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ORIGINAL ARTICLE

Prolonged standing increases lower limb arterial stiffness

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Abstract

Purpose Standing workstations have recently been promoted as a healthy alternative to sitting. However, it is unknown how prolonged standing affects arterial stiffness, a prognostic indicator of cardiovascular health. The purpose of this study was twofold: to observe changes in arterial stiffness, as assessed by pulse wave velocity (PWV), with a 2-h bout of standing, and to determine if short, intermittent walking bouts provide a comparative advantage to standing alone.

Methods Nineteen adults had arterial stiffness assessed by pulse wave velocity. Central (C_{PWV}), upper peripheral (U_{PWV}), and lower peripheral (L_{PWV}) PWV were assessed before (supine), during standing (min 10, 60, and 120), and after (supine) the 2-h standing bout. In one trial, the participants stood at a standing desk immobile for 2 h. In the other trial, participants performed 5-min walking breaks after every 25 min of standing.

Results After 2-h of standing, supine (85.8 ± 90.1 cm/s) and standing (303.4 ± 390.2 cm/s), L_{PWV} increased independent of trial (i.e., main effect of time; $p < 0.001$). Walking breaks during 2 h of standing did not significantly attenuate these changes. In addition, standing C_{PWV} decreased over time (− 38.5 ± 61.5 cm/s; $p = 0.04$). Yet, U_{PWV}, standing or supine, did not change over the course of standing ($p > 0.05$).

Conclusions These findings indicate that prolonged standing increases the measures of arterial stiffness and there is no evidence that walk breaks attenuate this response.

Keywords Pulse wave velocity · Physical activity · Occupational health · Sedentary

Abbreviations

C_{PWV}	Central pulse wave velocity
HR	Heart rate
L_{PWV}	Lower peripheral pulse wave velocity
MAP	Mean arterial pressure
PWV	Pulse wave velocity
STAND	Standing trial
U_{PWV}	Upper peripheral pulse wave velocity
WALK	Walking trial

Introduction

Modern occupations have reduced physical activity, thereby substantially increasing the risk for cardiovascular disease. Prolonged inactivity during the workday creates an atherogenic environment which increases the risk of cardiovascular disease and subsequent mortality (Padilla and Fadel 2017). This sedentary behavior appears to exert its pathological effects on the vasculature by reducing blood flow and shear stress, which causes vascular dysfunction (Restaino et al. 2016).

Prolonged standing has been recommended as replacement to sitting (Lopez-Jimenez 2015; Trinity 2017) to reduce cardiovascular risk; however, cardiovascular drawbacks to prolonged standing have also been found (Waters and Dick 2015). The conflicting evidence on the potential benefits and drawbacks of prolonged standing for cardiovascular health leaves a void in our understanding of arterial function during prolonged standing and the influence of physical activity breaks.

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The implementation of standing desks appears to have some metabolic benefits such as increased caloric expenditure and improved fasting glucose (Reiff et al. 2012; Healy et al. 2017), and acutely attenuates endothelial dysfunction in comparison to sitting (Morishima et al. 2017). Unfortunately, cardiovascular issues have also been found with prolonged standing (Waters and Dick 2015). Lower limb blood flow and shear rate are significantly reduced from standing (Morishima et al. 2017). Venous edema associated with standing greatly increases the risk of chronic venous insufficiency (Tomei et al. 1999) and worsens the progression of atherosclerosis (Krause et al. 2000) compared to those in sitting occupations. The venous edema that occurs with prolonged standing (Partsch et al. 2004) is also associated with vascular dysfunction (Restaino et al. 2016). However, it is unknown how standing affects overall measures of arterial function, such as arterial stiffness measured with pulse wave velocity (PWV).

A second recommendation in sedentary occupations is to incorporate physical activity into the workday (John et al. 2015). A physically active lifestyle appears to prevent, or at least attenuate, increases in arterial stiffness associated with aging (Vaitkevicius et al. 1993), as well as attenuating venous edema and preserving endothelial function (Morishima et al. 2016). Even acute bouts of physical activity appear to preserve endothelial function following long bouts of inactivity (Morishima et al. 2016, 2017; Restaino et al. 2015, 2016; Thosar et al. 2015) and can decrease arterial stiffness (Kingwell et al. 1997; Nickel et al. 2011). These effects can be isolated to a single exercising limb (Sugawara et al. 2003). Despite knowledge about physical activity and arterial stiffness in general, little is known about the specific effects of "walk breaks" throughout a long period of standing.

Arterial stiffness is typically measured by pulse wave velocity (PWV), and thus, it was the primary dependent variable in this investigation. Overall, PWV provides a measurement of the functional capacity of the arterial wall. PWV changes can be specific to the arterial branch (Ashor et al. 2014) with differences occurring between central (C_{PWV}), upper peripheral (U_{PWV}), and lower peripheral (L_{PWV}) arterial stiffness due to alterations in both the passive components (i.e., extracellular matrix and heart rate) as well as active components (i.e., endothelial function, nitric oxide availability, and vascular smooth muscle tone) of the arterial wall (Townsend et al. 2015). For example, acute changes in arterial stiffness due to vasodilatory stimuli such as exercise are more likely to occur in the muscular peripheral arteries (e.g., U_{PWV} and L_{PWV}) rather than the elastic central arteries (e.g., C_{PWV}) (Heffernan et al. 2007; Munir et al. 2008).

The purpose of this study was to examine the effects of prolonged (2 h) standing and standing with walking breaks on measures of central (C_{PWV}), upper peripheral (U_{PWV}), and lower peripheral (L_{PWV}) arterial stiffness. We specifically focused on arterial stiffness, as measured by PWV, because of its clinical applicability (Ben-Shlomo et al. 2014), prognostic value (Mitchell et al. 2010), and its sensitivity to acute interventions (Kingwell et al. 1997). We hypothesized that prolonged standing would result in increased C_{PWV} and L_{PWV}. We also hypothesized that walking breaks would attenuate increases in C_{PWV} and L_{PWV}. Finally, we hypothesized that U_{PWV} would be unchanged following prolonged standing or standing with walking breaks.

Materials and methods

Written informed consent was obtained from all participants prior to participation. Study procedures and informed consent were approved by the Institutional Review Board at the University of Arkansas, and were in accordance with the current guidelines of the Declaration of Helsinki. The exclusion criteria were: previous lumbar spine injury, previous history of lower limb cardiovascular issues, a history of contact dermatitis caused by isopropyl alcohol, the presence of an implanted pacemaker, or a history of fainting or dizziness. All participants were between the ages of 18–40 years and had a body mass index between 18 and 35 kg/m^2. A total of 20 participants were recruited to complete this study. One participant was unable to complete the study due to complaints of knee and back pain during the second experimental trial. A total of 12 men and 7 women ($N = 19$), age 22 ± 3 years, and a BMI of 23.2 ± 2.9 kg/m^2. Based on the previous research regarding PWV and menstrual cycle (Williams et al. 2001), we did not control for menstrual cycle within this study.

Experimental design

Figure 1 depicts the overall experimental design. Participants took part in two separate trials separated by at least 7 days. Each trial was completed on the same day of week and completed at the same time of day (within 1 h). For all experimental trials, participants arrived at the lab at least 3-h fasted, and 24-h without caffeine, alcohol, or exercise. In one trial, participants stood at a standing workstation with a treadmill beneath his or her feet for 120 min (STAND). In the other trial (WALK), participants stood for 120 min, but every 25 min, they completed 5 min of low-intensity walking (2 mph, 0% incline). The standing bouts were limited to 2 h due to pilot work indicating limited subject tolerance to bouts longer than this time period. Therefore, they had four bouts of walking (min 25, 55, 85, and 115). The order of trial completion was randomized.

Upon arrival to the laboratory, participants laid supine on a massage table. After 15 min of rest, baseline measures

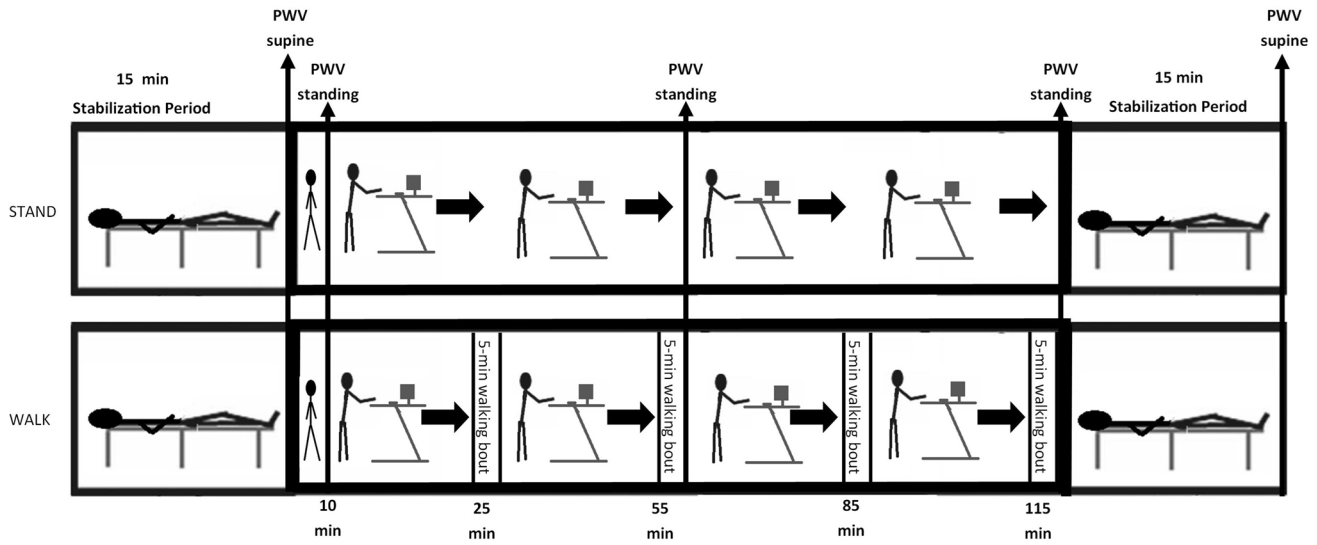

Fig. 1 Study design. Measurements of pulse wave velocity (PWV) occurred at the end of each stabilization period while supine, and after 10, 60, and 120 min of standing. Each box depicts a trial. The top box represents the standing trial (STAND) and the bottom box represents walking (WALK) trials. In the walking trial, participants had four 5-min walking breaks separated by 25 min

of PWV, blood pressure, and heart rate (HR) were obtained. Participants then stood and moved to a treadmill immediately adjacent to the massage table. Participants then stood, perpendicular to the treadmill belt, facing a standing workstation adjusted to his or her individual height. During the trials, participants had a non-stimulating documentary playing on the computer at the standing workstation (e.g., nature-related). At approximately 10, 60, and 120 min of standing, measures of PWV were obtained while the participant was standing. For the standing U_{PWV} measurement, participants rested his or her hand on the ultrasound technician's shoulder (i.e., level of the heart), while radial images were obtained. For the standing L_{PWV} and C_{PWV} measurements, individuals stood with feet planted at shoulder width and arms relaxed at their sides.

Measures

Arterial stiffness was indexed using PWV, which is the preferred method (Townsend et al. 2015). PWV is considered a valid measurement of arterial stiffness which is justified on the basis of the Bramwell–Hill and Moens–Korteweg equations (Vlachopoulos et al. 2011), and relies upon less assumptions regarding arterial stiffness than other measures (i.e., augmentation index) (Townsend et al. 2015). PWV was measured with duplex-mode Doppler ultrasound (GE GoldSeal LOGIQ eBT08; 4–12 MHz GE 8L-RS linear array transducer) using the foot-to-foot method (Calabia et al. 2011). Specifically, PWV was calculated as the distance between measurement sites divided by the time delay between the two waveforms from a recorded loop on the ultrasound using on screen calipers to directly measure the time delay between the R wave and the pulse wave. A three-lead ECG was utilized to calculate the time delay from the R wave to the foot of the pulse wave. The time delay was averaged from a minimum of ten cardiac cycles. The coefficient of variation of over the ten cardiac cycles was less than 3% at all measurement sites; similar to the previous work from our laboratory (Moyen et al. 2016). Central PWV (C_{PWV}) was calculated from the carotid and femoral arteries, while upper peripheral PWV (U_{PWV}) was calculated from carotid and radial arteries. Lower peripheral PWV (L_{PWV}) was calculated from femoral and dorsalis pedis arteries. The distance between arterial measurement sites for C_{PWV} was calculated as the combined distance from the suprasternal notch site to the umbilicus and from the umbilicus to femoral site minus the distance from carotid to the suprasternal notch. The distance between arterial sites for U_{PWV} was calculated as the distance between the suprasternal notch and the radial site minus the distance from the carotid to the suprasternal notch. The distance between arterial sites for L_{PWV} was calculated as the direct distance between the femoral and dorsalis pedis sites. Distances between sites were calculated for each individual trial by measuring from the distal edge of the ultrasound probe with a retractable cloth tape measure (Walmart, Bentonville, AR, USA). All PWV measures were performed on the left side of the body with consistent probe location being assured by marking the skin with a surgical marker. The day-to-day within-subject coefficient of variation for each of the measures was a 10%, 10%, and 9% for U_{PWV}, C_{PWV}, and L_{PWV}, respectively.

In this study, standing measures of PWV were obtained. Body posture influences hemodynamic regulation of parameters related to arterial stiffness (Reesink et al. 2007), but measuring arterial stiffness in the upright position is reliable (Nurnberger et al. 2011). Therefore, standing measures were only compared to other standing measures. Measurement site order was randomized between participants but consistent within participants for each trial.

In addition, participants were instrumented with an automated sphygmomanometer (Tango+; SunTech Medical, Inc., Morrisville, NC, USA). This device allowed for the measurement of blood pressure and HR. Mean arterial pressure (MAP) was measured by multiplying one-third systolic by two-third diastolic blood pressure.

Table 1 Heart rate and mean arterial pressure repeated-measures ANOVAs

	p	Partial η^2
HR		
Trial	0.347	0.055
Time	< 0.001	0.768
Time × Trial	0.173	0.094
MAP		
Trial	0.472	0.033
Time	< 0.001	0.498
Time × Trial	0.447	0.059

HR heart rate, MAP mean arterial pressure

Statistical analysis

Data were analyzed using Rstudio and the jamovi package (Selker et al. 2017). Two separate repeated--measures analyses were utilized: one with the supine data (baseline and post-trial) and one with standing data (10 min, 60 min, and 120 min of standing). A two-way (trial by time) repeated-measures ANOVA was run to determine the effect of STAND versus WALK on C_{PWV}, U_{PWV}, and L_{PWV} over the course of 2 h. Data are presented as mean ± standard deviation, unless otherwise stated. Graphical representation of the data was created using the ggplot2 package (Wickham 2009). Significance was set at an alpha of 0.05. If a significant ANOVA F test was observed, then pairwise comparisons were inspected. Effect sizes at the ANOVA level are represented by partial η^2, and by Hedges g_{rm} for the pairwise comparisons to aid in power and meta-analysis calculations in future studies (Lakens 2013).

Results

There was a main effect of time on MAP and HR (Table 1). Both HR (Fig. 2a) and MAP (Fig. 2b) were elevated throughout the standing period compared to the baseline measures, but there were no differences between trials at any time point. In other words, there was no two-way interaction between time and trial on MAP or HR (Table 1).

Supine PWV measures are displayed in Fig. 3. L_{PWV} increased over time (i.e., significant main effect of time; Table 2), regardless of trial (i.e., non-significant interaction and main effect of trial; Table 2). Post hoc comparisons indicated that, regardless of trial (STAND or WALK), standing for 2 h led to an increase ($p < 0.001$, $g_{rm} = 1.09$) in supine L_{PWV}. While the two-way interaction between time and trial was non-significant (Table 2), the degree to which L_{PWV} increased (Fig. 3c) was greater in the STAND trial ($g_{rm} = 1.24$) than in the WALK trial ($g_{rm} = 0.45$). Meanwhile, there were no changes in U_{PWV} or C_{PWV} when supine regardless of trial or time (Table 2; Fig. 3a, b for C_{PWV} and U_{PWV}, respectively).

Standing PWV measures are displayed in Fig. 4. C_{PWV} decreased over the course of standing, independent of trial (i.e., independent effect of time; Table 3) Post hoc comparisons (Fig. 4a) indicated a decrease in C_{PWV} from 10 to 120 min of standing ($p = 0.01$, $g_{rm} = 0.25$), but no differences between 10 and 60 min ($p = 0.12$, $g_{rm} = 0.15$), or 60–120 min ($p = 0.30$, $g_{rm} = 0.09$). However, L_{PWV} increased over the course of standing for 2 h (i.e., main effect of time; Table 3). Post hoc comparisons of standing L_{PWV} indicated that, regardless of trial (STAND or WALK), there was an increase (Fig. 4c) from 10 to 60 min ($p = 0.03$, $g_{rm} = 0.43$), 10–120 min ($p < 0.001$, $g_{rm} = 1.15$), and 60–120 min ($p = 0.002$, $g_{rm} = 0.69$). There were no changes in U_{PWV} over the course of standing (i.e., non-significant interaction or main effects; Table 3).

Discussion

Recent evidence (Morishima et al. 2017) suggests that standing may attenuate vascular dysfunction typically associated with long bouts of inactivity. However, studies, to date, have not considered arterial stiffness. Furthermore, no investigation has examined the effect of low-intensity, short-duration walk breaks during standing on vascular function. In this study, we measured arterial stiffness using C_{PWV}, U_{PWV}, and L_{PWV} during 2 h of standing with (WALK) and without (STAND) 5-min walk breaks every 25 min. As expected, U_{PWV} did not change in response to STAND or WALK. Contrary to our hypotheses, C_{PWV} decreased and L_{PWV} increased regardless of walking breaks. Walk breaks did not attenuate this response.

The primary effects of standing appear to be localized to the lower limbs (Figs. 3c, 4c). This is in agreement with the previous work, observing that while microvascular

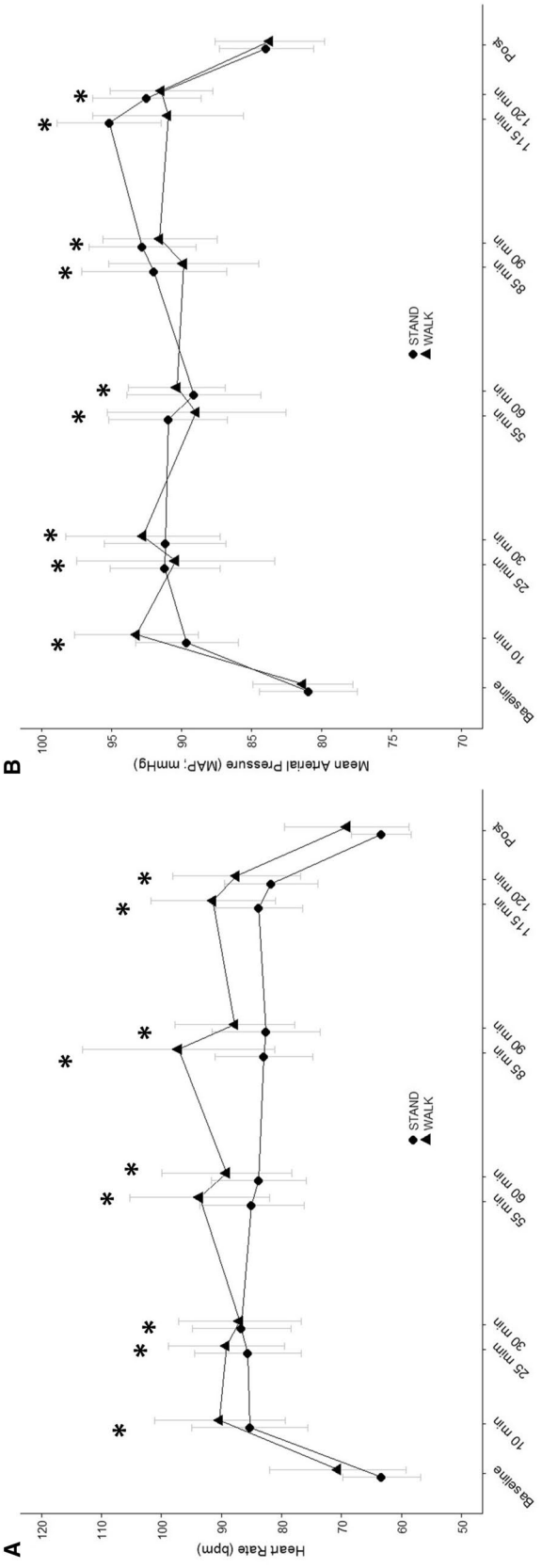

Fig. 2 **a** Heart rate and **b** mean arterial pressure (mean ± 95% confidence interval) throughout each experimental trial. *Significant difference ($p < 0.05$) from baseline

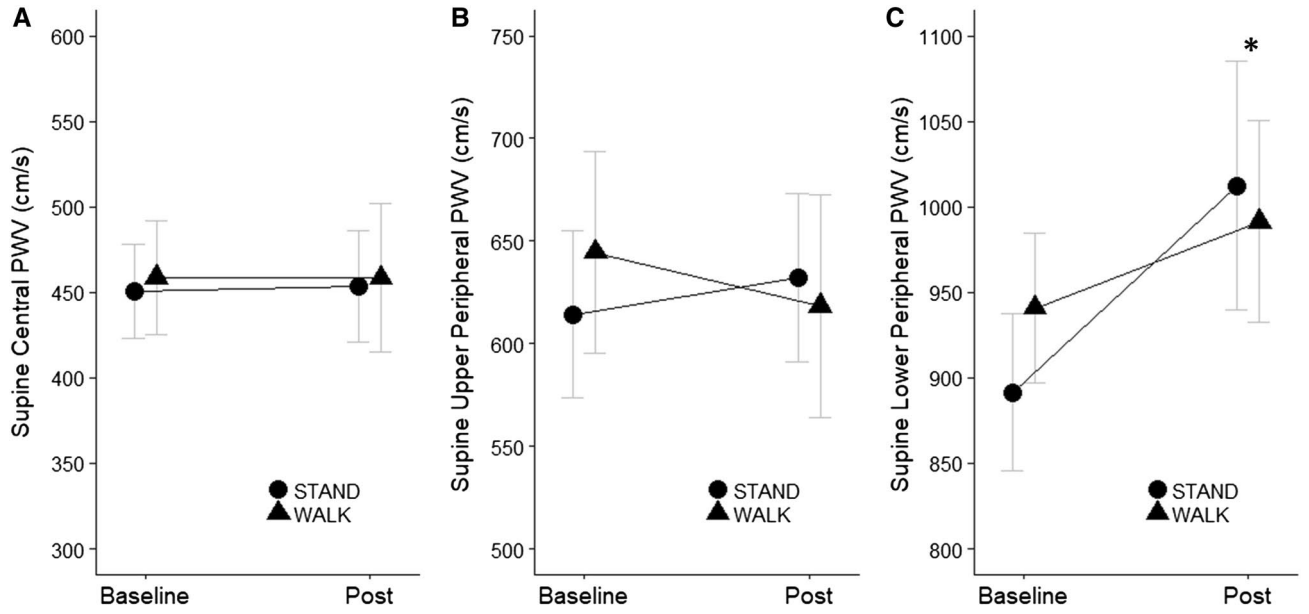

Fig. 3 Supine measures of **a** central, **b** upper peripheral, and **c** lower peripheral pulse wave velocity (mean ± 95% confidence interval) from before (baseline) and after (post) each experimental trial. *Significant difference ($p < 0.05$) from baseline. Markers are offset at each time point for clarity

Table 2 Supine pulse wave velocity repeated-measures ANOVAs

	p	Partial η^2
C_{PWV}		
Trial	0.663	0.011
Time	0.868	0.002
Time × Trial	0.820	0.003
U_{PWV}		
Trial	0.629	0.013
Time	0.782	0.004
Time × Trial	0.208	0.087
L_{PWV}		
Trial	0.533	0.022
Time	< 0.001	0.503
Time × Trial	0.155	0.109

C_{PWV} central pulse wave velocity, U_{PWV} upper peripheral pulse wave velocity, L_{PWV} lower pulse wave velocity

function in both the brachial and popliteal artery is reduced during prolonged (6 h) of sitting, macrovascular function was only affected in the lower limbs (Restaino et al. 2015). The increase in PWV observed during prolonged standing (Fig. 4c) may be due to the lack of muscle contraction and increased hydrostatic pressure, which can cause venous edema. This pooling of blood stretches the small veins and causes a venoarteriolar response resulting in vasoconstriction (Henriksen 1977; Brothers et al. 2009). During vasoconstriction, diameter decreases, whereas pressure within the artery increases, thereby increasing PWV in that arterial branch (Nichols and Edwards 2001). However, if this mechanism were the cause of increased L_{PWV}, physical activity should have been effective at preventing these changes, which was not the case in the present study (see below) (Quilici et al. 2009; Morishima et al. 2016). Future studies should make the measures of arterial diameter to provide insight into these mechanisms. Furthermore, the lower extremity arteries are more susceptible to atherosclerotic damage than other arterial branches (Li et al. 2014), perhaps explaining why we observed differences in the L_{PWV} and not at other measurement sites.

Two hours of prolonged standing led to an increase in lower limb arterial stiffness (i.e., L_{PWV}; Figs. 3c, 4c). This is in contrast to the previous research by Morishima et al. (2017) that indicated vascular function is preserved after standing for 2 h. Standing, despite the absence of a stimulus to increase shear stress, may provide some vascular benefit versus sitting likely due to changes in the anatomical position of the arteries in the lower limb (Morishima et al. 2017). However, comparing sitting versus standing is different, because the anatomical position of sitting forces the arteries into angulations that create turbulent flow within the femoral artery, thereby inducing vascular dysfunction. We did not compare sitting versus standing, because we were more interested in how arterial stiffness changed over 2 h of standing. Our results show that standing itself may not entirely protect against vascular derangements associated with inactivity.

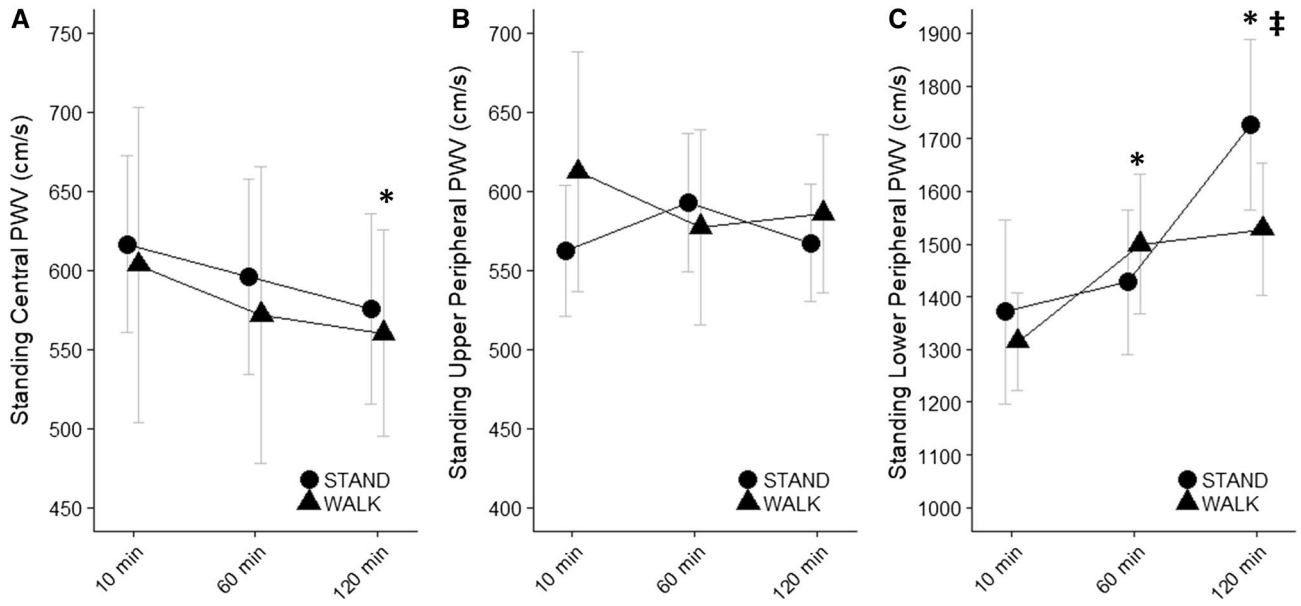

Fig. 4 Standing measures of **a** central, **b** upper peripheral, and **c** lower peripheral pulse wave velocity (mean ± 95% confidence interval) after 10, 60, and 120 min of standing. *Significant difference ($p < 0.05$) from 10 min, ‡Significant difference from 60 min ($p < 0.05$). Markers are offset at each time point for clarity

Table 3 Standing pulse wave velocity repeated-measures ANOVAs

	p	Partial η^2
C_{PWV}		
Trial	0.772	0.005
Time	0.039	0.173
Time × Trial	0.773	0.015
U_{PWV}		
Trial	0.104	0.148
Time	0.633	0.027
Time × Trial	0.103	0.125
L_{PWV}		
Trial	0.122	0.143
Time	< 0.001	0.505
Time × Trial	0.221	0.090

C_{PWV} central pulse wave velocity, U_{PWV} upper peripheral pulse wave velocity, L_{PWV} lower pulse wave velocity

The increase in L_{PWV} was not altered by four 5-min walking breaks (Figs. 3c, 4c). This may be partially explained by the fact that the walking bouts in this study were very low intensity as evidenced by similar HR and MAP responses in the two experimental trials (Fig. 2). We chose a light intensity because of the applicability in the work place. In other words, the walk break could be attained during the average workday without "breaking a sweat" (Schwartz et al. 2017). In other studies, Kingwell et al. (1997) and Nickel et al. (2011) have observed significant reductions in multiple measures arterial stiffness following low-to-moderate intensity cycling (i.e., a higher intensity than the current study). Therefore, the benefits of walking, or other types of physical activity, may occur at higher levels of intensity and volume.

Given that posture may change PWV, we chose to obtain measurements before and after the standing, while participants were supine for at least 10 min. Likewise, we obtained measures during the standing, while participants remained upright. For C_{PWV}, the measures just prior to standing and just after standing for 120 min, while supine, did not differ (Fig. 3a). This indicates that the decrease in C_{PWV} while standing for 120 min (Fig. 4a) did not persist when the participant moved to supine position. It is unclear why this postural change had an effect, especially since changes in L_{PWV} observed while standing (Fig. 4c) persisted when the participant returned to the supine position (Fig. 3c). Regardless of mechanism, the change in blood flow from standing to supine had more of an influence on C_{PWV} versus L_{PWV}. This finding has implications for participant positioning when measuring PWV and reinforces our decision to analyze supine and standing measures separately.

The effect of standing was localized to the lower limbs, while there were little-to-no changes in the other arterial branches. This is in agreement with the previous research documenting changes in endothelial function being localized to the lower limbs (popliteal artery) while observing little-to-no changes in the brachial artery (Thosar et al. 2014; Restaino et al. 2015). These changes are unlikely to directly contribute to coronary artery disease, but directly increase the risk for peripheral artery disease (Kulinski

et al. 2015; Padilla and Fadel 2017) which then indirectly increases cardiovascular mortality risk (McDermott 2006). Peripheral artery disease is characterized by atherosclerosis occurring primarily in the conduit arteries of lower limbs (Kroger et al. 1999). Therefore, repeated bouts of prolonged standing (e.g., the current study) or sitting (Restaino et al. 2015) may contribute to vasculopathy specific to the lower limb which increases the risk of peripheral artery disease.

It has been long established that prolonged inactivity at the workplace clearly has negative health implications (Morris et al. 1953). More scientific investigations comparing programs that promote physical activity or standing are needed to understand if either are effective public health strategies. The adoption of standing desks is now being promoted (Trinity 2017; Lopez-Jimenez 2015) as a healthier alternative to sitting; however, when standing desks are assessed in randomized-controlled trials, they offer very little benefit (Healy et al. 2017) and occupations that require standing are often related to number of health problems (Waters and Dick 2015). There is a possibility that implementing standing workstations may have several unintended consequences that negatively affect the health of the worker. Other possibly effective alternatives include walking breaks or vigorous exercise prior to prolonged sitting. In addition, sit-to-stand desks provide the ability to alternate body position, appear to offer some cardio-metabolic benefits (Graves et al. 2015), and offer some protection from low back pain associated with prolonged standing or standing (Agarwal et al. 2018). More physiological data on the vascular responses to prolonged standing are needed to determine the underlying benefits, and negative side effects, of the use of standing desks in comparison to seated desks.

As with any study, there were a number of limitations regarding our experimental design. First, our study had some broad inclusion criteria for BMI, but our participant pool was rather homogenous as evidenced by an average BMI considered "normal" and (23.2 ± 2.9 kg/m^2) and relatively small range of BMIs (19–29 kg/m^2). Second, our study did not consider participants' history of physical activity or exercise habits, and although it is not known to be a moderating factor when investigating PWV during prolonging standing or sitting, future studies may consider this. Third, the current study focused on responses in arterial stiffness to standing (STAND) and standing with walking breaks (WALK). While it is tempting to make conjectures regarding occupational health, we did not include a trial to compare sitting to standing in this study, so it is not possible to make direct statements regarding the usefulness of these two interventions in comparison to sitting. Fourth, the previous studies have documented that lower limb edema may influence vascular function following prolonged sitting (Morishima et al. 2016). Given the primary purpose of this study was to examine PWV, we did not measure lower leg edema.

In conclusion, we demonstrated that arterial stiffness in the lower limb increases after 2 h of standing. These increases in L_{PWV} were not significantly attenuated by having 5-min walking breaks every 25 min during standing. Furthermore, the effects of standing on arterial stiffness appear to be largely isolated to the legs with relatively no changes observed in C_{PWV} or U_{PWV}. Therefore, there may be negative changes in vascular function that occur during periods of prolonged standing that are not eliminated with bouts of walking.

Author contributions MG and KG conceived and designed the research study and acquired funding. BD and MP recruited and screened participants. MP, AC, BH, MRC, BD, and MP conducted the experiments. BH analyzed the ultrasound images for pulse wave velocity analysis. AC performed all the statistical analyses. AC, MRC, BH, MG, and KG wrote the manuscript. All authors read and approved the manuscript.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to report.

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