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High-Intensity Exercise Enhances Conduit Artery Vascular Function in Older Adults

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Abstract

Purpose—Modulation of vascular function follows an exercise intensity-dependent pattern in young adults. This study aimed to investigate the potential intensity-dependent effects of an acute bout of exercise on conduit and resistance artery function in healthy older adults.

Methods—Eleven healthy older adults (5 males/6 females, 66±1 years) completed 30 minutes of recumbent cycling at 50–55% (low-intensity) and 75–80% (high-intensity) of their age-predicted maximal heart rate on two separate study visits. Doppler ultrasound measures of brachial artery flow-mediated dilation (FMD) and reactive hyperemia (RH) were taken at baseline, ten minutes post-exercise, and one hour post-exercise. Additionally, cardiovascular hemodynamics and brachial shear rate were measured every five minutes during exercise.

Results—Brachial artery FMD was enhanced ten minutes after high-intensity (4.8±0.2 to 9.1±0.3%, $P<0.01$), but not low-intensity (4.7±0.2 to 6.2±0.3%, $P=0.54$) exercise. Peak and total (area under the curve) blood flow during RH (measures of resistance artery function) were enhanced ten minutes post-exercise for both intensities (peak low-intensity 372±31 to 444±37, peak high-intensity 391±30 to 455±28 ml/min; total low-intensity 142±16 to 205±20, total high-intensity 158±14 to 240±25 ml, main effect of time for both $P<0.05$). However, the magnitude of change in peak and total blood flow were not different between exercise intensities (interaction effect; $P=0.56$ and $P=0.97$, respectively). Independent of exercise intensity, FMD returned to baseline one-hour after exercise (high 5.9±0.3; low 5.1±0.1%, both $P>0.05$).

Conclusion—Our data indicate that high-intensity exercise acutely enhances conduit artery function in healthy older adults. Additionally, an acute bout of exercise enhances resistance artery function independent of intensity.

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Keywords

Exercise intensity; age; vascular function; flow-mediated dilation; reactive hyperemia

Introduction

Vascular endothelial dysfunction is characterized by impairment in endothelium-dependent vasodilation in conduit and resistance arteries serving as a predictor of pathologic cardiovascular events (1, 2). Flow-mediated dilation (FMD) is a noninvasive assessment of endothelium-dependent conduit artery function. Ischemia-induced reactive hyperemia (RH) can be obtained during the FMD measurement and reflects down-stream microvascular function (3). During dynamic exercise conduit artery shear stress is increased in working and non-working limbs, subsequently altering vasodilator function (4). Previous studies reported that brachial FMD immediately following acute, dynamic leg exercise is depressed (5–7), unchanged (6–8), or increased (6) in young subjects. These conflicting results could be derived from the intensity-dependent response in FMD and RH in young subjects (5, 9, 10). Additionally, young subjects exhibit a biphasic pattern in FMD following acute exercise characterized by an immediate reduction in FMD which normalizes 1–24 hours after exercise cessation (11–13), which emphasizes the importance of multiple post-exercise FMD assessments (4). Unlike young subjects, older adults appear to have an increased FMD response to acute exercise (14–16). Although exercise intensity and age are clearly important factors to consider when assessing post-exercise conduit artery function, only one study has examined the acute effect of exercise intensity on post-exercise FMD in older adults (16). However, the study by Bailey et al. (16) included subjects with cardiovascular risk factors (e.g., hypertension, obesity), as well as current medication use. Additionally, previous studies investigating post-exercise FMD responses (14, 15) in healthy older adults have made measurements at a single time point leaving the time course of change in vasodilator function unknown. To date, no studies in older adults have assessed microvascular function via RH following an acute bout of exercise. Therefore, this study sought to examine the effect of exercise intensity on the pattern of change in post-exercise FMD and RH in older adults. It is speculated that the post-exercise FMD enhancement in older adults is induced by increases in shear stress during exercise (14). We hypothesized that greater increases in shear stress during high-intensity exercise will induce more pronounced increases in brachial FMD and RH after acute cycling in older adults, and these measures of conduit and resistance artery function will remain elevated above baseline values for one-hour after exercise.

Method

Subjects

Eleven sedentary to recreationally active older adults (5 males/6 females, 66 ± 1 years, body mass index; 25.1 ± 0.7 kg/m²) participated in the study. All subjects completed written, informed consent and a health history screening. All subjects were considered healthy, non-obese, normotensive ($< 140/90$ mmHg), nonsmokers, and not taking any vasoactive medications. Subjects who engaged in structured physical exercise programs (greater than

30 minutes in duration more than 3 times per week) were excluded. Experiments were performed in the morning following an 8-hour overnight fast. Subjects were required to abstain from caffeine-containing foods and beverages, vitamin supplements, alcohol, and strenuous exercise for at least 24 hours before each test (15). All study protocols were approved by the Institutional Review Board at the University of Iowa.

Experimental protocol

Initially, subjects rested in a supine position for 20 minutes with the right arm supported in an outstretched position allowing the pre-FMD and pre-RH measurement to be performed. The subjects then moved to the recumbent cycle (PS50, True Fitness, St. Louis, MO) and rested for 15 minutes. Following rest, subjects performed 30 minutes of exercise during which, resistance was titrated to maintain target intensity. Exercise intensity was 50–55% (Low intensity) and 75–80% (High intensity) of age-predicted maximal heart rate (HR_{max}) which was randomized between two study visits. Age-predicted HR_{max} was calculated as $[208 - 0.7 \times \text{age}]$ (17). During exercise, subjects' right arm was supported in an outstretched, perpendicular position and elevated slightly above heart level allowing for shear rate (SR) measurements. Heart rate (HR), blood pressure (BP), and SR were recorded during exercise at five-minute increments. During exercise, HR was continuously monitored using a HR monitor with chest strap (CE0304, True Fitness, St. Louis, MO) and titrated such that target intensity was sustained throughout the 30 minutes of exercise. Immediately following exercise, subjects returned to the supine position where HR, BP, FMD, and RH measurements were repeated within ten minutes post-exercise (5). Following this, the subjects were moved to a seated position. Subjects were returned to a supine position 15 minutes prior to the final FMD measurement (Post 1 hour). The HR, BP, FMD, and RH measurements were repeated one hour after the cessation of exercise. BP and HR were measured via auscultation method and 3-lead electrocardiogram, respectively. Mean arterial pressure (MAP) was calculated as $(\text{Systolic BP} - \text{Diastolic BP})/3 + \text{Diastolic BP}$. Each subject participated in two separate study visits separated by at least 48 hours. All tests were performed at the same time of day within subjects and within one month to minimize variability of the primary outcome variables.

Measurements and analysis

FMD and RH—FMD was measured in accordance with standardized guidelines (18). Briefly, subjects were studied while supine with their right arm extended $<80^\circ$ laterally from the torso. Brachial artery FMD was measured using a high-resolution ultrasound machine with a 12 MHz multi-frequency linear probe machine (Vivid 7, General Electric, Milwaukee, WI). The ultrasound probe was placed on the distal one-third of the right upper arm with the cuff positioned on the right forearm immediately distal to the olecranon. Probe placement was recorded on the skin using a marker to ensure same location across all measurements within each study visit. Ultrasound settings were set to optimize longitudinal B-mode images of the lumen-arterial wall interface. Pulsed Doppler signals were recorded at an insonation angle of 60° with a sample volume encompassing the artery's diameter. After two minutes of baseline measurements, the cuff was inflated to 250 mmHg using a rapid cuff inflator (E-20 rapid cuff inflator, D. E. Hokanson, Bellevue, WA) then deflated after five minutes. During the FMD tests, artery diameter and mean blood velocity (V_{mean}) were

assessed for one minute at baseline, one minute prior to cuff deflation, and for three minutes following deflation. Arterial images and associated velocity waveforms were captured at 30 Hz using a capture box (VGA2USB LR, Epiphan, Palo Alto, CA) and stored in a computer (Optiplex980, DELL, Round Rock, TX).

Brachial diameter and V_{mean} were analyzed using custom-designed edge detecting and wall tracking software (S-13037 ver. 2.0.1, Takei Kiki Kogyo, Japan) (19). Post-deflation peak diameter (D_{peak}) was detected using a previously reported algorithm (20). FMD was calculated as the percent increase in D_{peak} from baseline diameter (D_{base}) using the formula; $[\text{FMD} = (D_{\text{peak}} - D_{\text{base}})/D_{\text{base}} \times 100 (\%)]$. SR was calculated as $4 \times V_{\text{mean}}/\text{diameter}$ and SR area under the curve (SR_{AUC}) was quantified as the area from the time of deflation to the time of D_{peak} , and calculated using trapezoidal rule as: $\sum [1/2 (x_{i+1} - x_i) (y_{i+1} - y_i) + (x_{i+1} - x_i) (y_i - z)]$, where x is time, y is SR and z is baseline SR.

RH was quantified as the difference in blood flow area under the curve (BF_{AUC}) between baseline and 100 seconds post-occlusion. BF_{AUC} was calculated using the same equation as SR_{AUC} . Peak RH was quantified as the peak hyperemic blood flow after cuff-deflation (BF_{peak}). From the synchronized arterial diameter and V_{mean} data, blood flow was calculated as $60 \times V_{\text{mean}} \times \text{cross sectional area}$.

SR during exercise—Measures of brachial SR were recorded at rest and during exercise in five-minute increments via Doppler ultrasound. Arterial diameter and V_{mean} were measured using custom-designed software described above. Mean, antegrade, and retrograde SR were calculated from the synchronized arterial diameter and V_{mean} data. SR at rest was averaged for one minute before exercise (baseline) and over 30 seconds every five minutes during exercise. Oscillatory shear index (OSI) was calculated as $|\text{retrograde SR}|/(|\text{antegrade SR}| + |\text{retrograde SR}|)$.

Statistics

Statistical analyses were performed using SPSS version 24 (IBM, Chicago, IL). The effect of exercise intensity on FMD and cardiovascular parameters, except Corrected-%FMD was evaluated using a two-way, repeated measures analysis of variance. Bonferroni post-hoc analyses were performed when significant F-ratios were detected. Dunnett's test was used to determine differences between baseline data and each time point during exercise. Corrected-%FMD, which accounts for changes in baseline diameter and SR_{AUC} after exercise, was calculated using an analysis of covariance, and multiple comparisons were performed using least significant difference method, as previously described (5, 21). The level of statistical significance was set at $P < 0.05$. All data are reported as mean $\pm$ standard error.

Results

Cardiovascular variables and brachial SR during exercise

All subjects completed both exercise bouts in their target HR ranges with the exception of one male subject. Subsequently, a target of 70–75% HR_{max} was used during this subject's high-intensity bout. Systolic BP and MAP were significantly elevated during high-compared to low-intensity exercise (Table 1). Antegrade and mean SR were also significantly higher

during the high-compared to the low-intensity bout (Figure 1A, C). However, retrograde SR and OSI during exercise did not differ between high- and low-intensity exercise (Interaction effects; $P=0.21$ and $P=0.81$, respectively) (Figure 1B, D).

Hemodynamics prior to each FMD measurement

No differences were observed between pre- and post-exercise measurements in BP for each exercise intensity (Table 2). In contrast, HR remained elevated above baseline ten minutes after high-intensity exercise ($P<0.05$), but not after low-intensity exercise, and returned to baseline one hour post-exercise.

Effect of exercise intensity on brachial FMD

The magnitude of change in absolute and %FMD following exercise were dependent upon exercise intensity (Interaction effects; both $P=0.02$) (Figure 2). Absolute and %FMD were increased ten minutes after high-intensity exercise (both $P<0.01$). There were no changes in absolute or %FMD ten minutes after low-intensity exercise (both $P>0.05$). Consequently, absolute and %FMD were greater in the high-intensity condition ten minutes after exercise compared to low-intensity exercise ($P=0.02$ and $P=0.01$, respectively). FMD corrected for baseline diameter and SR_{AUC} ten minutes after high-intensity exercise were also elevated above baseline (both $P<0.01$) and compared to low-intensity exercise (both $P<0.05$) (Table 2). One-hour after exercise cessation FMD was similar compared to baseline and between conditions (exercise intensities).

RH

Figure 3 illustrates the RH response following cuff deflation at each time point and exercise intensity. Both low- and high-intensity exercise resulted in an increased BF_{peak} and BF_{AUC} at the ten minute after exercise time point (Table 2, main effect of time; $P<0.01$ for both). However, the increase in BF_{peak} and BF_{AUC} was independent of exercise intensity (Table 2, interaction effect; $P=0.97$ and $P=0.56$, respectively).

Discussion

In this study, we explored the effect of acute exercise on FMD and RH in sedentary to recreationally active older adults and whether the responses were dependent on exercise intensity. Our principal finding was high-intensity exercise elicited significant increases in brachial artery FMD, whereas no change was observed following low-intensity exercise. We also found that FMD after high-intensity exercise exhibited a biphasic pattern in older adults; that is FMD increased immediately after exercise and returned to baseline within one hour post-exercise. The change in FMD induced by high-intensity exercise remained after post-exercise changes in SR_{AUC} and baseline diameter were accounted for. Lastly, we found microvascular function, as assessed by RH, was acutely improved after both low- and high-intensity exercise in older adults. Taken together, our data suggest that exercise intensity significantly affects conduit artery function following an acute bout of exercise; however, resistance artery function appears to be responsive to acute exercise independent of intensity in older adults.

In the current study, we demonstrated that brachial artery FMD following acute cycling exercise, showed an intensity-dependent response in healthy, older individuals (Figure 2). This significant increase in FMD remained after accounting for SR_{AUC} and baseline diameter (Table 2). These results suggest that exercise intensity has a direct influence on brachial artery FMD in older adults, with high-intensity exercise appearing to be most beneficial. To our knowledge, there have only been two previous studies which measured post-exercise FMD in healthy older adults (14, 15), and both studies observed an enhancement in FMD following acute exercise. Thijssen et al. reported that femoral FMD was increased immediately after maximal cycling exercise in older adults (15). Harvey et al. observed an increase in brachial FMD one hour after moderate-intensity treadmill exercise in middle-aged women (14). Additionally, Bailey et al. reported increased brachial FMD 60 minutes after high-intensity cycling exercise in males with higher cardiorespiratory fitness, some of which had hypertension and/or were obese (16). In our study, post-exercise FMD was increased following high-intensity exercise, but not low-intensity exercise in older adults. These current and previous results suggest that moderate- to high-intensity exercise is needed to observe a significant increase in FMD in older adults.

Interestingly, previous findings illustrate that high-intensity exercise has a deleterious effect on vascular function in young subjects (5, 6, 22, 23); however, our results indicate this paradigm does not persist with aging. Previous studies reported that the pattern of intensity-dependent FMD response in young and older adults could be associated with their physical activity level (12, 16). Our current results indicate that age is also a key factor to understanding the effects of exercise intensity on conduit artery vasodilator function. There are several contributing factors that possibly explain the discrepant findings in post-exercise FMD between young and older adults, most notably, differences in sympathetic tone. Recently, Atkinson et al. (24) demonstrated that α_1 -adrenoreceptor blockade abolished the immediate reduction in FMD after high-intensity cycling in young subjects. Their data suggest that exercise-induced increases in muscle sympathetic nerve activity (MSNA) contribute to the acute, post-exercise decrease in FMD in young subjects (24). Aging is accompanied by an increase in resting sympathetic outflow (25), potentially causing the impaired baseline FMD in older adults (15, 26). Floras et al. observed that subjects with higher resting MSNA showed greater reduction in blood pressure and MSNA after acute exercise with these findings being partially due to transient suppression of augmented baseline sympathetic tone (27). Moreover, studies have speculated that increased post-exercise FMD in middle-aged women could be attributed to the suppression of MSNA following exercise (28, 29). From these works, the observed increases in FMD after high-intensity exercise in this study may be attributed to a transient suppression of augmented basal sympathetic flow in older adults. Additionally, the decreases in FMD following acute high-intensity exercise in young adults may be related to increased production of reactive oxygen species and/or endothelin-1 (6, 30). In the present study, we did not measure oxidative stress or vasoactive substances in older adults; therefore, we cannot determine how high-intensity exercise affects these variables with aging.

While a reduction in MSNA following exercise is a potential explanation for improved FMD in older adults, augmented shear stress during the exercise bout (Figure 1) most likely contributed to the improved conduit artery function observed in the current study (Figures

2). Shear stress is a known stimulus for endothelial-derived NO production (31). More specifically, antegrade shear is the primary stimulus for NO production, whereas retrograde and turbulent shear may compromise NO bioactivity (32). Along these lines, augmented retrograde and oscillatory SR in the brachial artery during leg exercise has been shown to attenuate post-exercise brachial FMD (33). Although we did not assess endothelium-independent vasodilator function in the current study, previous evidence suggests smooth muscle function is unaffected by acute exercise in older women (28). From this, the change in FMD following exercise in older adults likely reflects endothelial-dependent vasodilation. While NO bioavailability is decreased with aging, it can be increased by acute exercise (12) via shear stress-mediated mechanisms. The examinations of changes in shear patterns during exercise on post-exercise FMD in older adults have not been previously reported (14–16). In the current study, we found intensity-dependent increases in antegrade and mean SR during exercise (Figure 1A, C) whereas the pattern of change in retrograde SR and OSI were not influenced by exercise intensity (Figure 1B, D). From this, we conclude that increases in antegrade and mean SR likely contributed to greater improvements in conduit artery vasodilator function following high-compared to low-intensity exercise in older adults. Most studies have evaluated the effects of acute exercise by assessing endothelial function immediately after exercise (5, 15). However, there is a possibility that the beneficial effects of a single bout of exercise on FMD may not be apparent for several hours (11). We examined the time course of change in FMD following an acute bout of exercise in healthy older adults. Evidence supports a biphasic response in FMD after an acute bout of exercise in young subjects with normalization occurring within one hour post-exercise (4, 6). Interestingly, we found a parabolic response in FMD following high-intensity exercise in older adults, whereby FMD appears to increase immediately following exercise and normalizing after one hour post-exercise (Figures 2 and 3). Our results indicate that high-intensity exercise improves conduit artery vasodilator function; however this improvement dissipates within one hour after exercise in healthy older adults. In contrast, it is well known that long-term exercise training improves conduit artery vascular function in older adults (34). Future studies are needed to elucidate the time course of vascular adaption in conduit arteries of older adults.

Acute aerobic exercise also has the potential to promote endothelium-dependent microvascular vasodilation, which is a surrogate marker of cardiovascular health (1, 35). We found that a bout of acute exercise has beneficial effects on RH in older adults; however, these effects were independent of exercise intensity. Our data show that although high-intensity exercise is needed to elicit a change in conduit artery function, microvascular function is increased following both low- and high-intensity exercise in older adults. These results support previous findings that described a disassociation between FMD and reactive hyperemia (36). The attenuation of RH following NO synthase inhibition suggests the change in RH partly reflects endothelial-dependent vasodilator function (37). However, multiple factors contribute to RH, and the macro- and microvascular vasodilator response following an acute bout of exercise could be attributed to different mechanisms, with the latter response being less dependent on NO-mediated vasodilation (10, 38). Collectively, these data illustrate the importance of future works to investigate both conduit and resistance

artery function following exercise, as these measures may provide a more global prospective on peripheral vasodilator responsiveness.

Conclusions

Exercise intensity plays a major role in modulating adaptations in endothelial function after chronic exercise (39). Changes in cardiovascular hemodynamics following acute exercise, such as the change in BP, can predict the degree of improvement after chronic exercise training (40, 41). Although there is a clear, positive relationship between exercise training and vascular health, the effect of acute exercise on vascular function has received relatively little attention. In the current study, we examined the effect of exercise intensity on magnitude of change in post-exercise vascular function in conduit and resistance arteries of healthy older adults. Our data demonstrate that exercise intensity impacts conduit, but not resistance artery vasodilator function in healthy older adults. Interestingly, recent studies revealed that long-term, high-intensity training is more effective at improving FMD than moderate-intensity training in older adults (34). The results of this study suggest that high-intensity aerobic exercise is effective in acutely improving conduit artery vasodilator function in elderly adults and thus could have implications for understanding the different effects of acute exercise on endothelium-dependent vasodilation as a function of age.

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Figure 1. Antegrade (A), retrograde (B), mean shear rate, (C) and oscillatory shear index (D) at rest and during exercise. High-intensity exercise (●) and low-intensity exercise (○). SR; shear rate, OSI; oscillatory shear index. * $P<0.05$ vs. Rest in Low, † $P<0.05$ vs. Rest in High, ‡ $P<0.05$ Low vs. High.

Figure 2. Absolute FMD (A) and %FMD (B) at pre, 10 minutes post-, and one hour post-exercise. High; high-intensity exercise, Low; low-intensity exercise. * $P<0.05$ vs. Low, † $P<0.05$ vs. Pre.

Figure 3.

Hyperemic responses over 100 seconds following cuff release at pre, ten minutes post-, and one hour post-exercise for low- and high-intensity exercise.

Table 1

Blood pressure and heart rate at rest and during exercise

		Exercise						
	Rest	5 min	10 min	15 min	20 min	25 min	30 min	Interaction
SBP (mmHg)	Low	122±3	138±5	137±5	136±5	138±5	137±5	<0.001
	High	121±3	181±6 [*] †	182±6 [*] †	178±6 [*] †	176±6 [*] †	174±5 [*] †	
DBP (mmHg)	Low	75±2	75±3	75±3	73±2	73±3	74±3	<0.001
	High	75±2	79±4	80±3	76±3	75±3	74±3	
MAP (mmHg)	Low	91±2	96±3	96±3	94±3	95±3	95±3	<0.001
	High	90±2	113±3 [*] †	114±3 [*] †	112±3 [*] †	108±3 [*] †	107±3 [*] †	
HR (bpm)	Low	63±3	85±1 [†]	86±1 [†]	85±1 [†]	86±1 [†]	86±1 [†]	<0.001
	High	63±2	121±2 [*] †	124±1 [*] †	125±1 [*] †	125±1 [*] †	124±1 [*] †	

Data reported as mean±standard error.

Low; low-intensity exercise, High; high-intensity exercise, SBP; systolic blood pressure, DBP; diastolic blood pressure, MAP; mean arterial pressure, HR; heart rate,

^{*} P<0.05 vs. Low,[†] P<0.05 vs. Rest.

Table 2

Cardiovascular parameters at FMD measurements

		Pre	Post 10 min	Post 1 hour	Interaction	Time	Intensity
SBP (mmHg)	Low	121±3	121±3	124±4	0.14	0.96	0.90
	High	123±4	123±5	119±4			
DBP (mmHg)	Low	77±2	72±2	75±2	0.54	<0.01	0.67
	High	77±2	74±2	75±2			
MAP (mmHg)	Low	92±2	88±2	91±2	0.22	<0.01	0.82
	High	92±2	90±3	90±2			
HR (bpm)	Low	67±3	65±2	62±2	<0.01	<0.01	<0.01
	High	64±2	90±4 ^{*†}	66±3			
D _{base} (mm)	Low	3.75±0.04	3.78±0.03	3.78±0.04	0.35	0.23	0.36
	High	3.64±0.03	3.74±0.03	3.73±0.03			
D _{peak} (mm)	Low	3.92±0.04	4.01±0.04	3.97±0.04	0.06	<0.01	0.80
	High	3.82±0.03	4.08±0.03	3.94±0.03			
Peak time (sec)	Low	51.0±1.5	57.8±1.9	51.2±1.3	0.26	0.01	0.11
	High	52.0±1.7	79.6±2.6	61.6±2.1			
SR _{AUC} ×10 ³ (arbitrary units)	Low	14.6±1.9	13.4±1.8	11.1±1.1	0.51	0.09	0.16
	High	14.2±1.3	16.8±2.7	14.0±1.5			
BF _{AUC} (ml)	Low	142±16	205±20	148±23	0.56	<0.01	0.28
	High	158±14	240±25	162±16			
BF _{peak} (ml/min)	Low	372±31	444±37	345±45	0.97	<0.01	0.57
	High	391±30	455±28	353±29			
Corrected-%FMD (%) (Covariate: D _{base})	Low	4.7±0.7	6.3±0.7	5.2±0.7	N/A	N/A	N/A
	High	4.6±0.7	9.1±0.7 ^{*†}	5.8±0.7			
Corrected-%FMD (%) (Covariate: SR _{AUC})	Low	4.5±0.7	6.4±0.7	5.6±0.7	N/A	N/A	N/A
	High	4.7±0.7	8.6±0.7 ^{*†}	5.8±0.7			

Data presented as mean±standard error.

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Low; low-intensity exercise, High; high-intensity exercise, SBP; systolic blood pressure, DBP; diastolic blood pressure, MAP; mean arterial pressure, HR; heart rate, D_{base}; baseline diameter, D_{peak}; peak diameter, Peak time; time from cuff deflation to peak diameter, SRAUC; shear rate area under curve, BFAUC; blood flow area under curve, BF_{peak}; peak hyperemic blood flow, Corrected-%FMD; covariate-adjusted flow-mediated dilation.

* P<0.05 vs. Low,
‡ P<0.05 vs. Pre.