

## ORIGINAL ARTICLE

# Resistance exercise training reduces arterial reservoir pressure in older adults with prehypertension and hypertension

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We examined changes in central blood pressure (BP) following resistance exercise training (RET) in men and women with prehypertension and never-treated hypertension. Both Windkessel theory and wave theory were used to provide a comprehensive examination of hemodynamic modulation with RET. Twenty-one participants (age  $61 \pm 1$  years,  $n=6$  male; average systolic blood pressure (SBP)/diastolic blood pressure (DBP) = 138/84 mm Hg) were randomized to either 12 weeks of RET ( $n=11$ ) or an inactive control group. Central BP and augmentation index (AIx) were derived from radial pressure waveforms using tonometry and a generalized transfer function. A novel reservoir-wave separation technique was used to derive excess wave pressure (related to forward and backward traveling waves) and reservoir pressure (related to the capacitance/Windkessel properties of the arterial tree). Wave separation using traditional impedance analysis and aortic flow triangulation was also applied to derive forward wave pressure (Pf) and backward wave pressure (Pb). There was a group-by-time interaction ( $P<0.05$ ) for central BP as there was a significant  $\sim 6$  mm Hg reduction in SBP and  $\sim 7$  mm Hg reduction in DBP following RET with no change in the control condition. There were also group-by-time interactions ( $P<0.05$ ) for Pf, excess wave pressure and reservoir pressure attributable to reductions in these parameters in the RET group concomitant with slight increases in the control group. There was no change in AIx or Pb ( $P>0.05$ ). RET may reduce central BP in older adults with hypertension and prehypertension by lowering Pf and reservoir pressure without affecting pressure from wave reflections.

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**Keywords:** augmentation index; blood pressure; exercise; hemodynamic

## INTRODUCTION

Although aerobic/endurance exercise has repeatedly been shown to reduce blood pressure (BP) in numerous cohorts,<sup>1</sup> resistance exercise training (RET) still remains an understudied and underappreciated exercise modality for BP modification. RET is currently recommended for general health promotion in persons with cardiovascular (CV) disease<sup>2</sup> and several studies note modest but clinically significant reductions in brachial BP with RET.<sup>3</sup> Yet despite these favorable reductions in BP, current professional guidelines do not acknowledge RET as a therapeutic option for the management of hypertension in older adults.<sup>4</sup>

RET may reduce central BP (that is carotid, aortic),<sup>5,6</sup> and this is important given that central BP is more predictive of target organ damage, CV morbidity and CV mortality compared with traditionally measured brachial BP.<sup>7–10</sup> The change in contour of the central BP

waveform with aging and in the presence of hypertension is due to a number of hemodynamic factors including increased forward wave pressure (Pf), increased pressure from wave reflections, increased arterial impedance and reduced arterial compliance.<sup>11,12</sup> The capacitance or Windkessel function of the large central arteries (that is the arterial reservoir) also has a significant role in modulating central BP with aging.<sup>13,14</sup> During left ventricular contraction, blood enters the aorta faster than it can leave; this increasing volume distends the aorta, increasing the reservoir pressure.<sup>13</sup> With advancing age and subsequent loss of arterial compliance, pressure in the arterial reservoir rises more rapidly for a similar increase in volume, having a significant impact on central BP.<sup>13</sup> An examination of this novel hemodynamic parameter may lead to greater understanding of the mechanism(s) responsible for BP reduction with RET, whereas simultaneously providing much needed

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exculpatory evidence on the use of RET to abrogate CV risk in at-risk cohorts such as older adults with prehypertension.

Current estimates suggest that 70 million Americans are prehypertensive.<sup>15,16</sup> Prehypertensive individuals are 11 times more likely to develop hypertension,<sup>17</sup> increasing CV risk substantially.<sup>18,19</sup> Moreover, preferential elevation of central BP in prehypertensive adults represents an intermediate phenotype in the pathogenesis of hypertension,<sup>20</sup> as it is well established that individuals with hypertension have elevated central BP.<sup>21</sup> Efficacy of RET to reduce central BP in prehypertensive and hypertensive older adults and the mechanisms by which it may do so merits further scrutiny.

The purpose of this study was to examine the effect of RET on central BP in older adults with prehypertension and newly diagnosed/never-treated hypertension. We sought to interrogate changes in the contour of the BP waveform using two different complementary hemodynamic theories: (1) reservoir theory (lumped-parameter model that examines the interaction of capacitance, compliance and resistance on the arterial system) and (2) wave-only theory (examines the interaction of outgoing/forward traveling pressure waves from the heart and reflected/backward traveling pressure waves from peripheral bifurcations and arterioles). Combining these approaches will allow for a comprehensive examination of pulse contour changes with RET. On the basis of our previous work<sup>5,6</sup> we hypothesized that RET would reduce central BP in prehypertensive and hypertensive men and women, and this would be related to a reduction in arterial reservoir pressure and not pressure from wave reflections.

## METHODS

### Subjects

Prehypertensive ( $n=11$ ) and newly diagnosed/never-treated hypertensive ( $n=10$ ) older adults participated in this study. All subjects were non-smokers and did not have any known CV, metabolic or inflammatory diseases, nor use CV medications or anti-inflammatory substances of any kind. None engaged in regular aerobic or resistance exercise. The subjects were randomly assigned to either 12 weeks of RET ( $n=11$ ) or an inactive control group ( $n=10$ ). The subjects were informed of the experimental procedures and possible risks involved in the present study, their right to withdraw from the study at any time and the measures taken to protect privacy. Written consent was obtained from all participants and all aspects of this study were conducted in accordance with ethical standards laid down in the Declaration of Helsinki.

### Study design

Previous work has noted reductions in central BP following RET of  $\sim 6$  mm Hg (effect size = 0.5) in older prehypertensive adults.<sup>5</sup> Sample size was thus determined from this study with the goal of seeing a similar reduction in central BP (power = 0.8 for a one-tailed test). Participants reported to the laboratory following an overnight fast. Hemodynamics were assessed following 15 min of supine rest. This was followed by assessment of body fat using bioelectric impedance analysis (Biospace, Inbody, Seoul Korea). A blood sample was then obtained from venipuncture and analyzed in a clinical laboratory using standard enzymatic techniques for blood lipids, fasting glucose and C-reactive protein. All measures were repeated following the 12-week intervention period.

Following baseline testing only, all participants underwent measurement of 24-hour BP with ambulatory monitoring to corroborate hypertensive status (previously established by repeated physician assessment). An automated ambulatory BP monitor (SpaceLabs 90207, SpaceLabs Medical, Redmond, WA, USA) was used for ambulatory BP measurements; measured every 30 min for daytime and 60 min for nighttime recordings. Discrimination of the daytime and the nighttime was obtained from individual self-reported sleep time. Subjects were encouraged to continue their usual daily activities and sleep patterns during the monitoring period but were instructed to avoid exercise and alcohol consumption.

Treadmill cardiopulmonary exercise testing was performed on a separate day (24 h after BP assessment) using a modified Bruce protocol. Expired gases were collected breath-by-breath using a one-way valve and analyzed using a metabolic cart (Q-stress/Trueone 2400, US). Peak oxygen uptake ( $\text{ml kg}^{-1} \text{min}^{-1}$ ) was defined as the highest value recorded during the test using established criteria and taken as an index of cardiorespiratory fitness.

### Resistance exercise training

RET was supervised by a personal trainer and performed 3 days a week. RET consisted of nine machine-based resistance exercises, four upper body (chest press, latissimus dorsi pulldown, back row, biceps curl), three lower body (leg press, leg extension and leg curl) and two core (abdominal crunch and lower back extension) exercises. The load was initially set at 40% of previously determined 1-RM values for upper body and 60% for lower body exercises in accordance with American Heart Association recommendations.<sup>2</sup> Two sets of 12–15 repetitions were performed during each session. The load was progressively increased by 5% every 3 weeks or when subjects could easily perform 15 repetitions.

### Pulse wave analysis

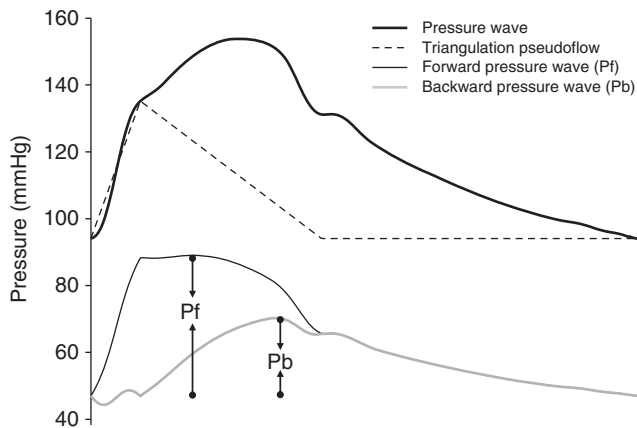
Resting BP was measured in duplicate in the brachial artery using an automated oscillometric device and the average systolic and diastolic values were used for subsequent analyses. Radial artery pressure waveforms were obtained in duplicate from a 10-s epoch using applanation tonometry and a high-fidelity strain-gauge transducer (Millar Instruments, Houston, TX, USA). Using a generalized validated transfer function,<sup>22,23</sup> a central aortic pressure waveform was reconstructed (SphygmoCor, AtCor Medical, Sydney, NSW, Australia). Mean pressure was derived from integrating the area under the central BP waveform. Left ventricular systolic ejection duration was taken as the time from the foot of the pressure wave upstroke to the incisura of the dirotic notch. Augmented pressure was defined as the difference between central systolic blood pressure (SBP) and the pressure at the primary wave peak ( $P_1$ ).  $P_1$  height was defined as the pressure at the first inflection point. Aortic pulse wave travel time (Tr) was determined from the time from the initial upstroke of the pressure wave to  $P_1$ . The systolic pressure tension-time integral and the diastolic pressure tension-time index were quantified to examine systolic-to-diastolic shifts in the proportion of pressure comprising the overall pressure waveform. Augmentation index (AIx) was calculated as the difference between the early- and late-systolic peaks of the arterial waveform to the total pulse pressure (PP) expressed as a percentage ( $(P_2 - P_1)/PP \times 100$ ). The intraclass correlation coefficient calculated for test–retest reproducibility for synthesized aortic SBP and AIx in this laboratory is  $>0.95$ .

The aortic pressure waveform was then separated into its forward (Pf) and reflected (Pb) components to calculate the transit time-independent parameters of wave reflection magnitude using a flow triangulation method as originally proposed by Westerhof *et al.*,<sup>24</sup> and later used by Wang *et al.*<sup>25</sup> Briefly, the shape of the truncated aortic flow wave can be estimated by using a triangular pseudoflow waveform. Flow is assumed to be zero during diastole and thus the flow waveform is constructed from interpolating a line from the timing of the onset of the pressure waveform foot to the inflection point/waveform shoulder (signaling arrival of the reflected pressure wave and approximating timing of peak aortic outflow) to end systole or the incisura of the dirotic notch (Figure 1). The forward and backward components of the pressure wave were constructed using the following equations:

$$Pf(t) = [Pm(t) + Zc \times F(t)]/2 \quad (1)$$

$$Pb(t) = [Pm(t) - Zc \times F(t)]/2 \quad (2)$$

where  $Pm(t)$  is the synthesized aortic pressure wave,  $F(t)$  is the approximated triangular-shaped flow wave,  $Pf(t)$  is the forward pressure component, and  $Pb(t)$  is the backward pressure component (Figure 1). Because calculation of Pf and Pb involves the product of flow and characteristic impedance ( $Zc$ ), which itself has flow in the denominator, calibration of the flow waveform is not needed (that is independent of flow calibration).<sup>24,25</sup> Pf and Pb are the pressure amplitudes of  $Pf(t)$  and  $Pb(t)$ , respectively. For a detailed description of wave separation and impedance analyses, the reader is referred to the original works and reviews cited herein.<sup>26–29</sup> The reflection index, analogous to the AIx and



**Figure 1** Sample wave separation using impedance analysis and a pseudoflow waveform approximated via triangulation from a central pressure waveform.

defined as the ratio of the reflected wave to the sum of the forward and reflected wave was calculated as the ratio of  $P_b/P_f + P_b \times 100$ .<sup>24,25</sup>  $P_f$  and  $P_b$  determined from this technique have previously been shown to be similar to values obtained using true aortic flow waves via invasive and non-invasive recordings.<sup>24,25</sup>

When aortic inflow exceeds outflow, the aorta is distended causing a rise in pressure. This arterial reservoir pressure was calculated by separating the aforementioned radial pressure waves into two components by iteration of the equation (below) and by fitting a monoexponential function to the falling pressure during diastole.<sup>13,30</sup>

$$P_{\text{reservoir}} - P_{\infty} = e^{-(a+b)t} \int_0^t [aP(t') + bP_{\infty}] e^{(a+b)t'} dt' + (P_d - P_{\infty}) e^{-(a+b)t}$$

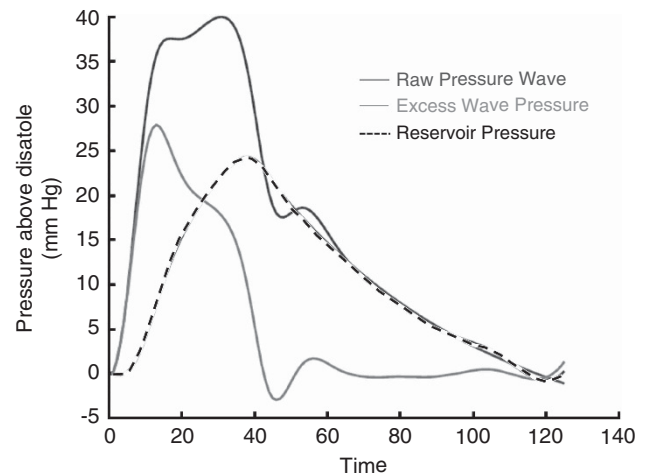
The excess wave pressure (pressure attributed to forward and backward traveling waves) was derived by the subtraction of arterial reservoir pressure from total pressure (Figure 2).<sup>31</sup> These waveform components provide information that is incremental to SBP and diastolic blood pressure (DBP)–time integrals. All of the reservoir and excess wave pressures are quoted with DBP subtracted.  $P_{\text{reservoir}}$  is reservoir pressure,  $P_{\infty}$  is the asymptotic pressure,  $P_d$  is the measured DBP at  $t=0$ ,  $b=1/RC$ , where  $R$ =resistance and  $C$ =compliance of the system;  $a$  is a rate constant that can be determined by fitting during the diastolic period.

### Statistical analysis

The average values obtained from the two radial measures was used for all subsequent analyses. Baseline comparisons were made using analysis of variance for continuous variables and  $\chi^2$ -tests for categorical variables. Analysis of variance with repeated measures (2 groups  $\times$  2 time points) was used to analyze the main outcome variables. If significant group-by-time interactions were detected, *post hoc* comparisons were made with *t*-tests. Analysis of covariance with repeated measures was also performed with sex as a covariate. Associations of interest were examined using Pearson's and Spearman's correlation coefficients. Change scores were computed as postvalues—prevalues. All statistical analyses were performed at the 0.05 level of significance and carried out by using IBM SPSS version 19 (IBM, Chicago, IL, USA).

## RESULTS

All participants successfully completed the exercise intervention (compliance to sessions >90%) without any CV complications. There were no group differences in age, sex (RET:  $n=2$  men *vs.* Control:  $n=4$ men;  $P>0.05$ ) or 24-hour BP at baseline (Table 1). Prevalence of hypertension ( $n=5$  per group) and prehypertension ( $n=6$  in RET



**Figure 2** Example of the reservoir wave separation technique obtained from a peripheral (radial) pressure waveform. Values are expressed after subtracting DBP.

**Table 1** Subject descriptive characteristics

Variable	RET	Control
Age (years)	60 $\pm$ 2	63 $\pm$ 2
Height (m)	1.6 $\pm$ 0.02	1.6 $\pm$ 0.02
<i>Ambulatory 24-h BP</i>		
SBP mean (mm Hg)	135 $\pm$ 5	136 $\pm$ 5
SBP day (mm Hg)	141 $\pm$ 5	140 $\pm$ 5
SBP night (mm Hg)	130 $\pm$ 5	132 $\pm$ 5
DBP mean (mm Hg)	81 $\pm$ 3	84 $\pm$ 3
DBP day (mm Hg)	84 $\pm$ 3	86 $\pm$ 3
DBP night (mm Hg)	78 $\pm$ 3	81 $\pm$ 3

Abbreviations: BP, blood pressure; DBP, diastolic blood pressure; RET, resistance exercise training; SBP, systolic blood pressure.

*vs.* 5 in control) was similar between groups ( $P>0.05$ ). RET significantly increased muscular strength (1-RM) for all exercises (data not shown,  $P<0.05$ ) confirming a training effect. There was no change in muscular strength in the control group or cardiorespiratory fitness in either group ( $P>0.05$ ).

There were similar reductions in glucose in both RET and control groups (Table 2,  $P<0.05$ ). A group-by-time interaction was detected for low-density lipoprotein cholesterol ( $P<0.05$ ) as there was a nonsignificant increase in LDL-cholesterol in the RET group ( $P>0.05$ ) coupled with a non-significant reduction in low-density lipoprotein cholesterol in the control group ( $P>0.05$ ).

There were no baseline group differences in any hemodynamic parameter ( $P>0.05$ ). There were significant reductions in brachial SBP, aortic SBP and mean pressure in the RET group compared with the control group (Table 3,  $P<0.05$ ). Group-by-time interactions were also detected for primary wave pressure ( $P_1$ ) height,  $P_f$ , excess wave pressure and reservoir pressure (Table 3,  $P<0.05$ ) as there were reductions in the RET group coupled with slight increases in the control group ( $P<0.05$  for all). There were no significant changes in augmented pressure,  $Tr$ ,  $Alx$ ,  $P_b$  or reflection index ( $P>0.05$ ). Adjusting for changes in low-density lipoprotein cholesterol, and/or glucose with analysis of covariance had no effect on aforementioned

**Table 2** Change in CV risk factors and metabolic parameters

Variable	RET		Control	
	Pre	Post	Pre	Post
Body mass index (kg m <sup>-2</sup> )	24 ± 1	24 ± 1	26 ± 1	26 ± 1
Body fat (%)	30 ± 2	30 ± 2	31 ± 2	31 ± 2
VO <sub>2</sub> max (ml kg <sup>-1</sup> min <sup>-1</sup> )	27 ± 6	28 ± 5	23 ± 4	23 ± 4
Glucose (mg dL <sup>-1</sup> ) <sup>a</sup>	102 ± 11	97 ± 8	104 ± 12	95 ± 8
Total cholesterol (mg dL <sup>-1</sup> )	233 ± 11	245 ± 10	212 ± 11	208 ± 11
LDL cholesterol (mg dL <sup>-1</sup> ) <sup>b</sup>	141 ± 11	151 ± 10	134 ± 12	122 ± 11
HDL cholesterol (mg dL <sup>-1</sup> )	57 ± 5	61 ± 4	51 ± 5	53 ± 4
Triglycerides (mg dL <sup>-1</sup> )	148 ± 22	146 ± 23	130 ± 23	124 ± 24
C-reactive protein (mg dL <sup>-1</sup> )	0.71 ± 0.45	0.30 ± 0.28	1.11 ± 0.48	0.84 ± 0.30

Abbreviations: CV, cardiovascular; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RET, resistance exercise training; VO<sub>2</sub>max, maximal oxygen uptake.

<sup>a</sup>Time effect ( $P < 0.05$ ).

<sup>b</sup>Group-by-time interaction ( $P < 0.05$ ).

**Table 3** Change in pressure waveform parameters

Variable	RET		Control	
	Pre	Post	Pre	Post
Brachial SBP (mm Hg) <sup>a</sup>	140 ± 4	134 ± 4	136 ± 4	139 ± 4
Brachial DBP (mm Hg) <sup>b</sup>	83 ± 2	77 ± 2	86 ± 2	82 ± 2
Aortic SBP (mm Hg) <sup>a</sup>	134 ± 5	129 ± 4	130 ± 5	133 ± 4
Aortic DBP (mm Hg) <sup>b</sup>	84 ± 2	77 ± 2	87 ± 2	84 ± 2
Mean pressure (mm Hg) <sup>a,b</sup>	106 ± 3	99 ± 3	105 ± 3	105 ± 3
Primary wave height (mm Hg) <sup>a</sup>	32 ± 2	30 ± 2	28 ± 2	30 ± 2
Augmented pressure (mm Hg)	18 ± 2	20 ± 2	17 ± 2	19 ± 2
Augmentation index (%)	36 ± 3	38 ± 3	37 ± 3	36 ± 3
Systolic ejection duration (ms)	337 ± 7	336 ± 5	346 ± 7	343 ± 6
Time to reflection (ms)	135 ± 3	132 ± 3	136 ± 3	137 ± 3
Systolic TTI (AUC) <sup>a</sup>	2552 ± 84	2397 ± 83	2465 ± 93	2483 ± 92
Diastolic TTI (AUC) <sup>a</sup>	3781 ± 114	3538 ± 109	3803 ± 119	3829 ± 114
Pf (mm Hg) <sup>a</sup>	33 ± 2	30 ± 2	29 ± 2	32 ± 2
Pb (mm Hg)	20 ± 2	21 ± 2	18 ± 2	20 ± 2
Reflection index (%)	38 ± 3	39 ± 4	39 ± 5	38 ± 4
Reservoir pressure (mm Hg) <sup>a</sup>	34 ± 2	31 ± 2	32 ± 2	35 ± 2
Excess wave pressure (mm Hg) <sup>a</sup>	37 ± 3	34 ± 3	35 ± 3	39 ± 3

Abbreviations: AUC, area under the curve; DBP, diastolic blood pressure; Pb, backward wave pressure; Pf, forward wave pressure; RET, resistance exercise training; SBP, systolic blood pressure; TTI, tension-time integral.

<sup>a</sup>Group-by-time interaction ( $P < 0.05$ ).

<sup>b</sup>Time effect ( $P < 0.05$ ).

changes in hemodynamic parameters. Adjusting for sex also had no effect on aforementioned group-by-time interactions.

Change in aortic systolic pressure was associated with change in  $P_1$  height ( $r = 0.56$ ,  $P < 0.05$ ), change in Pf ( $r = 0.73$ ,  $P < 0.05$ ), change in excess wave pressure ( $r = 0.67$ ,  $P < 0.05$ ) and change in reservoir pressure ( $r = 0.80$ ,  $P < 0.05$ ) but not change in AIx ( $r = 0.04$ ,  $P > 0.05$ ), reflection index ( $r = 0.02$ ,  $P > 0.05$ ) or Pb (0.26,  $P > 0.05$ ).

Change in aortic DBP was associated with change in reservoir pressure only ( $r = 0.46$ ,  $P < 0.05$ ). Change in aortic DBP was not associated with change in  $P_1$  height, excess wave pressure, Pf, Pb, AIx or reflection index ( $P > 0.05$  for all).

## DISCUSSION

Consistent with previous reports, we noted that RET had a favorable effect on BP, lowering both absolute brachial and aortic SBP and DBP by 6–7 mm Hg.<sup>5,6</sup> The reductions in BP found in the present study are clinically relevant, as a reduction in brachial SBP of 6 mm Hg on a population level may reduce CV morbidity by as much as 10%.<sup>32</sup> Similarly, according to a recent meta-analysis, a reduction in aortic SBP of 10 mm Hg was associated with an ~9% reduction in risk for CV events.<sup>33</sup> Thus, RET may be a useful lifestyle intervention to abrogate CV risk via reducing both peripheral and central BP in older prehypertensive and hypertensive adults.

With each cardiac contraction, a forward pressure wave is generated causing radial expansion of the vessel (that is potential energy of pressure). A portion of the ejected stroke volume (~40%) is temporarily stored within the elastic vessel wall, and upon cardiac relaxation the vessel recoils and stored blood is imparted back to the systemic circulation (that is kinetic energy of flow). When proximal aortic inflow exceeds terminal outflow capacity, the distension caused by the rise in volume generates a concomitant rise in pressure (that is reservoir pressure). With advancing age and subsequent loss of arterial compliance, pressure in the arterial reservoir rises more rapidly for a similar increase in volume<sup>13</sup> significantly contributing to age-associated changes in contour of the BP waveform. The capacitance function of the arterial tree ensures adequate runoff during diastolic decay to the periphery and almost completely explains the exponential reduction in pressure during diastole (when the aortic valve is closed and there is no inflow). Indeed, change in reservoir pressure in the current study was significantly associated with the change in DBP contour.

To our knowledge, this is the first study to examine the effect of an exercise intervention on reservoir pressure. Compared with control conditions, we noted reductions in reservoir pressure following RET. Changes in reservoir pressure were associated with changes in both SBP and DBP. Reservoir pressure is proportional to the volume of blood stored in the aorta, which in turn depends on the interactions of systemic arterial compliance and impedance to outflow.<sup>13</sup> The effect of RET on arterial compliance remains controversial with some studies noting reductions in compliance/increases in stiffness<sup>34,35</sup> and others noting no change.<sup>6,36,37</sup> RET has been shown to reduce arteriolar myogenic tone and peripheral vascular resistance (PVR)<sup>6,38</sup> and this can occur irrespective of changes in large artery stiffness.<sup>34</sup> Favorable changes in reservoir function can occur concomitant with increases in arterial stiffness<sup>39</sup> and this may be due to changes in PVR offsetting changes in arterial stiffness. Thus, it is possible that reductions in PVR and arteriolar tone with RET may alter terminal impedance enabling greater runoff into peripheral microvascular beds during diastole (outflow > inflow) leading to sustained reductions in reservoir pressure.<sup>40</sup>

We also noted reductions in Pf and other proxies of Pf ( $P_1$  height and excess wave pressure)<sup>41</sup> following RET. Changes in these pressure components were also associated with changes in aortic SBP. Pf is influenced by Zc (the association of regional pressure and flow in the proximal aorta) as well as transverse impedance (reservoir function or capacitance owing to radial expansion of the vessel). Thus, alterations in terminal and transverse impedance may subsequently have a favorable effect on upstream Zc contributing to reductions in Pf. This is important, given that increases in Pf with advancing age

contribute significantly to age-associated increases in BP.<sup>11</sup> RET may be a useful lifestyle intervention to favorably modify this important hemodynamic parameter.

Whether RET influences aortic Zc remains unknown. RET has been shown to increase aortic stiffness in older prehypertensive and hypertensive adults.<sup>34</sup> An inherent limitation of measuring aortic stiffness (via pulse wave velocity) is that proximal aortic mechanical properties are neglected. MRI studies have reported heterogeneity in aortic stiffness proceeding from proximal to distal regions.<sup>42,43</sup> Moreover, changes in aortic stiffness and Zc with aging and in the presence of hypertension are not uniform.<sup>44,45</sup> Therefore, disparate change in proximal aortic Zc and distal aortic pulse wave velocity (PWV) with RET is plausible. Strength-trained athletes have larger ascending aortic diameters;<sup>46</sup> thus, it is possible that RET may increase aortic root size. It has been suggested that this dilatation helps to offset wall stiffening by maintaining the capacity of the aorta to store volume during systole.<sup>42</sup> In general,  $Zc = (Eh/r^5)^{1/2}$ , where  $r$  is radius,  $E$  is Young's elastic modulus and  $h$  is wall thickness. As can be seen from this equation, Zc is modulated substantially by radius (raised to an approximate power of 2.5) and less so by  $E$  and  $h$  (owing to the square root function). According to the Moens-Korteweg equation,  $E = (PWV^2 \times D \times \rho)/h$ , thus PWV is directly proportional to the square root of the wall thickness and indirectly proportional to the square root of the radius. As such PWV is relatively insensitive to diameter, whereas Zc and volume elastance are highly dependent on diameter and these parameters may change divergently if diameter changes.<sup>47</sup> RET may not effect vascular wall thickness.<sup>35,38,48</sup> Therefore, an increase in diameter without a proportional increase in vessel wall thickness would offset an increase in PWV. More research is needed to examine the effects of RET on Zc in prehypertensive and hypertensive adults.

Similar to previous reports<sup>5,6,35-37,49</sup> we noted no change in AIx following RET although this is not a universal finding.<sup>50</sup> AIx as a measure purely attributable to wave reflections has been challenged as factors that influence forward wave genesis and impedance also affect AIx.<sup>13,51</sup> Therefore, we also employed a more refined measure to quantify pressure from wave reflections using impedance analysis and flow waveform triangulation. Using this novel approach we noted no changes in Pb. Numerous studies have acknowledged the importance of pressure from wave reflections as it relates to age-associated increases in BP,<sup>12</sup> target organ damage and CVD mortality.<sup>25,33</sup> Although RET appears able to reduce Pf and reservoir pressure, RET might not be a useful lifestyle intervention to attenuate age-associated increases in pressure from wave reflections.

Limitations to this study should be acknowledged. Previous studies have reported sex differences in the vascular and BP response to RET.<sup>52</sup> Given the small sample size of the current study and relatively few men, we lacked statistical power to perform subgroup analyses to adequately explore this possibility. Statistically adjusting for sex did not alter observed findings. In conclusion, RET may be an effective lifestyle intervention to reduce central BP in men and women with prehypertension and hypertension. Reductions in central BP with RET are related to changes in Pf and reservoir pressure, suggesting that capacitance and impedance properties of the arterial system have an important role in governing reductions in BP with RET. RET does not appear to be a useful intervention to reduce pressure from wave reflections in prehypertensive and hypertensive older adults.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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