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Exercise Increases Arterial Stiffness Independent of Blood Pressure in Older Veterans

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Abstract

Background: Exercise induced changes in arterial function could contribute to a hypertensive response to exercise in older individuals. We performed the present analysis to define the acute arterial stiffness response to exercise in ambulatory older adults.

Methods: 39 Veterans (>60 years old), without known cardiovascular disease, participated in this study, including 19 Veterans who were hypertensive (70.8±6.8 years, 53% female) and 20 Veterans who were normotensive (72.0±9.3 years, 40% female). Arterial stiffness parameters were measured locally with carotid artery ultrasound and regionally with carotid-femoral pulse wave velocity (cfPWV) before and during the 10 minutes after participants performed a Balke maximal exercise treadmill stress test.

Results: The arterial stiffness response to exercise was similar for control and hypertensive participants. At 6-minutes post-exercise, cfPWV was significantly increased (Δ 1.5±1.9 m/s, p=0.004) despite mean blood pressure (BP) having returned to its baseline value (Δ 1±8 mmHg, p=0.79). Arterial mechanics modeling also showed BP-independent increases in arterial stiffness with exercise (p<0.05). Post-exercise cfPWV was correlated with post-exercise systolic BP (r=0.50, p=0.004) while baseline cfPWV (r=0.13, p=1.00), and post-exercise total peripheral resistance (r=−0.18, p=1.00) were not.

Conclusion: In older Veterans, exercise increases arterial stiffness independently of BP and the arterial stiffness increase with exercise is associated with increased post-exercise systolic BP. BP-independent increases in arterial stiffness with exercise could contribute to a hypertensive response to exercise in older adults.

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Introduction

Arterial stiffness increases with both age and high blood pressure[1] which is clinically important, as population studies show resting measures of arterial stiffness are associated with incident hypertension, cardiovascular disease (CVD), and mortality[2–4]. However, resting arterial stiffness measures alone are likely insufficient to fully understand how arterial stiffness impacts the development and progression of hypertension and cardiovascular disease with aging. Excessively high blood pressure during exercise, or a hypertensive response to exercise (HRE), is commonly seen in clinical practice[5]. Though the prognostic implications of HRE have been debated, the acute changes in arterial stiffness as a result of physical activity are likely important[6,7]. HRE can occur even in individuals with normal resting blood pressure (BP)[8] and is associated with age[9], traditional CVD risk factors[9], incident hypertension[10–12], left ventricular hypertrophy[13], and CVD events and mortality[8]. Higher arterial stiffness during exercise may be an important mechanism contributing to HRE in older adults.

Past meta-analyses have shown that exercise acutely increases central arterial stiffness in the initial post-exercise recovery period[14]. Arterial stiffness is strongly dependent on the acute distending effect of BP although limited human data shows that central arterial stiffness can be modified independent of the change in BP[15,16]. It is unclear whether acute exercise increases arterial stiffness through BP-independent in addition to BP-dependent mechanisms. As a preliminary step towards understanding how exercise induced changes in arterial stiffness contribute to the exercise blood pressure response in older individuals, we performed the present study with the aim to define the acute arterial stiffness response to exercise in older Veterans.

Methods and Materials

This study was reviewed and approved by the University of Wisconsin Institutional Review Board and was endorsed by the Veterans Affairs (VA) Research and Development Committee. All participants gave written, informed consent to participate in this study.

Study Participants

This analysis included 39 Veteran participants (20 normotensive controls and 19 with a diagnosis of hypertension) from the ongoing Functional Arterial STiffness in Veterans (FAST-Vets) study at the Madison Veterans Affairs Hospital (MVAH). Ambulatory, community-dwelling, hypertensive, older Veterans (>60 years old) were recruited from the MVAH and surrounding clinics. Inclusion criteria were: male and female participants over the age 60 years. Exclusion criteria were: known CVD, secondary hypertension, chronic kidney disease, changing antihypertensive medication in the last month, active cancer (other than untreated, non-metastatic prostate cancer and non-melanoma skin cancer), hypoxemic pulmonary disease, active rheumatologic diseases (i.e., systemic lupus erythematosus, rheumatoid arthritis, etc.), human immunodeficiency virus, or illness with any infectious etiology or fever >38°C or hospitalization for any reason within the prior 4 weeks. Participants who were unable to walk on a treadmill were also excluded. A diagnosis of hypertension was assessed based on medical record review: two or more office systolic BP

measurements >140 mmHg, a mean home BP reading of >135 mmHg for over 7 days, active use of antihypertensive medications, or ICD codes.

Study Protocol

All studies were performed at the University of Wisconsin Atherosclerosis Imaging Research Program (UW AIRP) lab, which is a nationally recognized core ultrasound reading, training, and scanning laboratory. Visits began between 7AM and 11AM and participants withheld morning antihypertensive medications until after the study visit. For eight hours prior to the visit participants were asked to fast and refrain from smoking, caffeine, and sildenafil. On visit day 1 participants rested in a supine position in a temperature-controlled room for 10 minutes and serial baseline oscillometric brachial blood pressure (Cheetah Starling Fluid Management System, Baxter Healthcare, Deerfield, IL, USA), bioimpedance derived cardiac output measurement (Cheetah Starling Fluid Management System, Baxter Healthcare, Deerfield, IL, USA), and radial artery tonometry (Atcor Sphygmacor, Atcor Medical, Sydney, Australia) were performed. Central systolic blood pressure was calculated using a validated and US Food and Drug Administration approved transfer function[17]. Baseline arterial stiffness measurements were performed in duplicate. Participants then completed a maximal exercise treadmill stress test. Immediately post exercise participants returned to a supine position and repeat measurements of arterial stiffness were performed every 1–2 minutes for 10 minutes. An overview is shown in Figure 1. Following visit day 1 participants were fitted with a 24hr ambulatory blood pressure monitor (ABPM) (SpaceLabs Healthcare, Snoqualmie, WA, USA).

Treadmill Exercise Stress Test

Stress testing was conducted by a certified exercise physiologist in the UW AIRP lab. Heart rate was monitored continuously with a twelve channel ECG device (Schiller CS-200 Exercise Stress System, Baar, Switzerland) using a modified Balke protocol[18] to a target heart rate of ≥85% of the maximum age-predicted heart rate (220-age in years). The Balke protocol was used to ensure safety in participants[18–20]. Subjects walked at a comfortable speed determined during a warm-up period and speed was kept constant for the duration of testing. Following a two-minute warm up at 0% grade, the treadmill grade was increased by 2.5% every two minutes until the participant reached volitional exhaustion or indicated that they could not continue. A continuous ECG was recorded, and participants had BP and symptoms recorded every 2–3 minutes until peak exercise was reached. Immediately post exercise participants were returned to an ultrasound examination table adjacent to the treadmill. For safety purposes, exercise stress testing was not performed if a participant presented with a resting heart rate (HR) > 120 beats per minute (BPM), HR < 40 BPM, systolic blood pressure (BP) > 180 mmHg, or diastolic BP > 100 mmHg. HRE was defined as a peak brachial SBP > 210 mmHg.

Arterial Stiffness Measurements

Carotid-to-femoral pulse wave velocity (cfPWV) was measured using an AtCor SphymoCor Px tonometry system (Atcor Medical, Sydney, Australia), which uses a Millar micromanometer (Millar, SPT-301B, Houston, TX, USA). Simultaneous vascular ultrasound was performed with a Philips CX-50 (Philips Ultrasound, Bothell, WA) ultrasound system

with a 14L5 transducer by trained and registered sonographers from the UW AIRP lab. Longitudinal views of the distal 1cm of the right common carotid artery (CCA) were obtained with the imaging depth set at 4 cm, placing the artery between 2–3 cm deep on the screen, adjusting the focus and gain preferably stacking the jugular vein over the CCA to improve near and far wall resolution. B-mode ultrasound 5 beat DICOM clips were analyzed using Medical Imaging Applications Tools Carotid Analyzer (MIA Inc, Coralville, IA) software to measure artery lumen diameters over the cardiac cycles.

All baseline arterial stiffness measurements were performed in duplicate and averaged. The post-exercise stiffness measures repeated every 1–2 minutes for a 10 minute recovery period. Post-exercise measurements were grouped into 2-minute time periods. If multiple measurements were performed within a 2-minute time-period these values were averaged.

Arterial Stiffness Calculation and Modeling

Peterson's Elastic Modulus (PEM) of the carotid artery was calculated[21]:

$$PEM = \frac{\Delta p D d^2}{\left(Ds^2 - Dd^2\right)} \quad \#(1)$$

where Ds represents the internal arterial diameter at peak systole, Dd represents the internal diameter at end-diastole, and Δp represents the brachial blood pressure difference between the systolic and diastolic measurements (pulse pressure).

To examine the effect of changes in blood pressure with exercise, a participant-specific exponential curve was used to describe the blood pressure dependence of arterial mechanics[22–25]. The mathematical equations are included as a supplement. Using the non-linear curves, two models of changes in carotid artery stiffness with exercise were considered (Figure 2). In model 1 the pre-exercise pressure-diameter curve was kept constant, and the post-exercise BP values were used to calculate arterial stiffness. In model 2 the pre-exercise BP was kept constant, and the post-exercise pressure-diameter curves were used to calculate arterial stiffness. Model 1 represents the BP-dependent effects of exercise on arterial stiffness and model 2 represents the BP-independent effects of exercise on arterial stiffness. The blood pressure dependence of cfPWV was similarly adjusted using exponential relationships. Guideline statements recommend adjusting cfPWV to MAP[26] but because the waveform features used to calculate cfPWV occur at DBP it may be more appropriate to adjust cfPWV to DBP. We adjusted to both MAP and DBP in separate analyses.

Statistical Analysis

Continuous variables are presented as mean and standard deviation. Categorical variables are presented as number and percentage. Participant characteristics were compared between control and hypertensive groups with two-sided t-tests and Chi-squared tests. The arterial stiffness response to exercise was analyzed with a repeated-measures linear model with time after exercise as a within-subjects factor. For the primary analysis, hypertension status was included as a between-subjects factor. For secondary analysis, repeated measures analysis

was performed with sex and age as between-subjects factors. Associations between cfPWV and total peripheral resistance (TPR) with peak post-exercise SBP were analyzed with Pearson correlation coefficients. A Benjamini-Hochberg procedure was applied to p-values from Pearson correlations to control for multiple comparisons. For all statistical tests $p<0.05$ was considered statistically significant.

Results

Participant Characteristics

Participant characteristics are shown in Table 1. Control and hypertensive Veterans participating in this study were similar in age (72.0±9.3 vs 70.8±6.8 year, p=0.67), sex (40% female vs 52.6% female, p=0.43), and smoking status. 84.2% of hypertensive participants were using antihypertensive medications and had a self-reported an average of 15.1±14.6 years since hypertension diagnosis (median 10 years; range 2–60 years). From 24-hour ambulatory blood pressure monitoring (ABPM), both SBP and DBP were not significantly different between hypertensive and control participants. 53% of control and 46.6% of hypertensive participants had well controlled 24-hour ABP (<125/75) according to 2017 AHA/ACC guidelines[27].

Hemodynamic Response to Exercise

For all participants, the treadmill stress test was stopped due to fatigue. During the treadmill stress test, control participants achieved 7.7±2.7 METS and hypertensive participants achieved 7.3±2.4 METS. Exercise duration was 10:14 ± 3:27 (range 4:00 – 16:00) minutes for control participants and 11:43 ± 3:02 (range 8:00 – 19:08) minutes for hypertensive participants. The peak brachial SBP and HR during exercise were similar for control and hypertensive participants (185±19 vs 187±18 mmHg, 133±18 vs 137±16 BPM, respectively). A similar percentage of control and hypertensive participants had a peak exercise SBP > 210mmHg (30% vs 26.3%, p=0.80). Brachial BP and HR responses to exercise are shown in Figure 3. As expected, exercise produced a significant increase on early post-exercise supine SBP, MAP and DBP. At 10 minutes into recovery, SBP and MAP were decreased compared to baseline (p=0.014 and p=0.028). Hypertensive participants had significantly elevated MAP (p=0.023) and DBP (p=0.015) throughout the monitoring period, but the group-time interaction was not significant for SBP, MAP, or DBP (p=0.68, 0.86, and 0.98). Exercise increased HR for the entire 10-minute monitoring period post-exercise. Hypertensive participants had significantly elevated HR (p=0.002), but the group-time interaction was not statistically significant for HR (p=0.80). TPR decreased with post-exercise for the entire 10-minute recovery period. Hypertensive participants had significantly decreased TPR (p=0.004), but the group-time interaction was not significant (p=0.99). Exercise induced changes in cardiac output (CO) and stroke volume (SV) are shown in supplemental figure S1. CO was increased during the recovery from exercise but SV was not different from baseline.

Arterial Stiffness Response to Exercise

Arterial stiffness responses to exercise are shown in Figure 3. Exercise had a statistically significant effect on both cfPWV and carotid PEM in both groups. cfPWV was increased

at 2-, 4-, and 6-minutes post exercise compared to baseline (8.9±2.2 vs 13.3±3.5, 11.6±3.2, and 10.4±2.6 m/s, p<0.01). Carotid PEM was increased at 2- and 4-minutes post exercise compared to baseline (47.5±22.4 vs 79.7±31.7 [p<0.001], and 69.5±46.3 [p=0.012] kPa). Hypertensive participants had greater cfPWV and carotid PEM (p<0.001 and p=0.001). No significant group-time interactions were observed for arterial stiffness measures. Exercise did not cause significant changes in carotid artery diameters post-exercise. Hypertensive participants had greater carotid artery diameters (p<0.01). Additional repeated measures analysis of both cfPWV and carotid PEM found that male participants had increased arterial stiffness compared to female participants and increasing age was associated with increased arterial stiffness (Supplement Figure S2 and S3). The sex-time and age-time interactions were not statistically significant.

Due to MAP decreasing throughout the recovery period from exercise, changes in arterial stiffness with exercise are plotted against changes in MAP in Figure 4. At 6 minutes post-exercise, cfPWV was significantly increased (Δ 1.5±1.9 m/s, p=0.004) despite MAP having returned to its baseline value (Δ 1±8 mmHg, p=0.79). At 10-minutes post-exercise MAP had dipped below its baseline value (Δ −4±8 mmHg, p=0.028), but cfPWV and carotid PEM were similar to their baseline values (Δ 0.6±1.6 m/s, p=0.25 and Δ 2.7±18.3 kPa, p=0.81).

Associations with Blood Pressure Response to Exercise

Correlations of cfPWV with the peak post-exercise SBP are shown in Figure 5 and additional correlations are presented in the supplemental material (Figure S3). Baseline SBP, baseline TPR, and baseline cfPWV were not significantly associated with the maximum post-exercise SBP (r=0.18, 0.03, and 0.13, p=1.0, 1.0, and 1.0). Post-exercise cfPWV and the pre-post exercise change in cfPWV were moderately associated with the maximum post-exercise SBP (r=0.50 and r=0.52, p=0.004 and p=0.002). The slope of the association between baseline cfPWV (1.43 95% CI [−2.21 – 5.07] mmHg/m/s) with post-exercise SBP was not statistically different compared to post-exercise cfPWV (3.51 95% CI [1.48 – 5.54] mmHg/m/s, p=0.16 vs baseline) or the pre-post exercise change in cfPWV (4.49 95% CI [2.00 – 6.99] mmHg/m/s, p=0.068 vs baseline). Post-exercise TPR and the pre-post exercise change in TPR were not significantly associated with the maximum post-exercise SBP (r=−0.18 and −0.21, p=1.0 and 1.0). The correlation of post-exercise cfPWV with post-exercise SBP was significantly greater than the correlation of post-exercise TPR with SBP (p=0.001). Correlations of the pre-post exercise change in DBP-independent cfPWV were significantly associated with post-exercise SBP (Supplemental Figure S4).

Arterial Mechanics Modeling

Arterial mechanics modeling was performed to analyze the BP-dependent and BP-independent contributions to increased arterial stiffness after exercise (Figure 6). Because the hemodynamic and arterial stiffness responses to exercise were similar for both groups, control and hypertensive participants were analyzed together. For cfPWV, BP-independent increases in arterial stiffness (Model 2) accounted for the majority of the post-exercise changes. For example, at 2-minutes post exercise the BP-independent increase in cfPWV was Δ 3.0±2.8 m/s (p<0.001) while the BP-dependent increase in cfPWV was only Δ

1.3±0.8 m/s (p=0.062). For carotid PEM at 2-minutes the BP-dependent and BP-independent effects on increasing stiffness were similar (Δ 15.0±8.4 [p=0.019] and 12.4±22.4 kPa [p=0.005] respectively). However, at 4-minutes post-exercise the BP-independent increase in carotid PEM was Δ 13.8±31.1 kPa (p=0.047) while the BP-dependent increase in carotid PEM was only Δ 4.9±7.3 kPa (p=0.34). Modeling of cfPWV was insensitive to using MAP or DBP (Supplemental Figure S5). Modeling of change in carotid diameters found no statistically significant changes to either BP-dependent or BP-independent effects (Supplemental Figure S6).

Discussion

This study assessed the acute effects of exercise on central arterial stiffness in older Veterans. The major novel finding was that exercise increased arterial stiffness beyond the effect of increased BP. We did not tackle this problem with traditional statistical models because arterial stiffness depends on BP non-linearly. Instead, we utilized direct measurements at a post-exercise time-point when BP had returned to baseline and non-linear models of arterial mechanics. Additionally, post-exercise arterial stiffness was also correlated with maximum post-exercise SBP while baseline arterial stiffness was not. BP-independent increases in arterial stiffness during exercise could contribute to excessively high exercising blood pressures and hypertensive response to exercise (HRE) in older adults. The acute change in arterial stiffness with exercise is a potential mechanistic explanation for the variability in HRE across the age spectrum, regardless of baseline hypertensive status[8,28,29]. The prognostic significance of increased arterial stiffness in response to exercise in the general population and older adults is unclear. Increased arterial stiffness during exercise could contribute to HRE, and there is evidence that increased arterial stiffness in response to exercise has negative consequences for patients with heart failure with preserved ejection fraction (HFpEF)[30,31]. Increased arterial stiffness and wave reflections in response to exercise in HFpEF patients are associated with increased LV filling pressure[32]. It is plausible that increased arterial stiffness in response to exercise in healthy individuals could increase LV afterload and increase the risk of developing HFpEF. Future research should identify the mechanisms through which acute exercise increases arterial stiffness. This may lead to novel therapeutic approaches to decrease the hypertensive response to exercise and development of cardiac dysfunction in older adults. Arterial stiffness is an important component of the blood pressure response to exercise due to the effects of arterial stiffness on pressure pulse propagation, wave reflection, and impedance[33–35]. Our results showed that post-exercise systolic BP was correlated with post-exercise arterial stiffness, but not pre-exercise arterial stiffness. Post-exercise TPR was not associated with SBP, indicating that HRE in older adults is primarily a problem of high arterial stiffness, not resistance. These findings highlight that the arterial stiffness response to exercise contributes to HRE more so than the resting arterial stiffness. Analysis of adults from the Framingham Offspring cohort found that resting cfPWV was significantly associated with SBP during the second stage of a Bruce protocol treadmill stress test[9] however, these data were acquired in a younger cohort and BP was measured during moderate exercise rather than maximal exercise.

It is unlikely that the association of post-exercise SBP and arterial stiffness was due to higher BP increasing stiffness. Our results showed for the first time that exercise increases arterial stiffness independent of the effect of BP. During the recovery phase, when MAP returns to baseline, cfPWV remained significantly elevated. Additionally, when BP dipped below baseline at 10-minutes, both cfPWV and carotid PEM were comparable to their baseline values. Past meta-analyses of the effects of acute exercise on central arterial stiffness have been performed [14,36,37], although no prior studies have quantified the BP-dependent versus BP-independent effects of exercise on arterial stiffness. In this study we were able to take advantage of the rapid changes in BP during recovery from exercise by performing arterial stiffness measurements at time points when BP was greater than, equal to, and less than baseline BP. By doing this we showed that arterial stiffness is increased independent of BP during the recovery from exercise.

Our arterial mechanics modeling analysis further supports that BP-independent effects are a major contributor to increased arterial stiffness following exercise. Similar arterial mechanics modeling analysis also suggest that exercise increases central arterial stiffness independent of BP in adults with type 2 diabetes mellitus[38]. In this same cohort of older Veterans as the present study, we have recently shown that nitroglycerin-induced vasodilation increases central arterial stiffness despite a decrease in BP[39]. Nitroglycerin-induced vasodilation and lower limb venous occlusion also cause changes in arterial stiffness independent of the change in BP in middle-aged hypertensive individuals[16,40]. This study shows that exercise is another physiological stressor that can cause BP-independent changes in arterial stiffness and that exercise-induced changes in arterial stiffness are related to the BP response to exercise.

The mechanisms by which exercise increases arterial stiffness independent of BP are unclear. Increased heart rate could partially contribute to increased arterial stiffness through viscoelastic effects although the effect of viscoelasticity on *in vivo* arterial stiffness is modest[41,42]. Based on prior analysis of heart rate and cfPWV[43], the increase in heart rate observed 6-minutes post exercise (Δ 15.9±8.1 BPM) would only account for approximately 0.2–0.3 m/s of the increase in cfPWV (Δ 1.5±1.9 m/s), although the effect of HR could be greater at higher BP[43]. Exercise induced changes in cfPWV are independent of the change in heart rate in stroke patients[44]. Vasodilation and decreased vascular smooth muscle tone can paradoxically increase arterial stiffness in older individuals[15,39,45] by shifting mechanical load from smooth muscle onto the extracellular matrix[15]. TPR decreased after exercise, indicating peripheral vasodilation, but we did not find a significant change carotid artery diameter after exercise. Arterial mechanics modeling further suggests that the small increase in carotid diameter was primarily due to increased BP distending the carotid artery (Supplemental Figure S5). Myogenic tone increasing vascular smooth muscle contraction at higher BP[46,47] is another plausible mechanism for arterial stiffening post exercise, however this would not explain why arterial stiffness remained elevated when BP had returned to baseline levels. Vascular smooth muscle contraction is admittedly more complicated than can be explained only by actin-myosin cross-bridging and mechanical theories developed for striated muscle[48]. Airway smooth muscle exhibits glass-like transitions where the cytoskeleton rearranges in minutes[49,50] and a similar phenomenon could occur in vascular smooth muscle during exercise. Future research to understand what mechanisms underlie

the arterial stiffness response to exercise will require carefully designed experiments given the complex determinants of arterial mechanics, including: sympathetic nervous system activity[51–54], paracrine signaling between smooth muscle and the endothelium[55,56], and intrinsic myogenic responses[57,58].

Limitations of this study include the relatively small number of subjects and that findings are limited to an older, albeit less studied, patient population. Lipid profiles, renal function, and physical activity were not quantified in this study. In addition, peripheral brachial artery BP was used instead of central carotid artery BP to calculate carotid artery stiffness. This will affect the calculated values of carotid stiffness, but because similar results were found with cfPWV, which does not require measuring BP, we do not expect using carotid BP to calculate stiffness would alter the directionality of the changes. The single exponential models of arterial mechanics used in this study have been validated in resting and ex vivo conditions[22,59,60], but have not been validated during recovery from exercise. Lastly, a washout period for antihypertensive medications prior to the study visit was not used. Even though participants did not take medications the morning of their visit, medications taken the prior day could exert some vasoactive effects and have influenced results.

Conclusion

The primary novel finding of this study was that acute exercise increased arterial stiffness beyond effect of blood pressure in both control and hypertensive older Veterans. Post-exercise arterial stiffness was also correlated with post-exercise blood pressure while baseline arterial stiffness was not. Blood pressure independent increases in arterial stiffness during a treadmill stress test could cause hypertensive response to exercise in older adults. Future research should identify the mechanisms through which acute exercise increases arterial stiffness. This may lead to novel therapeutic approaches to decrease the hypertensive response to exercise in older adults.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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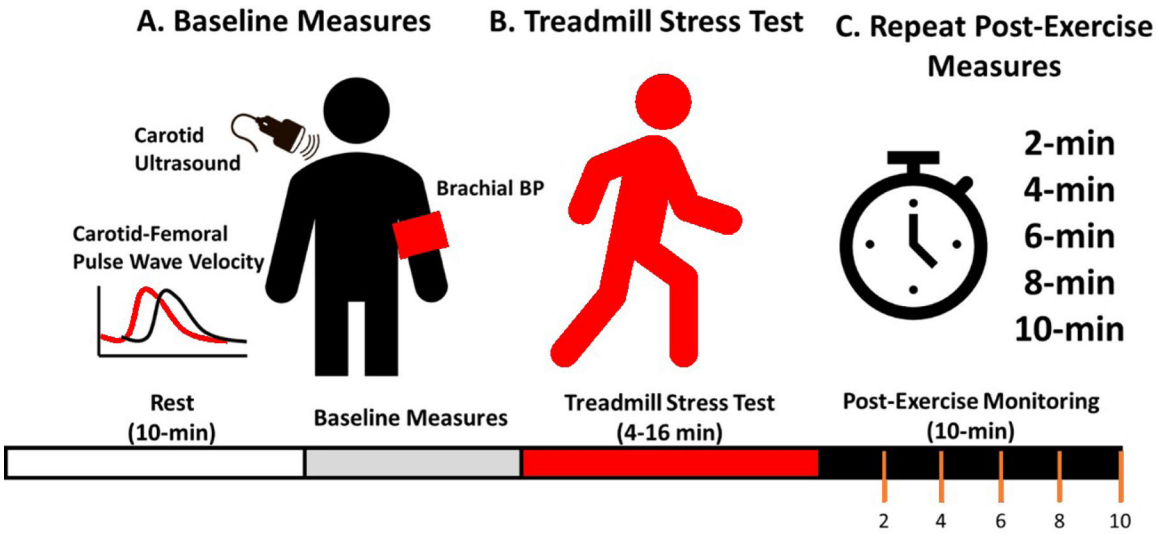

Figure 1:

Diagram of the study visit day 1 timeline. A. First, baseline measurements were performed including carotid ultrasound, brachial blood pressure (BP), and carotid-femoral pulse wave velocity. B. Second, a maximal exercise stress test was performed. C. Finally, immediately post-exercise the participant returned to examination table and measurements were repeated for 10 minutes.

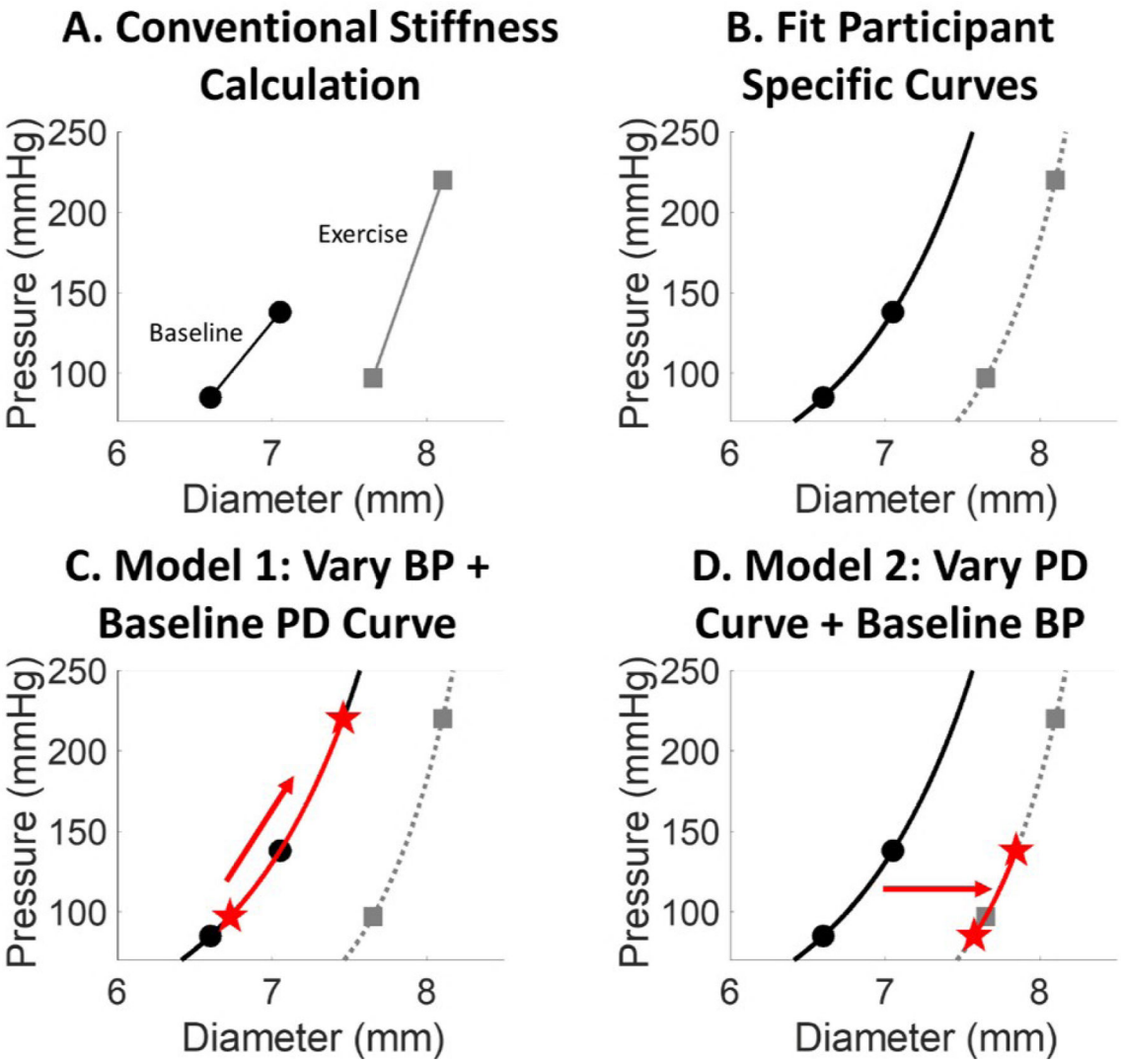

Figure 2:

Graphical representation of the participant specific models used to analyze the arterial stiffness response to exercise. Baseline data are shown as black circles, exercise data are shown as gray squares, and model calculations are shown as red stars. For Model 1, stiffness was calculated with the baseline pressure-diameter (PD) curve and post-exercise blood pressure (BP). For Model 2, stiffness was calculated with the baseline BP curve and post-exercise PD curve. The participant shown in Figure 2 is not representative as they had noticeable carotid artery vasodilation, however these data were chosen to show as the pre- and post-exercise PD curves are clearly separated.

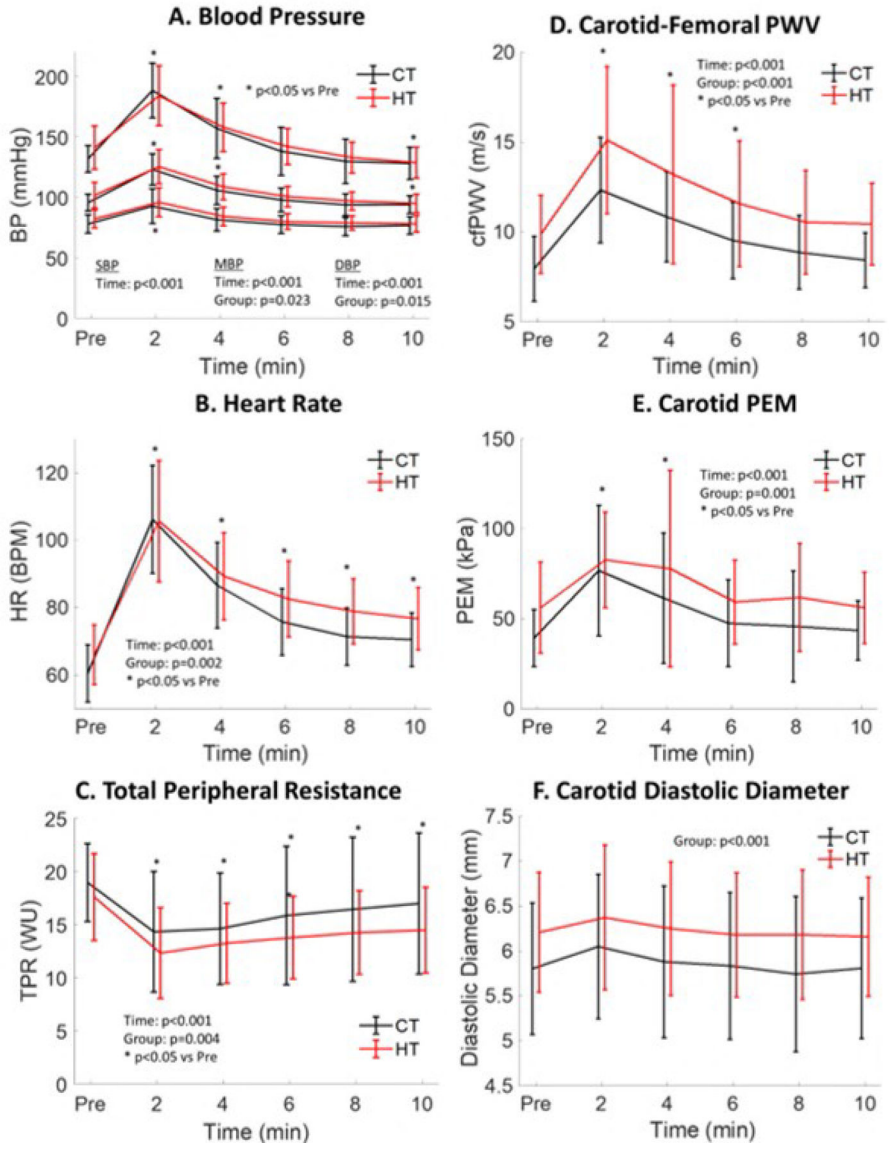

Figure 3:

Hemodynamic and arterial stiffness responses to exercise. Time refers to time after exercise. Exercise A. increased systolic blood pressure (SBP), mean arterial pressure (MAP), and diastolic BP (DBP), B. increased heart rate (HR), C. decreased total peripheral resistance (TPR), D. increased carotid-femoral PWV (cfPWV), E. increased carotid Peterson's elastic modulus (PEM), and F. did not change carotid artery diameter. Abbreviations: CT – Control, HT – hypertensive

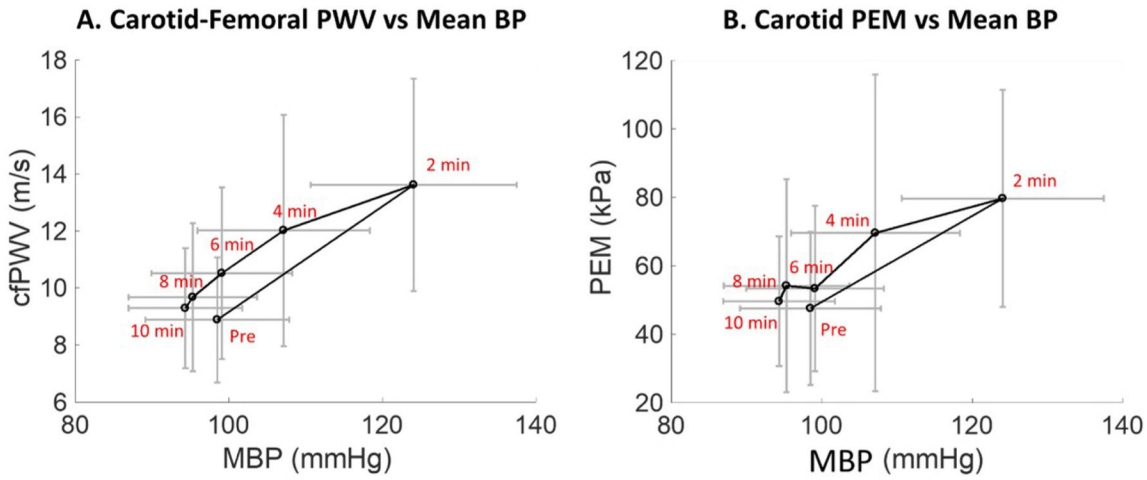

Figure 4:

Arterial stiffness response to exercise for all participants plotted against change in mean blood pressure (MAP). Abbreviations: cfPWV – carotid-femoral pulse wave velocity, PEM – Peterson's elastic modulus.

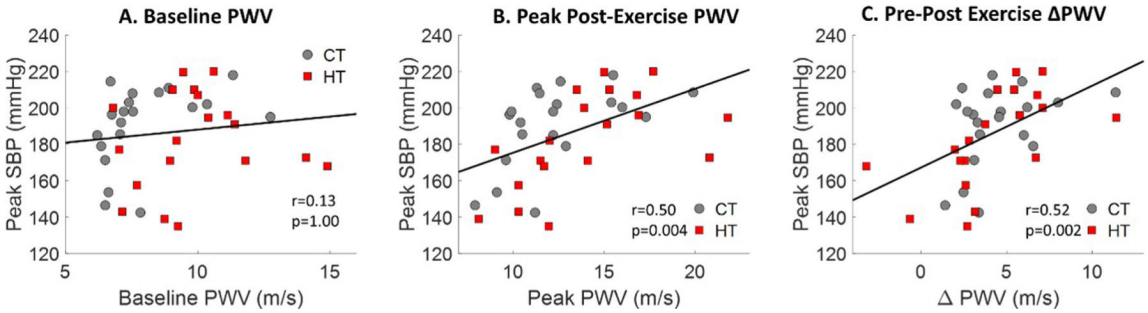

Figure 5:

Correlations of A. baseline, B. peak post-exercise, and C. pre-post exercise change in carotid-femoral pulse wave velocity (cfPWV) with the peak post-exercise systolic blood pressure (SBP) Abbreviations: CT – Control, HT – hypertensive, r – Pearson correlation coefficient

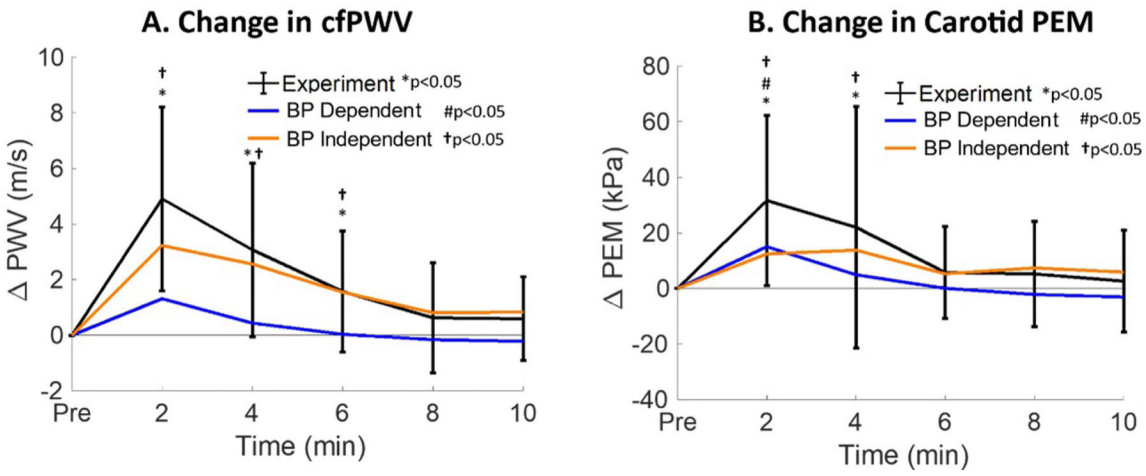

Figure 6:

Measured changes in arterial stiffness (black line) for both groups and arterial mechanics modeling of changes in arterial stiffness due to blood pressure dependent effects (blue line) and blood pressure independent effects (orange line) for A. carotid-femoral pulse wave velocity (cfPWV) and B. carotid Peterson's elastic modulus (PEM). Results show significant BP-independent increases in arterial stiffness following exercise. For clarity, error bars are only shown for the directly measured stiffness values. Changes in cfPWV were modeled based on mean BP. Results for diastolic BP were similar and are presented in the supplemental results.

Table 1:

Participant Characteristics

	Control (n=20)	Hypertensive (n=19)	p-value
Age (years)	72.0±9.3	70.8±6.8	0.67
BMI (kg/m^2)	27.6±4.5	27.3±6.6	0.90
Sex			0.43
Female (n, %)	8 (40%)	10 (52.6%)	
Race/Ethnicity			0.97
White (n, %)	19 (95%)	18 (94.7%)	
Black (n, %)	1 (5%)	1 (5%)	
Diabetes Mellitus (n, %)	2 (10%)	6 (31.6%)	0.10
Smoking Status			0.47
Current (n, %)	2 (10%)	3 (15.8%)	
Former (n, %)	9 (45%)	11 (57.9%)	
Never (n, %)	9 (45%)	5 (26.3%)	
Pack Years	14.7±19.2	16.8±19.2	0.74
Supine Blood Pressure			
SBP (mmHg)	132±11	141±18	0.06
DBP (mmHg)	78±8	82±7	0.09
MAP (mmHg)	96±7	102±11	0.04
cSBP (mmHg)	123±10	136±16	0.006
24hr ABPM	N=19	N=15	
24hr SBP (mmHg)	121±9	126±11	0.10
24hr DBP (mmHg)	69±6	73±7	0.15
24hr BP < 125/75 (n, %)	10 (53%)	7 (46.6%)	0.72
Antihypertensive Medications (n,%)			--
0		3 (15.8%)	
1	--	10 (52.6%)	
2		6 (31.6%)	
Antihypertensive Medication Classes (n,%)			--
ACE Inhibitor		2 (10.5%)	
Angiotensin Receptor Blocker		7 (36.8%)	
Calcium Channel Blocker		5 (26.3%)	
Beta Blocker		3 (15.8%)	
Thiazide Diuretic		3 (15.8%)	
Unknown		2 (10.5%)	
Self-Reported Years Since HT Diagnosis	--	15.1±14.6	--

Abbreviations: BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, MAP – mean arterial pressure, cSBP – central systolic blood pressure, ABPM – ambulatory blood pressure monitor, HT - Hypertension