Resistance exercise lowers blood pressure and improves vascular endothelial function in individuals with elevated blood pressure or stage I hypertension

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Running title: Resistance Training on Hypertension

NEW & NOTEWORTHY: This is among the first studies to investigate the effects of chronic resistance exercise training on blood pressure (BP) and putative BP regulating mechanisms in middle-aged and older adults with untreated elevated BP or stage 1 hypertension in a randomized, non-exercise, controlled trial. Nine weeks of resistance exercise training elicits 4–8 mmHg improvements in systolic and diastolic BP alongside improvements in vascular endothelial function and total peripheral resistance without influencing central arterial stiffness or cardiovagal function.

Abstract

Lifestyle modifications are the first-line treatment recommendation for elevated blood pressure (BP) or stage 1 hypertension (E/S1H) and include resistance exercise training (RET). The purpose of the current study was to examine the effect of a 9-week RET intervention in line with the current exercise guidelines for individuals with E/S1H on resting peripheral and central BP, vascular endothelial function, central arterial stiffness, autonomic function, and inflammation in middle-aged and older adults (MA/O) with untreated E/S1H. Twenty-six MA/O adults (54±6 y; 16F/10M) with E/S1H engaged in either 9 weeks of 3 days/week RET (n=13) or a non-exercise control (CON; n=13). Pre- and post-intervention measures included peripheral and central systolic (SBP and cSBP) and diastolic BP (DBP and cDBP), flow-mediated dilation (FMD), carotid-femoral pulse wave velocity (cfPWV), cardiovagal baroreflex sensitivity (BRS), cardiac output (CO), total peripheral resistance (TPR), heart rate variability (HRV), and c-reactive protein (CRP). RET caused significant reductions in SBP (mean change±95%CI = (-7.9 [-12.1, -3.6] mmHg; $p < 0.001$), cSBP (6.8 [-10.8, -2.7] mmHg; $p < 0.001$), DBP (4.8 [-10.3, -1.2] mmHg; $p < 0.001$), and cDBP (-5.1 [-8.9, -1.3] mmHg; $p < 0.001$), increases in FMD (+2.37 [0.61, 4.14] %; $p = 0.004$) and CO (+1.21 [0.26, 2.15] L/min; $p = 0.006$) and a reduction in TPR (-398 [-778, -19] mmHg·s/L; $p = 0.028$). RET had no effect on cfPWV, BRS, HRV, or CRP relative to CON ($p \geq 0.20$). These data suggest that RET reduces BP in MA/O adults with E/S1H alongside increased peripheral vascular function and decreased TPR without affecting cardiovagal function or central arterial stiffness.

Introduction

It is estimated that roughly 1.39 billion people have hypertension worldwide and that nearly 10 million deaths are attributed to hypertension-related complications annually (1, 2). There are multiple categories that define a higher than optimal blood pressure (BP), including elevated BP (systolic BP (SBP) of 120–129 mmHg and a diastolic BP (DBP) of less than 80 mmHg), stage 1 hypertension (SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg), and stage 2 hypertension (SBP over 140 mmHg or a DBP over 90 mmHg) (2). Lifestyle interventions are the recommended first-line treatment for individuals who have elevated BP and stage 1 hypertension (E/S1H) in an attempt to prevent or delay the need for future pharmaceutical intervention (3). Resistance exercise training (RET) effectively reduces BP and is one of the recommended lifestyle interventions for individuals with E/S1H (4). Notably, however, the majority of studies examining the impact of RET on BP include BP only as a secondary outcome, and the mechanism by which RET lowers BP is unclear (5), particularly in middle-aged (MA/O) adults with untreated E/S1H. Therefore, there is a clear and urgent need for high-quality investigations examining the effects of RET on BP and putative BP-regulating mechanisms in individuals with E/S1H (5).

The limited body of evidence available on the mechanism by which RET lowers BP suggests improvements in peripheral vascular endothelial function may be a major contributing factor (5, 6). However, the only study examining RET's impact on vascular function in untreated MA/O adults with hypertension did not have a true non-exercise control group, utilized a short 4-week RET program, did not measure FMD, and included individuals with stage 2 hypertension under the updated BP categories (7). Additionally, while endothelial dysfunction and hypertension are related, the directionality and causality of this association is less clear (8). Interestingly, RET has been shown to worsen central arterial stiffness and cause alterations in autonomic nervous system function that result in impaired BP control in some (7, 9-17), but not all studies (18-24). These effects would be particularly worrisome in MA/O adults with E/S1H

and would also seemingly be at odds with the potential beneficial effects of RET on BP. However, the effects of RET on central arterial stiffness and autonomic function in this population are, as of yet, not well-described.

Therefore, the purpose of the current study was to examine the effect of a 9-week RET intervention in accordance with current exercise guidelines provided by the American College of Sports Medicine (ACSM) for individuals with high BP (25) on resting peripheral and central BP, vascular endothelial function, central arterial stiffness, cardiovagal function, and inflammation in MA/O with E/S1H.

Methods

Participants

Thirty-six individuals completed a screening visit for the current study, however, six of these individuals had BPs below the inclusion cutoff and thus were not eligible. Therefore, 30 physically inactive, male and female MA/O adults (aged 45–64 y) were determined to be eligible for the current study and were randomized into either a RET or a non-exercise control (CON) group **(Table 1)**. Out of the enrolled participants, there were 4 individuals in RET and 6 individuals in CON who met ES1H criteria based on their SBP alone, whereas the remaining participants were classified as ES1H due to both their SBP and DBP. Following screening but prior to the first experimental visit, two participants in CON and one in RET dropped out of the study for the following reasons: scheduling conflicts (n=1), unrelated injury (n=1), and unresponsiveness to study-related communication (n=1), whereas one participant in CON dropped out following the first experimental visit due to scheduling conflicts. As a result, 26 participants completed this investigation (Table 1). To determine eligibility, participants arrived at the laboratory for a screening visit after a 6-hour fast, abstaining from caffeine consumption for at least 12 hours, and having not engaged in moderate-to-vigorous intensity exercise for at least 24 hours. During the screening visit, participants completed an informed consent form,

health history questionnaire, and the Physical Activity Readiness Questionnaire (PAR-Q+), had their menopause status determined via STRAW-10 principal criteria (26), and had a resting brachial BP measured. During the screening visit, BP was recorded as the average of duplicate recordings following a 5-minute seated rest period with a 1-minute interval between measurements. For all measurements, participants were seated with an appropriately sized cuff placed on the upper right arm, which was supported and at heart level. The screening BP was collected using an automatic oscillometric BP device (OMRON Platinum Model BP5450, OMRON Healthcare Co., JPN) that has been validated for clinical accuracy that is on the US BP Validated Device Listing. If the first and second SBP or DBP measurements differed by ≥ 5 mmHg or ≥ 4 mmHg, respectively, a third measurement was completed, and the average of the two closest measurements was recorded. To be eligible, participants must have been 45–64 years old, had a body mass index of 18.5–39.9 kg/m^2, have not been meeting the physical activity guidelines for at least 6 months, have been determined to have no known cardiovascular, metabolic, or musculoskeletal disease (excluding hypertension), nor to be taking any medications treating such disease, according to self-reported health history, determined to be ready to begin an exercise program according to the PAR-Q+, and had a SBP between 120–139 mmHg and/or DBP between 80–89 mmHg as measured during the in-person screening visit. Participants were recruited using IRB-approved emails via the university mass email system and by word of mouth. All study procedures and documents complied with the Declaration of Helsinki, except for preregistration in a publicly accessible database, and were approved by the University's Institutional Review Board for the protection of human subjects (IRB Approval #: 202201319). All participants consented to participate by signing an informed consent form explaining the nature, benefits, and risks of the study before participation.

Experimental Design

An overview of the experimental design can be viewed in **Figure 1**. All eligible participants visited the laboratory for two experimental visits occurring 3–7 days prior to (T0) and 5–7 days following (T1) the 9-week intervention period. For all experimental visits, participants abstained from exercise for at least 5 days, caffeine for 12 hours, and food for 6 hours prior to arrival, and were studied at the same time of day during pre- and post-testing. During the experimental visits, participants had their body composition measured before laying supine for at least 10 minutes prior to a venipuncture. An additional 10-minute supine rest was then provided before vascular endothelial function and central arterial stiffness were measured via FMD and carotid-femoral pulse wave velocity (cfPWV), respectively. Participants then transitioned into a seated position and sat quietly for 10 minutes prior to having their resting BP collected and their beat-by-beat BP and heart rate recorded for 5 minutes. At the end of each visit, participants engaged in strength testing, where their 10-repetition maximum (RM) was determined using a cable-loaded bench press and plate-loaded hack squat machine. Prior to strength testing, participants were provided with a 180-kcal hypoallergenic snack (Organic Strawberry Crispy Squares, MadeGood Foods, USA). There were two premenopausal participants in each group. Two premenopausal women had an IUD (RET, n =1; CON, n =1), whereas the other two completed their experimental visits in the follicular phase (RET, n =1; CON, n = 1) to control for changes in circulating sex hormones.

A Priori Sample Size Determination: The estimated sample size required to observe mixed-factors interaction effect for changes in BP, cfPWV, and FMD, were determined in G*Power (Autenzell, Germany). Collier *et al.* (7) observed an effect size of RET on BP and cfPWV of d=0.65 and d=0.67, while Ramirez-Valez *et al.* (23) observed an effect size of RET on FMD of 0.51. Combining these effect sizes with a standard power (1-β) of 0.8, 2 groups (RET and CON), and 2 measurements (T0 versus T1) with a conservative correlation between

measurements of 0.5, it was determined that 8, 8, and 10 participants would be needed per group to achieve adequate power for BP, cfPWV, and FMD outcomes. Therefore, assuming a 20% dropout rate, we aimed to recruit at least 12 participants into each group.

Intervention Period

During the 9-week intervention period, individuals in the RET group came to the lab every Monday, Wednesday, and Friday to complete a ~40-minute RET session. Each RET session was led and supervised by one of three trained lab members and no more than four participants trained in the same sessions in order to maintain adequate supervision while allowing sufficient flexibility to accommodate participants' schedules. During each RET session, participants completed (in order) bench press, hack squat, latissimus dorsi pulldown, leg extension, seated row, leg curl, and plank resistance exercises. Specific set and repetition schemes for the RET program are shown in **Figure 1**. All exercises were cable-loaded except for the hack squat, which was plate-loaded, and the plank, which was completed using only body weight. The initial weight was estimated based on strength testing at the end of T0 and used for week 1. During weeks 2 and 3, participants were queried and monitored to determine if they would have been able to complete 2 or more repetitions beyond the prescribed 12 repetitions on the final set of each lift. If this was the case, the weight was increased by 5–10% for the following workout. From week 4 and onward, participants were instructed to complete as many repetitions as possible on the final set of each lift (excluding plank) but were stopped if they completed 3 repetitions more than the prescribed amount. Weight was then increased by 5–10% if participants completed more than the prescribed repetitions on the final set for two workouts in a row for a particular lift. For planks, participants completed the same number of sets as the other exercises, but did so for time instead of repetitions, with a prescription of 15 seconds for week 1 and 20 seconds for week 2, followed by a 5-second increase in time for each workout thereafter. Participants rested for at least 1-minute, but not longer than 3-minutes,

between sets and were instructed to allow sufficient rest in order to ensure lingering fatigue did not affect subsequent set performance. All sets and repetitions were completed for a given exercise before moving to the next exercise in the session during weeks 1–4. During weeks 5–9, participants completed supersets with an upper and lower-body exercise paired (e.g., bench press and hack squat). At the end of each session, participants were asked for their rating of perceived exertion (RPE) between 0–10, with 0 representing no exertion (i.e., rest) and 10 representing maximal exertion. Those in CON were asked to maintain their current lifestyle and dietary habits throughout the 9-week period and did not come to the laboratory outside of the screening and experimental visits.

Conduit Artery Vascular Function

The brachial artery FMD technique was used to assess vascular endothelial function and reactive hyperemia (RH) in accordance with the most recent guidelines (27). Prior to data collection, participants laid in a supine position in a dark, temperature-controlled room for 10 minutes. With the participant's left arm laterally extended, a segmental cuff (TMC7, Hokanson, USA) was placed just distal to the medial epicondyle of the humerus and a 12-MHz ultrasound probe (12L-RS, General Electric, USA) was used to visualize the brachial artery and measure blood flow, while a screen capture device (AV.io HD, Epiphan Systems, USA) was used to record the ultrasound screen. Positioning of the segmental cuff distally to the ultrasound probe was chosen because the increase in post-occlusive artery diameter is largely NO-mediated using this technique (28). Blood flow velocity was collected using an insonation angle of 60° to the axis of the vessel and a sample volume encompassing the entire width of the artery (29). FMD testing included a 2-minute baseline period, a 5-minute cuff occlusion period at 240 mmHg using a rapid cuff inflation system (E20, Hokanson, USA), and a 3-minute post-occlusive period. A previously validated (30), continuous, semiautomated edge detection software (FMD Studio, Quipu srl, Italy) was utilized to continuously measure brachial artery diameter and blood flow

velocity throughout the protocol, which were used to calculate shear rate ($4 \cdot$ blood flow velocity (cm/s) / brachial diameter (cm)) (27). Baseline diameter (D_{base}) and shear rate (SR_{base}) were calculated as the average value during the 2-minute baseline period, while peak diameter, shear rate (SR_{peak}), and shear rate area under the curve (SR_{AUC}) were calculated following cuff release up until peak diameter was observed using FMD Studio software, as previously described (31-33). RH was calculated as the difference in AUC of blood flow between baseline (BF_{base}) and the first 90 seconds of the post-occlusive period. Relative and absolute FMD (FMD_{abs}) was calculated as relative (%) and absolute (mm) the change from D_{base} to maximal diameter, whereas FMD normalized to SR (FMD_{SR}) was calculated as FMD/SR_{AUC}. Probe location was measured from the superior border of the antecubital fossa during pre-testing to ensure a similar placement of the probe during post-testing.

Carotid-femoral Pulse Wave Velocity

Central arterial stiffness was assessed using cfPWV (SphygmoCor XCEL, AtCor Medical, Inc. USA). While remaining in a supine position following the FMD test, participants had their carotid pulse palpated and marked on the left side of the neck and had a cuff placed on their upper left thigh to acquire the femoral pulse wave via volumetric displacement. The pulse waves of the carotid and femoral arteries were then recorded simultaneously by a tonometer and the femoral cuff, respectively. The distance between the site of the carotid and femoral pulse was then divided by the difference in pulse wave transit time between the two arteries (e.g., distance/time) to determine cfPWV. To correct for the known impact of distending pressure on cfPWV and the hypothesized reduction in BP expected in the RET group, change in mean arterial pressure (MAP) was added as a covariate in cfPWV analyses.

Resting Blood Pressure

During experimental visits, resting BP was collected in a seated position following a 10-minute resting period in accordance with the American Heart Association guidelines (34) using a

SphygmoCor XCEL cuff device (SphygmoCor XCEL, AtCor Medical, Inc. USA). SBP, DBP, MAP, and pulse pressure (PP) were determined automatically by standard oscillometric brachial BP measurement using an appropriately-sized BP cuff. Immediately after, the cuff was inflated and held at a sub-diastolic pressure level for 5 seconds, during which cuff displacement waveforms were measured and calibrated to the brachial SBP and DBP. Next, a generalized transfer function was applied to estimate the central BP waveform, from which central SBP (cSBP), and central DBP (cDBP) were determined using the device's proprietary software (35).

Hemodynamic Monitoring

While seated, participants had a finger photoplethysmograph placed on the middle finger of the right hand, which was utilized to collect beat-by-beat BP (NOVA Finometer, Finapres Medical Systems, The Netherlands). The participants held their right hand over their heart during all hemodynamic testing, with their arm supported. Modelflow technology was used to calculate cardiac output (CO) and total peripheral resistance (TPR). Additionally, heart rate was collected using a 3-lead electrocardiogram, and respiratory rate was collected using a respiratory belt with participants instructed to breathe at a normal rate during all testing (TN1132/ST; ADInstruments). Data was collected at 1000 Hz using a data acquisition system (Powerlab Series 26; ADInstruments, USA) and stored offline.

Cardiovagal Baroreflex Sensitivity and Heart Rate Variability

Raw beat-by-beat BP waveforms and ECG data were uploaded to Ensemble-R software, and the sequence method was utilized to assess cardiovagal BRS and HRV. BRS_{pooled} was assessed by averaging the slope between three sequences of either increasing (BRS_{up}) or decreasing (BRS_{down}) pulse waveform peak pressures with subsequent decreases or increases in R-R interval length, respectively, with a minimum correlation of r = 0.8, increase in SBP of 1 mmHg, and an R-R interval length of 4 ms. The log-transformed root mean square of

252 successive differences (lnRMSSD), high-frequency power (lnHF), and low-frequency power
253 (lnLF), were calculated to represent both time and frequency domain HRV.

254 C-reactive Protein

255 Whole venous blood was collected in a lithium heparin plasma separator tube (BD
256 Vacutainer, Becton Dickinson, USA) before being spun for 15 minutes at 1000 g. Plasma was
257 then transferred to 1.7-mL microcentrifuge tubes for storage at -80°C. Samples were later
258 thawed, and high-sensitivity CRP was assessed using a commercially available enzyme-linked
259 immunosorbent assay (CRP ELISA, Immundiagnostik AG, Germany). The detection range of
260 the CRP ELISA kit was 1.8–150 ng/mL, with a sensitivity of 0.124 ng/ml, and an inter-assay
261 coefficient of variation of < 10%. All assays were performed in accordance with the
262 manufacturer's instructions and read using a microplate photometer (Multiskan^{TM} FC Microplate
263 Photometer, ThermoFisher Scientific^{TM}, USA).

264 Body Composition

265 At both experimental visits, participants' body composition was assessed via BodPod
266 (COSMED, USA) to assess body fat percent (BF%), fat mass (FM), and fat-free mass (FFM).

267 Lifestyle Controls

268 All participants were asked to refrain from any other forms of exercise outside of the
269 study and maintain their current dietary habits throughout the study period. Calories, protein, fat,
270 and carbohydrate intake, along with physical activity in metabolic equivalent of task (MET)
271 minutes per week were collected via self-report using 3-day dietary food logs and the Short Last
272 7 Days International Physical Activity Questionnaire (IPAQ), which were completed during both
273 pre- and post-testing.

Statistical Analysis

Residual normality was assessed using Shapiro-Wilk tests, while homoscedasticity was assessed using Levene's test. In the case of violation of either normality or homoscedasticity, data was transformed with a natural logarithm before being reverted to their original scale for reporting. Multiple independent two-way mixed linear models (group [RET vs. CON] × visit [pre- vs. post-intervention]) were run to determine the impact of the intervention period on all resting BP, vascular endothelial function, RH, cfPWV, HRV, BRS, dietary, and physical activity variables with sex included as a covariate. cfPWV was analyzed using a two-way mixed linear model with ΔMAP and sex included as covariates. To decompose significant group × visit interactions, Tukey-adjusted post hoc comparisons were performed. Between-group effect sizes were determined using Cohen's *d*. Pearson's product correlations (r) or Spearman rank correlation coefficients (ρ) were used to explore the relationship between the changes in SBP, DBP, CO, TPR, FMD, and selected secondary variables of interest where residuals were normally or non-normally distributed. Partial correlations ($r_{xy,z}$ or $\rho_{xy,z}$) were also performed to remove the effect of sex and are reported in Figure 5. Within and between group differences are reported in text as mean differences with [95% CI Lower Bound, 95% CI Upper Bound] unless denoted otherwise. Confidence Intervals were adjusted using the Bonferroni method. Significance was set at $p \leq 0.05$. Statistical analyses were performed using JASP (JASP Team 2020, v. 0.13.1) or jamovi (v. 2.3.21.0) and figures were created using GraphPad Prism (v. 9.5.1).

Results

Body Composition

There were no significant group × visit interactions, group main effects, or visit main effects for weight, FFM, FM, or BF% **(Table 2)**.

Strength

There was a significant group × visit interaction for both squat 1RM and bench 1RM. RET significantly increased both squat 1RM (+79.6 [64.1, 95.1] kg; $p < 0.001$) and bench 1RM (+22.7 [18.8, 26.6] kg; $p < 0.001$) from T0 to T1. Additionally, both squat 1RM (+79.7 [39.8, 119.5] kg; $p < 0.001$; d = 2.33) and bench 1RM (+30.9 [15.6, 46.2] kg; $p < 0.001$; d = 2.37) were significantly greater at T1 in RET compared to CON. There were no significant changes in CON from T0 to T1 ($p \geq 0.05$) **(Table 2)**.

Blood Pressure

There were significant group × visit interactions for SBP, DBP, cSBP, cDBP, MAP, and PP **(Figure 2)**. Specifically, RET experienced a significant reduction in SBP (-7.9 [-12.1, -3.6] mmHg; $p < 0.001$), DBP (-4.8 [-10.3, -1.2] mmHg; $p < 0.001$), cSBP (-6.8 [-10.8, -2.7] mmHg; $p < 0.001$), cDBP (-5.1 [-8.9, -1.3] mmHg; $p < 0.001$), and MAP (-5.7 [-9.9, -2.0] mmHg; $p < 0.001$) from T0 to T1; however the decrease in PP from T0 to T1 (-3.1 [-6.6, 0.5] mmHg; $p = 0.089$) in RET was not significant. There were no significant changes in any BP variable from T0 to T1 in CON ($p \geq 0.05$). Accordingly, RET had significantly lower SBP (-9.8 [-17.3, -2.4] mmHg; $p = 0.004$; d = 1.52), cSBP (-9.7 [-17.0, -2.3] mmHg; $p < 0.001$; d = 1.52), and MAP (-6.1 [-11.9, -0.4] mmHg; $p = 0.026$; d = 1.22) than CON at T1. While there were large effect size differences between RET and CON at T1 for DBP (-4.5 [-10.3, 1.2] mmHg; $p = 0.142$; d = 0.90), cDBP (-4.3 [-10.1, 1.4] mmHg; $p = 0.173$; d = 0.86), and PP (-5.3 [-11.3, 0.7] mmHg; $p = 0.081$; d = 1.02), these differences were not statistically significant.

Resting Hemodynamics

There were significant group × visit interactions for both CO and TPR (**Figure 3**). CO significantly increased in RET (+1.21 [0.26, 2.15] L/min; $p = 0.006$), but there was no difference in CO between RET and CON at T1 (+0.9 [-0.6, 2.3]; $p = 0.33$; d = 0.70). TPR significantly decreased from T0 to T1 in RET (-398 [-778, -19] mmHg·s/L; $p = 0.028$), and while there was a

large effect size difference between RET and CON at T1 (-369 [-849, 110] mmHg·s/L; p = 0.158; d = 0.87), this difference was not significant. There were no significant changes in CO or TPR in CON from T0 to T1 ($p \geq 0.64$) **(Figure 3)**. There was no significant group × visit interaction, group main effect, or visit main effect for RHR (**Table 3)**.

Conduit Artery Vascular Function

There were significant group × visit interactions for FMD (p = 0.011; η_p^2 = 0.25), $cFMD_{SR}$ (p = 0.017; η_p^2 = 0.22), FMD_{abs} (p = 0.006; η_p^2 = 0.29), as well as BF_{base} (p = 0.023; η_p^2 = 0.20). There was no significant interaction for D_{base} (p = 0.67; η_p^2 = 0.14). RET experienced significant increases from T0 to T1 in FMD (+2.37 [0.61, 4.14] %; p = 0.004), $cFMD_{SR}$ (+1.25 [0.23, 2.27] %; p = 0.009), and FMD_{abs} (+0.09 [0.03, 0.16] mm; p = 0.002). There were no significant changes in any of these variables from T0 to T1 in CON (all $p \geq 0.99$). Consequently, $\Delta cFMD_{SR}$ (+2.1 [0.04, 4.09] %; p = 0.035; d = 1.18) and FMD_{abs} (+0.14 [0.005, 0.283] mm; p = 0.048; d = 1.12) were greater in RET than CON at T1, whereas there was a large, but non-significant difference in FMD (+3.8 [-0.7, 8.4]%; p = 0.104; d = 0.98). RET also experienced significant increases from T0 to T1 in BF_{base} (+28.6 [5.1, 52.1]; p = 0.009). While there was a large effect size difference between RET and CON at T1 for BF_{base} (+26.4 [-3.6, 56.4]; p = 0.085; d = 1.00), this difference was not significantly different. There were no significant group × visit interactions, group main effects, or visit main effects for RH, SR_{base}, SR_{peak}, or SR_{AUC} **(Figure 4 and Table 3).**

Central Arterial Stiffness

There was no significant group × visit interaction, group main effect, or visit main effect for cfPWV **(Table 3)**.

Cardiovagal Baroreflex Sensitivity and Heart Rate Variability

An average of 26.9 ± 10.7 valid sequences were acquired per participant at the pre- and post-intervention visits. There was no significant group × visit interaction, group main effect, or

visit main effect for BRS_{pooled}, BRS_{up}, or BRS_{down} **(Table 3)**. There was also no significant group × visit interaction, group main effect, or time main effect for lnRMSSD, lnLF, or lnHF **(Table 3)**.

C-reactive Protein

There was no significant group × visit interaction, group main effect, or time main effect for CRP **(Table 3)**.

Correlations

Relations among the changes in hemodynamic, vascular, cardiovagal, and body composition variables are depicted in **Figure 5**. ΔSBP was significantly correlated with ΔFMD (r = -0.48; $p = 0.012$), $\Delta cFMD_{SR}$ (r = -0.54; $p = 0.005$), ΔBF_{base} (r = -0.47; $p = 0.016$), and ΔD_{base} (r = -0.45; $p = 0.021$), as well as with Δsquat (ρ = -0.52; $p = 0.007$), and Δbench (r = -0.67; $p < 0.001$). ΔDBP was significantly correlated with Δbench (r = -0.49; $p = 0.012$). ΔCO was significantly correlated with ΔFFM (ρ = 0.58; $p = 0.002$), as well as with ΔTPR (r = -0.69, $p < 0.001$). ΔTPR was also significantly correlated with ΔD_{base} (r = -0.44; $p = 0.023$), ΔBRS_{down} (r = -0.47; $p = 0.016$). ΔTPR was not related to ΔSBP (r = 0.26; $p = 0.20$) or ΔDBP (r = 0.30; $p = 0.13$). ΔPP was significantly related to ΔPWV (ρ = -0.51; $p = 0.008$).

Lifestyle Controls

The average total exercise session attendance was (mean ± SD) 96 ± 6%. There were no significant group × visit interactions, group main effects, or time main effects for physical activity, nor the consumption of calories, fat, carbohydrates, or protein **(Table 4)**.

Discussion

This was the first study to explore the putative vascular mechanisms driving RET-induced improvements in BP in MA/O adults with untreated E/S1H. The main finding of the current study was that a 9-week RET program reduced peripheral and central BP which was accompanied by an increase in FMD and a decrease in TPR. Additionally, we reported

increases in BF_{base} and CO, with no changes in either RH or cfPWV. Lastly, the RET intervention did not cause any changes in autonomic function as measured by cardiovagal BRS or HRV, or changes in systemic inflammation as reflected by CRP. Further, our data indicate that chronic RET does not positively or negatively affect central arterial stiffness, autonomic function, or inflammation in MA/O adults with untreated E/S1H.

This is the first study to examine the impact of a RET intervention on BP in untreated MA/O adults with untreated E/S1H. Our data indicate that RET is effective at reducing both peripheral and central BP. RET reduced SBP and DBP by 8 and 5 mmHg, respectively, which is similar to reductions reported following other RET interventions (20, 36-39), aerobic exercise interventions (40), and slightly greater than the average pharmacological reductions reported over 6 months (41). Thus, these reductions in BP are clinically relevant, and every 5-mmHg reduction in SBP is associated with a 10% decrease in CVD risk (42). Collier *et al.*, previously reported a 4 and 4 mmHg reduction in SBP and DBP, respectively, following just 4 weeks of RET in MA/O adults with hypertension (7). Additionally, middle-aged men with untreated stage 2 hypertension experienced 16 and 12 mmHg reductions in SBP and DBP, respectively, following a 12-week RET program that was similar to the current study (39). In younger adults with untreated E/S1H who engaged in an 8-week RET intervention, Beck *et al.* reported a 10 and 8 mmHg reduction in peripheral SBP and DBP, and 9 and 8 mmHg reductions in cSBP and cDBP (20). Our data agree with and extend this previous work and indicate that RET lowered cSBP and cDBP by 7 and 5 mmHg in MA/O with E/S1H. Further, RET promoted a 3 mmHg decrease in PP, which provides important prognostic information above and beyond SBP and DBP (43-45) and is largely determined by a mismatch of distal (e.g., conduit) to proximal (e.g., abdominal aorta) arterial diameters (45). Overall, our data strengthen prior evidence regarding the effect of RET on BP in MA/O with hypertension (7) by (i) experimentally isolating the effects of RET via inclusion of a non-exercise control group, and also by (ii) specifically studying MA/O adults with untreated E/S1H, for whom lifestyle interventions such as RET are explicitly recommended as a

first line strategy for BP control. Accordingly, we build upon these prior studies and present important evidence that supports RET as a viable lifestyle intervention to improve BP, showing for the first time that just 9 weeks of RET in MA/O adults with untreated E/S1H exhibit reductions that are slightly greater than those experienced following 6 months of pharmacological treatment (41).

We further extended existing evidence by examining the effect of RET on putative BP-regulating mechanisms in relation to RET-induced BP changes. BP is the product of CO and TPR and in addition to lowering BP, RET increased CO and decreased TPR in the present study. The measure that was most strongly correlated with ΔCO in the current study was ΔFFM ($r = 0.56$; $p = 0.003$). Thus, while it is tempting to speculate that these relations may be explained by a training-induced increase in blood flow demand to supply a greater volume of metabolically active tissue and/or an increase in venous capacity or return (46-49), we did not observe significant RET-induced changes in whole body FFM (50). However, we also observed a 40% RET-induced increase in resting blood flow (e.g., BF_{base}) and a non-significant 3.1% (+0.11 mm) increase in brachial artery diameter (e.g., D_{base}). Prior studies have suggested that RET promotes increases in resting arterial lumen size in the conduit arteries feeding active muscle beds (51), likely due to arterial remodeling and/or a decrease in resting arterial tone in response to large, repeated, chronic increases in blood flow and the resultant arterial shear stress (51, 52). Further, changes in conduit artery blood flow reflect changes in the tone of the downstream resistance vessels, which are so named because they are the major arterial bed that modulates vascular resistance. Hypertension is characterized by increased peripheral resistance caused by decreased resistance vessel lumen diameters, decreased resistance vessel density due to rarefaction, and/or reduced vasomotor function (53, 54). Thus, it is likely that the increases in BF_{base} observed herein reflect a decreased resistance to flow in the resistance vessels, perhaps by reversal of microvascular rarefaction and decreased constrictor tone (54, 55). Notably and in support of this hypothesis, both changes in resting brachial artery

diameter and blood flow were inversely associated with changes in SBP in the present study (Figure 5). In addition, it is also plausible that RET-induced increases in conduit artery diameter contributed to decreases in PP by reducing the ratio between proximal and distal conduit artery diameters (45), although this is highly speculative and will require future investigation. Therefore, taken together, our data suggest that the BP-lowering effect of RET may be explained by decreases in TPR secondary to changes in peripheral vascular tone. However, due to the lack of significant relationships between TPR and both SBP and DBP, additional mechanistic research is necessary to confirm this hypothesis.

Multiple indices of vascular endothelial function examined in the current study also improved following the RET intervention. Our data indicated that RET elicited improvements in both FMD and $cFMD_{SR}$ in MA/O with untreated E/S1H, a finding that is largely in agreement with prior work in individuals with high BP (56-58). RET causes dramatic increases in blood flow to the muscles active in each exercise (59), causing acute increases in shear stress on the vascular endothelium (60). Notably, chronic exposure to repeated, transient increases in shear stress derived from exercise promotes an endothelial phenotype that is characterized by increased endothelial NO synthase (eNOS) expression and greater NO bioavailability (61). Additionally, the observed significant improvements in both FMD and $cFMD_{SR}$ suggest that increases in FMD were not caused by an increase in the shear stimulus on the vascular endothelium, but rather improvements in endothelium-dependent function (28, 62). While macrovascular function improved, we did not see any improvements in microvascular function as measured by RH. Unlike FMD, which is endothelium-dependent (63), RH provides insight into the dilation of the downstream resistance vessels and is minimally dependent on NO (29, 64). Our data disagree with those of Heffernan *et al.* and Collier *et al.,* who have previously reported that multi-week RET interventions improved RH. However, this difference could be due to the use of strain-gauge plethysmography versus the use of Doppler ultrasound to measure RH (7, 22), or due to a lack of power in the present study considering that RET improved RH in

all but one participant. An improvement in RH may have been hypothesized given that TPR is primarily regulated at the level of the resistance vessels, but changes in resting tone rather than the response to ischemia are likely more important to resting blood pressure control. Accordingly, and as previously described, BF_{base} was elevated following RET, potentially suggesting greater dilation of downstream resistance vessels at rest, although we cannot rule out the possibility that the increase in BF_{base} was caused by elevated CO. Still, it is noteworthy that changes in SBP were inversely associated with increases in both FMD and BF_{base} (Figures 5A, B, and D). Overall, these data indicate that RET improves vascular endothelial function and resting peripheral blood flow that may contribute to RET-mediated improvements in BP, and which are also likely to improve long-term cardiovascular risk in individuals with E/S1H.

While there is consistent cross-sectional evidence suggesting that individuals who engage in RET have stiffer central arteries (65-68), the experimental evidence regarding the influence of RET on arterial stiffness is less clear. Notably, RET had no effect on cfPWV in the present study. Whereas the majority of studies do not report increases in central arterial stiffness following RET (18, 20-24), there are multiple reports indicating RET may promote increased stiffness (7, 9-11). A potential methodological explanation for this discrepancy is the timing of post-test measurements, with all but one of the studies that have reported increases in arterial stiffness following a RET intervention having completed post-testing within 24 hours of the final exercise session (7, 9-11, 19). However, acute RET may increase central arterial stiffness for up to three days alongside transiently increased SNS activity and inflammation, and decreased parasympathetic nervous system activity (69-71). Therefore, it is plausible that the increases in aortic stiffness reported in these studies are due to transient changes in response to acute exercise, but do not reflect chronic maladaptive structural changes. It is also possible that RT interventions lasting several weeks or months are either not long enough to persistently alter the stiffness of the aorta, or other uncontrolled factors may be confounding the cross-sectional findings. Nevertheless, our data, collected 5–7 days (133 ± 19 h) after the last bout of

476 RET, indicate that short-term RET does not change central arterial stiffness as measured by
477 cfPWV among MA/O adults with E/S1H.

478 Our findings also indicate that RET had no adverse effects on cardiovagal function as
479 assessed by cardiovagal BRS and HRV. Prior evidence suggests that RET may reduce BRS in
480 MA/O with untreated hypertension (72), and either reduces (73) or does not influence BRS in
481 young healthy adults (74, 75). In the former study, Collier *et al.* reported that aerobic exercise
482 training and RET caused divergent changes in BRS in response to spontaneous decreases in
483 BP, as well as in the low- to high-frequency HRV ratio suggesting that aerobic and resistance
484 exercise training may have different effects on sympathovagal balance in MA/O with
485 hypertension (72). The authors also reported increases in central arterial stiffness that may have
486 resulted in a decreased ability of the aorta to return to smaller diameters during periods of
487 decreasing BP, and thus smaller changes in baroreceptor firing and lower BRS_{down} (72).
488 However, it is important to highlight that because a non-exercise control group was not included
489 and because residual transient effects may have influenced the post-study measurements
490 which were performed 24–48 h after the final exercise session (72), central questions remained
491 regarding the effects of RET in this population. In the present study, RET did not result in
492 chronic changes in central arterial stiffness or vagal modulation, which may explain the lack of
493 change in cardiovagal BRS. It is also notable that while the slope of the association between
494 changes in BP and heart rate did not change, BP did, suggesting that some degree of
495 baroreceptor resetting to operate at lower arterial pressures may have occurred. Therefore, our
496 data indicate that a 9-week RET program does not adversely impact cardiovagal function in
497 MA/O with E/S1H.

498 The RET intervention in the current study significantly improved both squat and bench
499 press strength, but surprisingly did not significantly influence FFM, FM, or BF%. In contrast,
500 Moraes *et al.* reported that a 12-week RET intervention promoted a 3 kg increase in FFM, a 4
501 kg decrease in FM, and a 4% reduction in BF% among middle-aged men with untreated stage 2

hypertension (39). On the other hand, Collier *et al.* report no changes in BF% following 4 weeks of RET in middle-aged to older adults with elevated BP or hypertension (7). RET programs typically result in immediate improvements in neuromuscular function during the first several weeks of training, with changes in FFM becoming increasingly detectable with longer durations of training (76, 77). In addition, it is likely that changes in FFM with RET are less robust among aging individuals with sub-clinical or clinical vascular dysfunction, which is associated with anabolic resistance (78). Thus, it is likely that neural adaptations explain the marked RET-induced improvements in strength, whereas the current program was not long enough to promote significant increases in FFM. However, this increase in strength without an increase in FFM is likely still to be of benefit relative to improved functional capacity, and possibly also given the independent relationship between strength and all-cause mortality (79). We also observed no changes in circulating CRP concentrations, which is in contrast to prior studies showing that chronic RET reduces CRP (80, 81) but may also be explained by the lack of change in body composition in this study (82, 83). Future studies may wish to directly examine whether E/S1H is associated with blunted skeletal muscle hypertrophy in response to RET in MA/O adults.

There were several limitations to our study. First, we studied a mixed sample of males and females which included both pre- and post-menopausal women. Men may be more susceptible to potential RET-induced increases in central arterial stiffness than postmenopausal women (84), and since the current study was not powered to detect sex differences and was comprised of mostly females, we are unable to determine if this explained our lack of findings regarding cfPWV. However, biological sex served as a covariate in all of our analyses. In addition, the distribution of pre- and post-menopausal women was balanced between groups. Second, the short nature of the study limits our ability to understand the long-term impact of RET participation in this population. It is possible that the differences in cross-sectional and intervention data regarding the impact of RET on central arterial stiffness may result from the

progressive nature of changes in stiffness, and interventions longer than 9 weeks may be necessary to induce changes. Additionally, participants did not have clinically diagnosed E/S1H in the current study due to the lack of an in-office clinical measurement (85), and participants were also not required to complete their screening visit at the same time as the first experimental visit. However, it should be noted that all participants had a BP consistent with E/S1H classification at both their screening and first experimental visit. There was also no change from pre- to post-intervention among individuals in CON who all still had a BP consistent with E/S1H classification at post-testing. Together, these serve to validate the E/S1H classification of the individuals included in this study. Lastly, we did not conduct regular check-ins with CON throughout the intervention period, which would have assisted with ensuring protocol compliance. However, all participants in CON confirmed compliance at the end of the study, and this is supported by a lack of significant changes from pre- to post-intervention in the CON group in this study.

The current study indicates that 9 weeks of RET performed in accordance with the current exercise guidelines for individuals with E/S1H is effective for lowering BP to a degree consistent with the effects that may be expected by prescription of BP lowering medications (41). These improvements were observed alongside a decrease in TPR and an increase in vascular endothelial function, as measured by the FMD technique. Moreover, we observed no effects of RET on central arterial stiffness or cardiovagal function. Therefore, our findings suggest habitual RET lowers BP and improves vascular endothelial function among MA/O adults with E/S1H. Future studies should continue to investigate the acute and long-term effects of RET on BP and vascular function, as well as the influence of training status to better understand the potential discrepancies in the literature regarding RET and central arterial stiffening.

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AUTHOR CONTRIBUTION STATEMENT

The study was conceptualized and planned by NFB, AES, KMW, and NDMJ. Data collection and entry was completed by NFB and EMR. Data analysis was performed by NFB, EMR, and NDMJ. NFB was the primary creator of all figures and tables. NFB and NDMJ completed original draft and all authors contributed to review and editing. NFB was responsible for project administration and NDMJ provided resources to complete the project. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

CONFLICTS OF INTEREST

Within the last two years, NFB and EMR have received graduate assistant stipend funding from Woodbolt, LLC. NFB and NDMJ have received grant funding from the National Strength and Conditioning Association Foundation. EMR has received grant funding from the American College of Sports Medicine. NDMJ has received grant funding from the American Heart Association, the Center for Integrative Research on Childhood Adversity (Award P20GM109097 through the NIGMS), the Injury Prevention Research Center (Award R49 CE003095 through the NCIPC/CDC), the National Institutes of Aging through the Research Network on Animal Models

to Understand Social Dimensions of Aging, Woodbolt Distribution, LLC, and Applied Food Sciences, Inc, and has been the recipient of an NIH Clinical Research Loan Repayment Award. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. AES and KMW declare no conflict of interest.

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FIGURE CAPTIONS

Figure 1. Overview of the experimental design. In week 1, load (10RM) for the prescribed repetitions was determined based on baseline strength testing. During weeks 2 and 3, loads (12RM) were initially determined by baseline strength testing and adjusted (+5–10%) whenever participants felt they could complete 2 repetitions more than prescribed on the final set of each exercise. During weeks 4–9, participants completed as many repetitions as possible during their final set of each exercise. Whenever a participant completed 2 or more repetitions than prescribed for 2 consecutive training sessions, the load was increased 5–10% for the next exercise training session (e.g., 2+2 rule). Created with BioRender.com.

Figure 2. Peripheral systolic blood pressure (SBP), peripheral diastolic blood pressure (DBP), central SBP (cSBP), central DBP (cDBP), mean arterial pressure (MAP), and pulse pressure (PP) collected prior to and following either 9 weeks of resistance exercise training (RET) or a non-exercise control period (CON). All data are displayed as estimated marginal means (± 95% CI). * = significant within-group decrease from T0 to T1 ($p \leq 0.05$); † = significantly lower in RET at T1 than in CON at T0; # = significantly lower in RET at T1 than in CON at T1 ($p \leq 0.05$).

Figure 3. Resting cardiac output (CO) and total peripheral resistance (TPR) collected prior to and following either 9 weeks of resistance exercise training (RET) or a non-exercise control period (CON). All data are displayed as estimated marginal means (± 95% CI). * = significant within-group increase from T0 to T1 ($p \leq 0.05$).

Figure 4. Percent flow-mediated dilation (FMD), FMD corrected to shear rate ($cFMD_{SR}$), reactive hyperemia (RH), and baseline blood flow (BF_{base}) collected prior to and following either 9 weeks of resistance exercise training (RET) or a non-exercise control period (CON). All data are displayed as estimated marginal means (± 95% CI). * = significant within-group increase from T0 to T1 ($p \leq 0.05$); # = significant difference between RET and CON at T1 ($p \leq 0.05$).

Figure 5. Relations between the changes (Δ) in **A**: SBP and flow-mediated dilation (FMD); **B**: SBP and FMD corrected for shear rate stimulus ($cFMD_{SR}$); **C**: systolic blood pressure (SBP) and resting brachial artery diameter (D_{base}); **D**: SBP and resting blood flow (BF_{base}); **E**: total peripheral resistance (TPR) and D_{base}; **F**: TPR and cardiovagal baroreflex sensitivity down (BRS_{down}); **G**: cardiac output (CO) and fat-free mass (FFM); and **H**: pulse wave velocity (PWV) and pulse pressure (PP) following a 9-week RT program (RET; yellow filled circles) or non-exercise control period (CON; dark grey filled circles). Note that relations between CO versus FFM and PWV versus PP are depicted as rank correlations due to non-normality of residuals. Inset text boxes also display partial correlation coefficients ($r_{xy,z}$ or $\rho_{xy,z}$) for the relation with the effect of sex removed.

Table 1. Baseline Participant Characteristics

	RET (n=13; 5M/8F)	CON (n=13; 5M/8F)
Age (y)	52 (6)	55 (6)
Height (cm)	171.5 (10.5)	171.5 (7.4)
Weight (kg)	84.6 (9.7)	81.3 (15.5)
BMI (kg/m^2)	29.9 (4.2)	28.0 (4.3)
Post-Menopausal (n)	6	6
Years Post-Menopause (y)	6 (7)	8 (4)
Race		
White (n)	11	11
Asian (n)	1	1
Black (n)	1	1
Elevated Blood Pressure		
Participants (n)	4	5
SBP (mmHg)	122 (1)	125 (3)
DBP (mmHg)	73 (9)	74 (9)
Stage 1 Hypertension		
Participants (n)	9	8
SBP (mmHg)	130 (5)	133 (6)
DBP (mmHg)	84 (3)	85 (8)

All data are displayed as mean (SD); BMI = body mass index; CON = control group; RET = resistance training group.

Table 2. The effect of resistance exercise versus control on body composition and muscle strength

	RET (n=13; 8F/5M)		CON (n=13; 8F/5M)		Group × Visit		Group		Visit	
	T0	T1	T0	T1	*p*	η_p^2	*p*	η_p^2	*p*	η_p^2
Weight (kg)	86.3 (6.1)	87.0 (6.1)	83.0 (6.1)	82.9 (6.1)	0.21	0.07	0.37	0.03	0.99	<0.01
FFM (kg)	55.6 (3.2)	56.2 (3.2)	51.8 (3.2)	52.2 (3.2)	0.66	<0.02	0.08	0.13	0.65	<0.01
FM (kg)	30.6 (4.7)	30.8 (4.7)	31.1 (4.7)	30.7 (4.7)	0.41	0.03	0.95	<0.01	0.66	<0.01
BF (%)	35.6 (3.6)	37.4 (3.6)	37.4 (3.6)	36.9 (3.6)	0.61	0.01	0.51	0.02	0.39	0.03
Squat 1RM (kg)	175.3 (21)	255.2 (21)$^{\#\dagger\ddagger}$	169.1 (21)	175.5 (21)	<0.001*	0.81	-	-	-	-
Bench 1RM (kg)	34.2 (7.9)	56.4 (7.9)	25.2 (7.9)	25.5 (7.9)	<0.001*	0.85	-	-	-	-

All data are displayed as estimated means (± model 95% CI); *significant interaction effect ($p \leq 0.05$); $^{\#}$significant within-group increase from T0 to T1 ($p \leq 0.05$); †significantly greater than in CON at T0 ($p \leq 0.05$); ‡significantly greater than in CON at T1 ($p \leq 0.05$); CON = non-exercise control group, RET = resistance exercise training group, FFM = fat free mass, FM = fat mass, BF = body fat, 1RM = estimated one repetition maximum.

Table 3. The effect of resistance exercise versus control on central arterial stiffness, vascular function and reactive hyperemia, inflammation, and autonomic function

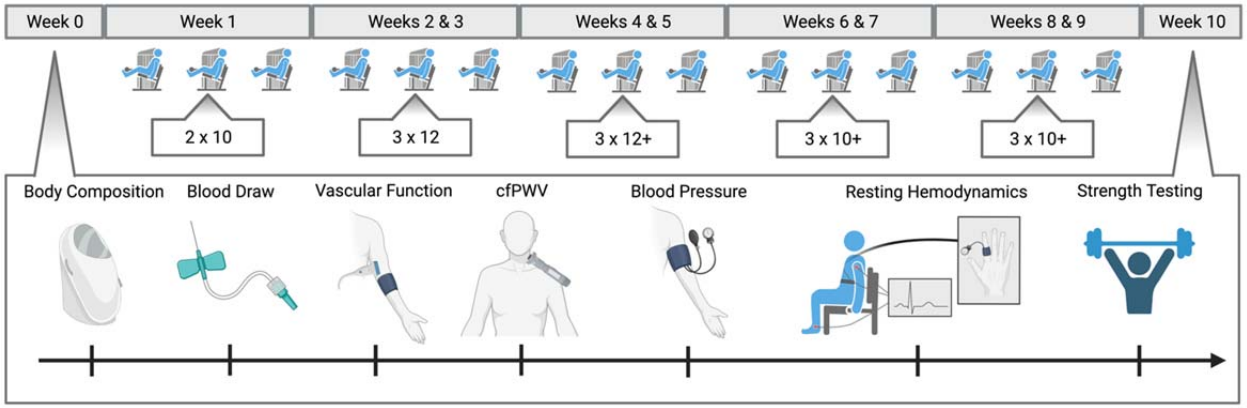
	RET (n=13; 8F/5M)		CON (n=13; 8F/5M)		Group × Visit		Group		Visit	
	T0	T1	T0	T1	*p*	η_p^2	*p*	η_p^2	*p*	η_p^2
cfPWV (m/s)	7.0 (0.5)	6.8 (0.6)	7.3 (0.6)	7.2 (0.5)	0.20	0.07	0.72	<0.01	0.23	0.07
D_{base} (mm)	3.53 (0.2)	3.64 (0.2)	3.76 (0.2)	3.73 (0.2)	0.07	0.14	0.22	0.06	0.39	0.03
FMD_{abs} (mm)	0.24 (0.1)	0.33 (0.1)$^{\#\dagger\ddagger}$	0.20 (0.1)	0.21 (0.1)	0.006*	0.29	-	-	-	-
SR_{base} (s^{-1})	164.9 (40.2)	202.0 (40.2)	165.9 (40.2)	192.3 (40.2)	0.73	<0.01	0.81	<0.01	0.71	<0.01
SR_{peak} (s^{-1})	1044.8 (140)	1031.3 (140)	937.2 (140)	1003.9 (140)	0.32	0.04	0.46	0.03	0.69	<0.01
SR_{AUC} ($au \cdot 10^{-3}$)	2.04 (0.5)	2.17 (0.5)	2.11 (0.5)	2.11 (0.5)	0.58	0.01	0.99	<0.01	0.93	<0.01
CRP (mg/L)	3.16 (1.4)	2.17 (1.3)	2.23 (1.4)	2.25 (1.3)	0.33	0.05	0.39	0.04	0.75	<0.01
BRS_{pooled} (ms/mmHg)	5.83 (1.1)	5.87 (1.1)	5.22 (1.1)	5.14 (1.1)	0.81	<0.01	0.37	0.03	0.12	0.10
BRS_{up} (ms/mmHg)	5.67 (1.2)	5.60 (1.2)	4.72 (1.2)	5.24 (1.2)	0.39	0.03	0.41	0.03	0.47	0.02
BRS_{down} (ms/mmHg)	6.19 (1.2)	5.98 (1.2)	5.41 (1.2)	5.01 (1.2)	0.78	<0.01	0.25	0.06	0.28	0.05
lnRMSSD (ms)	3.18 (0.2)	3.09 (0.2)	3.08 (0.2)	2.97 (0.2)	0.92	<0.01	0.43	0.03	0.22	0.07
lnLF (ms^2)	5.21 (0.7)	4.97 (0.7)	5.09 (0.7)	4.65 (0.7)	0.63	0.01	0.60	0.01	0.37	0.04
lnHF (ms^2)	4.78 (0.6)	4.32 (0.6)	4.24 (0.6)	4.10 (0.6)	0.32	0.04	0.28	0.05	0.11	0.11
RHR (bpm)	68.9 (5.1)	70.2 (5.1)	71.8 (5.1)	72.1 (5.1)	0.65	<0.01	0.48	0.02	0.66	<0.01

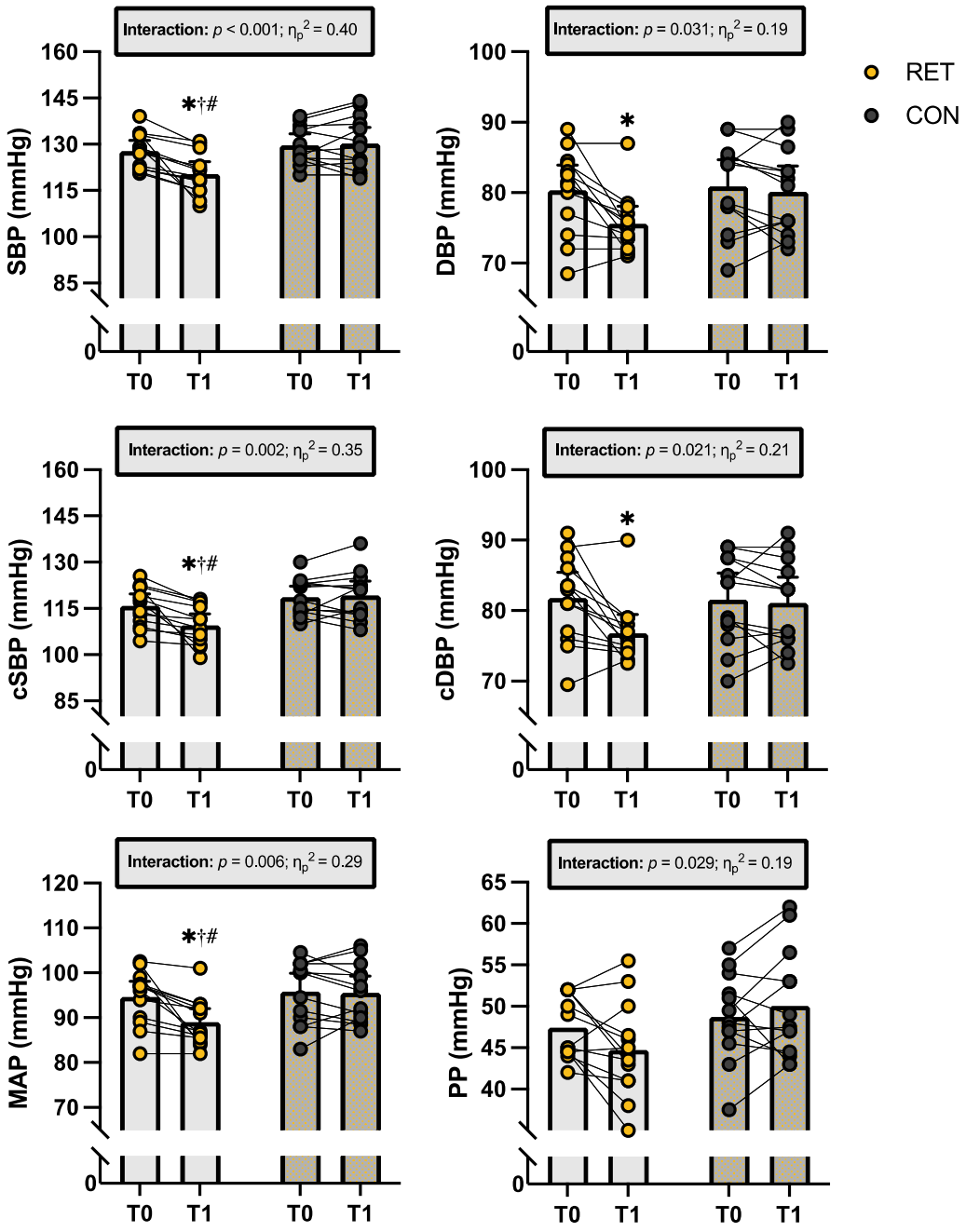
All data are displayed as mean (± 95% CI); *significant interaction effect ($p \leq 0.05$); $^{\#}$significant within-group increase from T0 to T1 ($p \leq 0.05$); †significantly greater than in CON at T0 ($p \leq 0.05$); ‡significantly greater than in CON at T1 ($p \leq 0.05$); AUC = area under the curve, BRS = cardiovagal baroreflex sensitivity, CON = non-exercise control group, RET = resistance exercise training group, D_{base} = baseline diameter, D_{max} = maximal diameter after cuff release, lnRMSSD = log transformed root mean square of successive differences, lnHF = log transformed high frequency power, lnLF = log transformed low frequency power, RHR = resting heart rate, SR = shear rate

Table 4. Dietary and physical activity control data pre- and post-intervention in the resistance exercise and control groups

	RET (n=13; 8F/5M)		CON (n=13; 8F/5M)		Group × Visit		Group		Visit	
	T0	T1	T0	T1	*p*	η_p^2	*p*	η_p^2	*p*	η_p^2
Physical Activity (MET·min/week)	395.7 (148)	406.2 (148)	445.2 (148)	472.3 (149)	0.58	0.01	0.65	<0.01	0.46	0.02
Calories (kcal)	2135.7 (272)	2161.8 (272)	1995.9 (272)	2027.5 (272)	0.95	<0.01	0.45	0.03	0.62	0.01
Carbohydrate (g)	224.4 (34.3)	226.7 (34.3)	185.6 (34.3)	198.3 (34.3)	0.53	0.02	0.14	0.09	0.42	0.03
Protein (g)	101.5 (15.7)	98.8 (15.7)	97.6 (15.7)	104.0 (15.7)	0.22	0.06	0.95	<0.01	0.35	0.04
Fat (g)	92.6 (17.1)	96.1 (17.1)	97.6 (17.1)	94.5 (17.1)	0.44	0.03	0.87	<0.01	0.67	<0.01

All data are displayed as estimated marginal mean (± model 95% CI); CON = non-exercise control group, RET = resistance exercise training group, MET = metabolic equivalent of task


Week 0
Week 1
Weeks 2 & 3
Weeks 4 & 5
Weeks 6 & 7
Weeks 8 & 9
Week 10
2 x 10
3 x 12
3 x 12+
3 x 10+
3 x 10+
Body Composition
Blood Draw
Vascular Function
cfPWV
Blood Pressure
Resting Hemodynamics
Strength Testing


Interaction: p < 0.001; ηp2 = 0.40
SBP (mmHg)
160
145
130
115
100
85
0
*†#
T0
T1
T0
T1
Interaction: p = 0.031; ηp2 = 0.19
DBP (mmHg)
100
90
80
70
0
*
T0
T1
T0
T1
RET
CON
Interaction: p = 0.002; ηp2 = 0.35
cSBP (mmHg)
160
145
130
115
100
85
0
*†#
T0
T1
T0
T1
Interaction: p = 0.021; ηp2 = 0.21
cDBP (mmHg)
100
90
80
70
0
*
T0
T1
T0
T1
Interaction: p = 0.006; ηp2 = 0.29
MAP (mmHg)
120
110
100
90
80
70
0
*†#
T0
T1
T0
T1
Interaction: p = 0.029; ηp2 = 0.19
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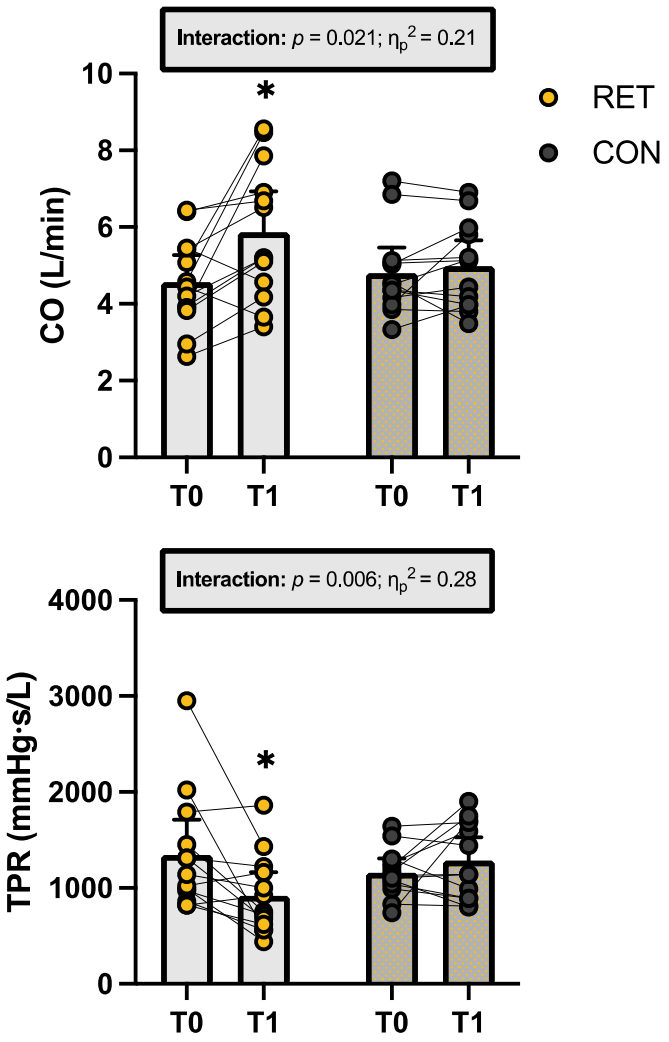
55
50
45
40
0
T0
T1
T0
T1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RET
CON
CO (L/min)
10
8
6
4
2
0
*
T0
T1
T0
T1
Interaction: p = 0.006; η_p^2 = 0.28
TPR (mmHg·s/L)
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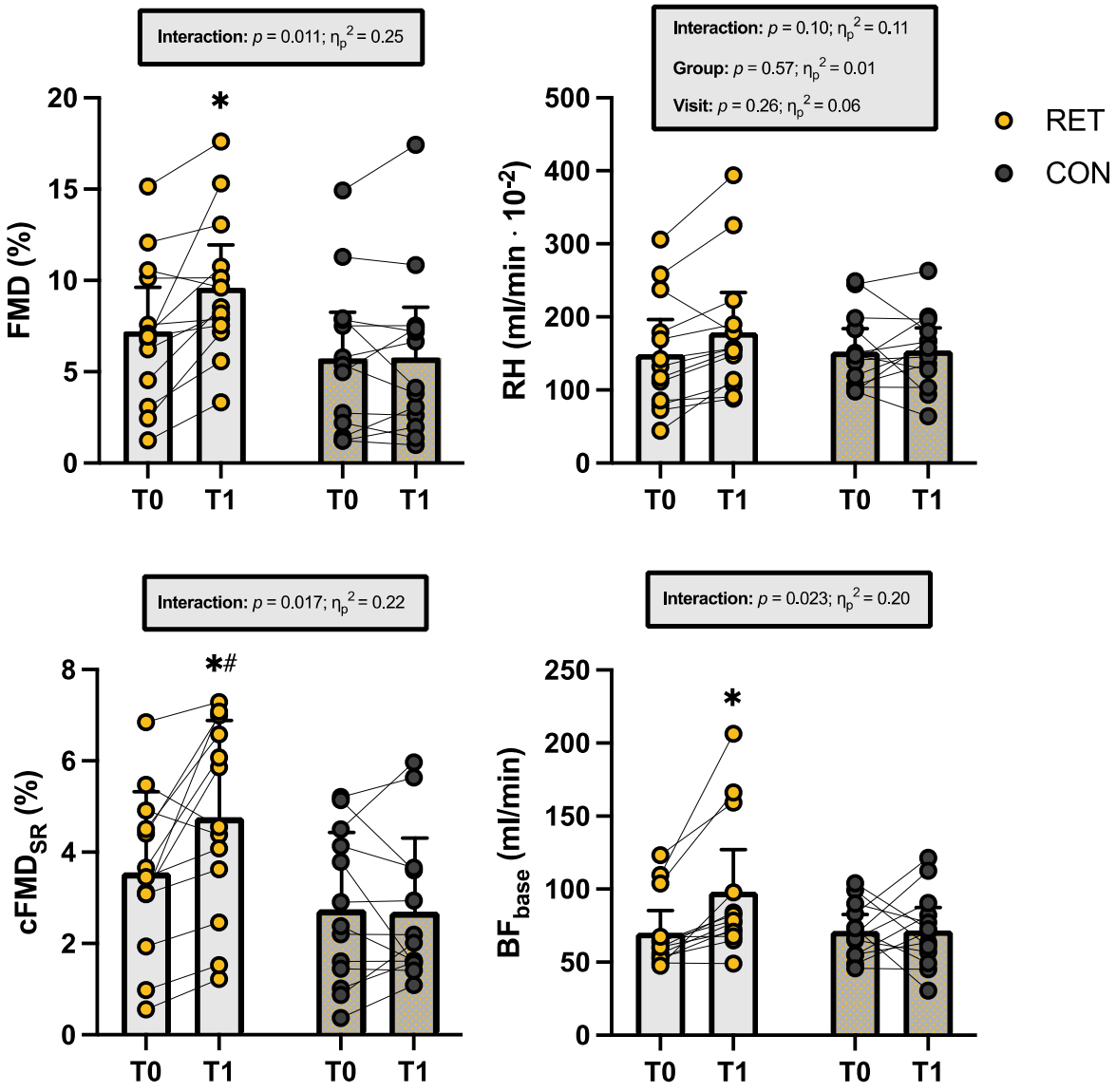
3000
2000
1000
0
*
T0
T1
T0
T1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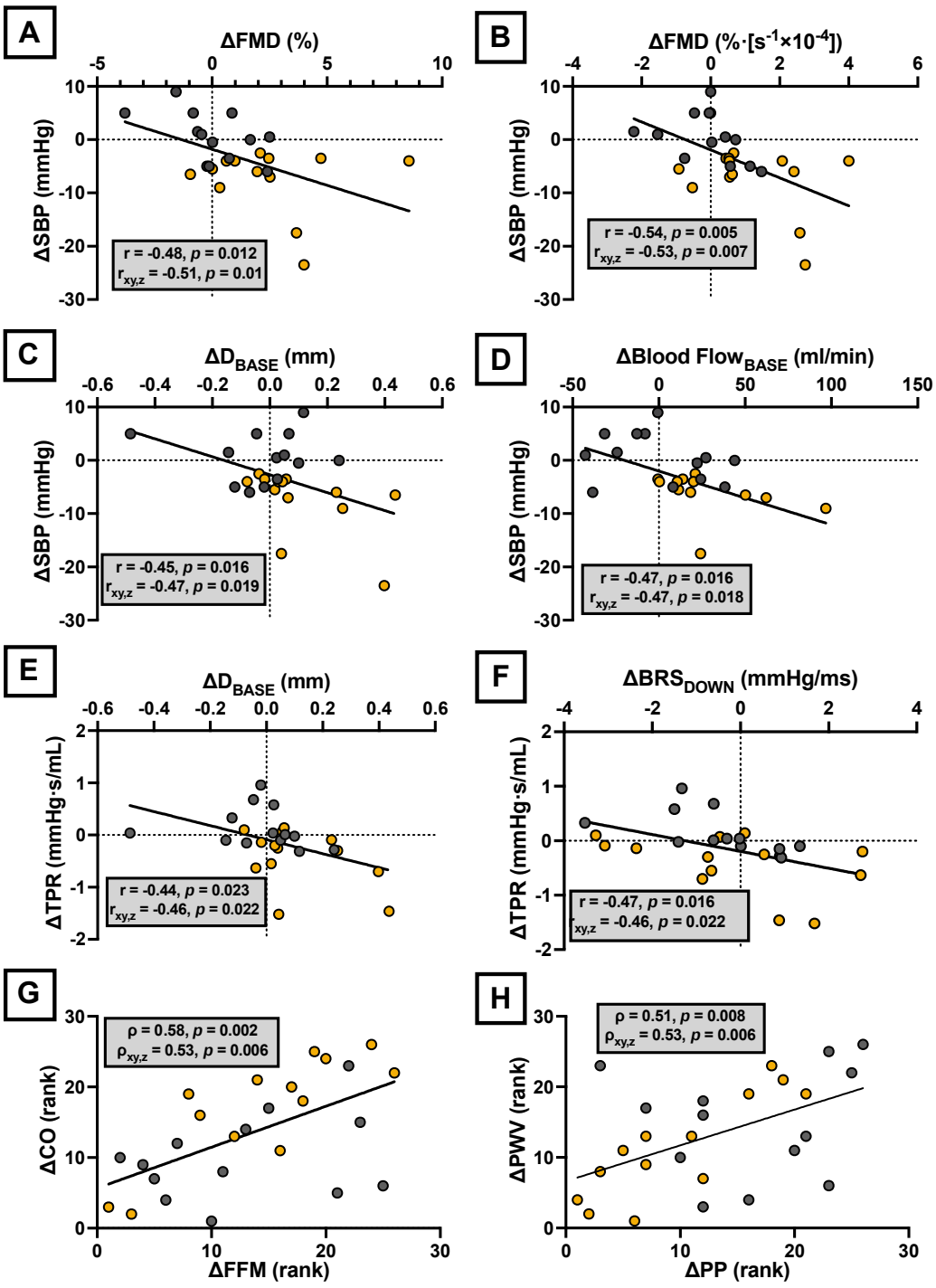
FMD (%)
20
15
10
5
0
*
T0
T1
T0
T1
Interaction: p = 0.10; ηp² = 0.11
Group: p = 0.57; ηp² = 0.01
Visit: p = 0.26; ηp² = 0.06
RH (ml/min · 10-2)
500
400
300
200
100
0
T0
T1
T0
T1
RET
CON
Interaction: p = 0.017; ηp² = 0.22
cFMDSR (%)
8
6
4
2
0
*#
T0
T1
T0
T1
Interaction: p = 0.023; ηp² = 0.20
BFbase (ml/min)
250
200
150
100
50
0
*
T0
T1
T0
T1


A
ΔFMD (%)
ΔSBP (mmHg)
r = -0.48, p = 0.012
r_xy,z = -0.51, p = 0.01
B
ΔFMD (%·[s^-1×10^-4])
ΔSBP (mmHg)
r = -0.54, p = 0.005
r_xy,z = -0.53, p = 0.007
C
ΔD_BASE (mm)
ΔSBP (mmHg)
r = -0.45, p = 0.016
r_xy,z = -0.47, p = 0.019
D
ΔBlood Flow_BASE (ml/min)
ΔSBP (mmHg)
r = -0.47, p = 0.016
r_xy,z = -0.47, p = 0.018
E
ΔD_BASE (mm)
ΔTPR (mmHg·s/mL)
r = -0.44, p = 0.023
r_xy,z = -0.46, p = 0.022
F
ΔBRS_DOWN (mmHg/ms)
ΔTPR (mmHg·s/mL)
r = -0.47, p = 0.016
r_xy,z = -0.46, p = 0.022
G
ρ = 0.58, p = 0.002
ρ_xy,z = 0.53, p = 0.006
ΔCO (rank)
ΔFFM (rank)
H
ρ = 0.51, p = 0.008
ρ_xy,z = 0.53, p = 0.006
ΔPWV (rank)
ΔPP (rank)