abbreviation: BPM, beats per minute. Figure courtesy of the authors.*

1:1 ratio change in CO to change in SV is expected. The authors' results for SV and CO are counter to this expectation. One potential explanation could be that although there were no significant changes in HR in either condition during the period, the range of HR values among participants was highly varied, which might have obscured changes that would have explained the different effects seen for SV and CO. Another explanation could relate to the fact that the continuous-wave Doppler ultrasound device used in the study estimates HR from a 3-second sample at each timepoint. Because of this, typical variations in HR, such as that due to the respiratory cycle,[24] might have been enough to produce variability in the data during each measurement. Additional measurements for each timepoint might reduce some of this variability and clarify a potential effect.

One additional possible explanation for the observed lack of an effect for HR could be related to the variable start time for visits. All participants began testing between 6:00 AM and 9:00 AM. High intersubject variability in HR values between those who started at 6:00 AM compared with those who started closer to 9:00 AM is possible. For example, participants who began testing at 6:00 AM but typically wake up at approximately 7:00 AM might have experienced a cortisol awakening response during testing, resulting in a rapid increase in HR from baseline that could have confounded results. Although the variability of HR found in this study is within the range of values typically reported in the literature,[25] it could be that this degree of change from baseline was sufficient to obscure a potential interaction effect.

Limitations and Strengths

Improving the study's internal validity ensured the results were factually sound; however, there are limits on their generalizability. The study demonstrates changes in hemodynamics among young, healthy participants, and likely are not applicable to older populations or those with cardiometabolic diseases. Older adults and adults with cardiometabolic disease have a more limited ability to adapt to stresses on the cardiovascular system caused by venous blood pooling,[26,27] which might lead to increased acute stress on the cardiovascular system due to venous blood pooling.

This trial maintained high internal validity by standardizing procedures for each participant, thereby limiting confounders. The experimental conditions were as consistent as possible and previsit guidelines reduced confounding factors from diet, caffeine, alcohol, and exercise. In addition, menstrual cycles of female participants were controlled for by only testing in the follicular phase to minimize hormonal effect of estradiol on vascular response. Lastly, the study included a washout period of 48 hours to 1 week between treatments, generating participant's baseline state while limiting variations in stress, hormones, and other physiological factors.

Conclusion

Venous blood pooling during prolonged sitting might cause hemodynamic changes that affect CO via SV and put increased burden on the heart to maintain mean arterial pressure in the body. However, the role of venous blood pooling in these changes had not been assessed previously. This study assessed the role of venous blood pooling on changes in central hemodynamic parameters during prolonged sitting and found increases in venous blood pooling related to decreases in SV, which supports the study's hypothesis. However, the changes in CO detected were different than those detected for SV. Although the sample of young, healthy adults might have had adaptive responses in HR that were able to maintain CO despite decreases in SV, populations of older adults or those with cardiometabolic disease might be unable to similarly compensate, rendering them vulnerable to increases in cardiac burden. Future research can investigate the relationship between venous blood pooling and central hemodynamic parameters in populations that might be more vulnerable to changes in cardiac homeostasis.

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