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Independent and combined effects of aerobic and resistance training on blood pressure (ART-B)

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by

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NOMENCLATURE

US	United States
CVD	Cardiovascular disease
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
BMI	Body Mass Index
HDL-C	High Density Lipoprotein Cholesterol
LDL-C	Low Density Lipoprotein Cholesterol
RM	Repetition Maximum

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ABSTRACT

The health benefits of aerobic exercise have been well established, with less data existing on the benefits of resistance exercise. Furthermore, most early studies on physical activity and hypertension investigated either aerobic or resistance training alone, and have primarily been done on healthy individuals. Therefore, data on individuals who are hypertensive, overweight or obese, sedentary, and at an increased risk for cardiovascular disease are scarce. **Purpose**: The purpose of this study was to compare the effects of aerobic training only, resistance training only, and a combination of both on blood pressure and other cardiovascular disease risk factors compared with a non-exercising control group. **Methods**: Pre- or stage-1 hypertensive, overweight or obese, and sedentary men and women (ages 58 ± 7 years) were randomized to one of three 8-week exercise programs (aerobic only, resistance only, or a combination of both), or a non-exercise control group. The exercise programs were all 3 days per week for 1 hour. **Results**: Of the 69 randomized participants, 66 completed the protocol and all 69 were used in an intention-to-treat analysis. At baseline, the mean (SE) for systolic and diastolic blood pressure was 131 (13) mmHg and 91 (9) mmHg, respectively. Eight weeks of exercise did not significantly change systolic blood pressure in any of the groups ($p > 0.05$), and only the combination group saw a significant decrease in diastolic blood pressure (-3.7 mmHg, 95% CI -6.8, -0.6). Significant increases [mean (95% CI); p value] were also seen in treadmill time for the aerobic [72 seconds (38, 107); $p < 0.01$] and combination groups [51 seconds (17, 86); $p < 0.01$], whereas significant lower body strength gains were seen in the resistance [29.4 lbs (9.1, 49.7); p=0.01] and combination groups [24.4 lbs (4.7, 44.2); p=0.02]. Lastly, significant improvements [mean (95% CI; p value)] in body composition were seen for all three exercise groups: aerobic [weight: -1.0 kg (-1.9, -0.1; p=0.03) and fat mass -0.9 kg (-1.5, -0.2; p=0.01)], resistance [waist circumference: -1.7 cm (-3.3, -0.1; p=0.04)], and combination [weight 0.9 kg (0.02, 1.8; p=0.04) and lean body mass 0.8 kg (0.0, 1.5; p=0.04)]. **Conclusion**: Overall, the combination of aerobic and resistance exercise training seemed to be the most effective in improving blood pressure and other cardiovascular disease risk factors.

CHAPTER 1

INTRODUCTION

Although the health benefits of aerobic exercise are well established (Blair & Kampert, 1996; Kodama et al., 2009; Lee et al., 2012; Lee et al., 2011), little data exist in regards to the health benefits of resistance exercise. The recommendations from the World Health Organization and the United States (US) government both put more emphasis on aerobic exercise for health benefits (U.S. Department of Health and Human Services, 2008; World Health Organization, 2010). According to a recent national survey, 44% of Americans met the aerobic physical activity guidelines requiring an individual to exercise 150 minutes at a moderate intensity, 75 minutes at a vigorous intensity, or a combination of both each week; whereas only 22% of Americans met the resistance guidelines of performing muscle strengthening activity 2 or more times per week (Carlson, Fulton, Schoenborn, & Loustalot, 2010; U.S. Department of Health and Human Services, 2008).

Studies have investigated the effects of resistance training on bone health, quality of life in older adults, and metabolic health in type 2 diabetes. Resistance training prevents a decline in skeletal muscle mass and function; prevents osteoporosis, sarcopenia, and accompanying falls, fractures, and disabilities; decreases HbA1c levels; lowers blood pressure; causes a decrease in visceral adipose tissue; and creates an increase in resting energy expenditure (Banz et al., 2003; Braith & Stewart, 2006; Cornelissen, Fagard, Coeckelberghs, & Vanhees, 2011).

In regards to cardiovascular disease (CVD), there have been few studies evaluating the effect of resistance exercise either independent of or combined with aerobic exercise. It is possible that aerobic and resistance exercise have different physiological responses. Aerobic exercise induces greater improvements in cardiorespiratory fitness and cardiometabolic variables, whereas resistance exercise enhances muscular strength and has positive effects on body composition, muscle, adipose tissue, and bone. If the addition of resistance exercise to aerobic exercise could have an additive effect and further decrease the risk of hypertension, it would be beneficial to the public, as well as practitioners and their exercise prescription (Braith & Stewart, 2006), as high blood pressure is the number one leading risk factor for mortality according to the World Health Organization (2009). Most of the earlier studies on physical activity and hypertension have investigated either aerobic or resistance training alone, and have had limitations such as lack of random assignment or no control group (Cornelissen et al., 2011). Previous studies were also primarily done on healthy individuals and had no consideration of nutritional counseling (Cornelissen et al., 2011). Therefore, data on individuals who are hypertensive, overweight or obese, sedentary, and at an increased risk for cardiovascular disease, are scarce.

From a public health perspective, any additional modifiable factors that decrease the risk of mortality among hypertensive individuals would be of great interest. It has already been established that aerobic exercise can have a significant blood pressure lowering effect: 3.8 mm Hg for systolic blood pressure and 2.6 mmHg for diastolic pressure (Whelton, Chin, Xin, & He, 2002). Even with this apparently small decrease, it has been estimated to reduce cardiac morbidity by 5%, stroke by 8% to 14%, and all-cause mortality by 4% in the average population (Whelton et al., 2002).

The purpose of this study was to compare the effects of either aerobic training only, resistance training only, or a combination of both on blood pressure and other CVD risk factors compared with a non-exercising control group, while providing dietary counseling as a control for all groups, by conducting a 8-week randomized controlled trial in 45-74 year old, pre- or stage 1 hypertensive, overweight or obese, sedentary adults. The hypothesis was that all three exercise groups would exhibit significantly lower blood pressure and improvement in other CVD risk factors compared with a non-exercise control group. Also, the combination of aerobic and resistance exercise would have lower blood pressure and greater improvement in other CVD risk factors compared with either the aerobic exercise only or the resistance exercise only groups.

CHAPTER 2

REVIEW OF LITERATURE

Hypertension, defined by a chronic elevation in systolic blood pressure (SBP) ≥140 mm Hg or diastolic blood pressure (DBP) ≥ 90 mm Hg, and pre-hypertension (SBP 120-139 mm Hg or DBP 80-89 mm Hg) are both complex disorders, leading to an increased risk of CVD and mortality (Chobanian et al., 2003). In the US alone, an estimated 78 million adults over the age of 20 (33% of population) have hypertension, and approximately 36% are pre-hypertensive (Go et al., 2014). By the year 2030, hypertension is predicted to affect 37.3% of Americans and cost $42.8 billion dollars (Heidenreich et al., 2011).

With the large prevalence and economic burden, it is important to establish methods to reduce the risk of hypertension and elevated blood pressure. Aerobic exercise has many health benefits on CVD (Blair & Kampert, 1996; Kodama et al., 2009; Lee et al., 2011, 2012), however, less data exists regarding the health benefits of resistance exercise, independent of or combined with aerobic exercise (World Health Organization, 2009).

This literature review will cover 1) the risks of CVD morbidity and mortality in reference to aerobic and resistance exercise including cardiorespiratory fitness and muscular strength, 2) the mechanisms by which aerobic and resistance exercise can alter blood pressure and other CVD risk factors, and 3) the magnitude of blood pressure reduction seen by different modes of physical activity (aerobic exercise, resistance exercise, or a combination of both).

Physical Activity and Health Risks

Being active and exercising decreases the risk for coronary heart disease, stroke, type 2 diabetes, and some forms of cancer (Physical Activity Guidelines Advisory Committee, 2008). Physical activity has also been shown to have positive effects for the risk of CVD morbidity and mortality.

CVD and CVD Risk Factors

Some common predictors of hypertension are a family history of hypertension, increased body mass index, and low physical activity and fitness (Pescatello et al., 2004). Even with a blood pressure as low as 115/75 mm Hg, a positive relationship has been found with the risk of CVD, doubling for each 20/10 mm Hg increase (Pescatello et al., 2004). Being hypertensive is associated with an increased incidence of all-cause and CVD mortality, stroke, coronary heart disease, heart failure, peripheral arterial disease, and renal insufficiency (Pescatello et al., 2004). Several risk factors, other than hypertension, have also been identified for CVD, specifically, obesity, metabolic syndrome, dyslipidemia, and inflammatory factors (Artero et al., 2012).

Consequently, individuals with pre-hypertension are also at higher risk for cardiovascular events compared to individuals with optimal blood pressure (Pescatello et al., 2004; Vasan et al., 2001). When using data from the Women's

Health Initiative to evaluate the risk of a myocardial infarction or stroke, risk was increased 76% and 186% for myocardial infarction, and 93% and 262% for stroke, for pre-hypertensives and hypertensives, respectively (Hsia et al., 2007). When assessing any cardiovascular event, risk increased 66% and 189%, respectively (Hsia et al., 2007).

Fitness and fatness are also predictors of hypertension, metabolic syndrome, and total cholesterol (Lee et al., 2012). An increase in fitness shows a negative association, whereas an increase in fatness has a positive association with hypertension, metabolic syndrome, and total cholesterol (Lee et al., 2012). Maintaining or improving fitness levels reduced the risk of metabolic syndrome by 42% and 52%, respectively, compared with those who lost fitness in the Aerobics Center Longitudinal Study (ACLS) database (Lee et al., 2012). Fatness can be attenuated by either aerobic or resistance exercise, as both are beneficial for body composition (Banz et al., 2003; Wanderley et al., 2013). A reduction in fatness compensates for some CVD risks associated with losing fitness, where an increase in cardiorespiratory fitness also counteracts the adverse effects of fat gain (Lee et al., 2012).

Performing moderate-intensity physical activity for approximately 150 minutes per week, or an energy expenditure of approximately 1,000 kcal per week, lowers the rate of CVD (Garber et al., 2011). For each 1 MET increase in maximal aerobic capacity, the risk of coronary heart disease and CVD decreased 15% (95% CI 0.82, 0.88) (Kodama et al., 2009). In the Health Professionals Follow-up Study, both exercise intensity and volume of PA by quintiles of MET hours per week had a dose-response relationship with risk for coronary artery disease ($p < 0.001$) (Tanasescu et al., 2002). Accumulating more than 42 MET-hours per week had a 30% reduction of coronary heart disease compared to <6.3 MET-hours per week (Tanasescu et al., 2002).

Although little research has been done on resistance training, muscular strength has an inverse association with obesity, hypertension, and metabolic syndrome, and pro-atherogenic inflammatory proteins (Artero et al., 2012). Resistance exercise has also shown reductions in risk of type 2 diabetes in both men and women, independent of moderate-vigorous physical activity, with resistance in combination with aerobic exercise showing the greatest benefits (Grøntved et al., 2014; Grøntved, Rimm, Willett, Andersen, & Hu, 2012). In a study measuring strength with elbow flexion, handgrip, and knee extension, all measurements were inversely associated with disease risk, and handgrip strength was the best predictor for coronary heart disease (Silventoinen, Magnusson, Tynelius, Batty, & Rasmussen, 2009).

CVD Mortality

By changing from a sedentary to active lifestyle, or regularly engaging in physical activity of at least 150 minutes per week or approximately 1,000 kcal per week, all-cause and CVD mortality can be delayed (Garber et al., 2011; Physical Activity Guidelines Advisory Committee, 2008). Not only is aerobic exercise beneficial, but muscular strength has also had an inverse association with all-cause and CVD mortality (Fitzgerald et al., 2004; Gale, Martyn, Cooper, & Sayer, 2007).

These benefits have been seen in both hypertensive and normotensive individuals, with the greatest benefits seen with high strength and high CRF (Artero et al., 2011; T S Church, Kampert, Gibbons, Barlow, & Blair, 2001). This suggests high CRF and strength may both be protective against all-cause and CVD mortality in individuals with elevated blood pressure or diagnosed hypertension.

Low fitness, defined as the least fit 20% of participants in each age-sex group, increased risk of all-cause mortality by 52% in the ACLS database of men and 110% in women, and increased risk for CVD mortality, specifically, 70% (Blair & Kampert, 1996). An even greater risk for CVD mortality has been seen in pre-hypertensive and hypertensive women from the Women's Health Initiative with risks of 58% and 202%, respectively, compared to normotensive individuals (Hsia et al., 2007).

Being able to increase or maintain fitness has also shown positive benefits on mortality. Lee et al. (2011) found a 15% and 19% reduction of risk for all-cause and CVD mortality, respectively, with a 1 MET increase in aerobic capacity. Becoming fit or remaining fit reduces risk of all-cause and CVD approximately 40-50% compared to those remaining unfit. Furthermore, becoming unfit increases risk of all-cause mortality 38% and CVD mortality 89% (Lee et al., 2011). Similarly, moderately and high fit normotensive men from the ACLS cohort showed a risk reduction in CVD mortality 46% (95% CI 0.31, 0.91) and 56% (95% CI 0.23,0.84), respectively, after controlling for age, year of examination, alcohol use, smoking, family history of CVD, total cholesterol, BMI, and fasting glucose (Church et al., 2001).

In regards to strength, few studies have looked at its relationship with mortality risk. In one study, a relationship was found between tertiles of strength and all-cause mortality with the hazard ratio (95% CI) for the middle and high strength tertiles 0.74 (0.59, 0.91) and 0.80 (0.64, 0.996) compared to low strength, even after controlling for cardiorespiratory fitness in men (Ruiz et al., 2008). This effect has also been seen in hypertensive men, with those in the upper tertile of strength having a 36% lower risk of all-cause mortality, even after adjustment for cardiorespiratory fitness (Artero et al., 2011).

Mechanisms of Physical Activity on Blood Pressure

Aerobic Exercise

Upon meeting the physical activity guidelines, aerobic exercise in middle-aged and older persons improves hypertension, glucose intolerance, insulin resistance, dyslipidemia, and inflammatory markers, with both acute and chronic benefits (Chobanian et al., 2003; Church et al., 2001; Durstine, Grandjean, Cox, & Thompson, 2002; Garber et al., 2011; Pescatello et al., 2004). With more specifics pertaining to blood pressure reduction, aerobic exercise reduces peripheral vascular resistance (Fagard, 2006; Hamer, 2006), which is seen as one of the greatest benefits. This is accomplished through hormonal and structural changes. These adaptations are a reduction in sympathetic nerve activity by a decrease in norepinephrine levels, attenuating peripheral vasoconstriction and an increase in vasodilation (Church et al., 2001; Hamer, 2006). The structural mechanism noted was an increase in lumen diameter, but may be dependent on the individual (Hamer, 2006).

Resistance Exercise

Resistance exercise provides other mechanisms of reducing CVD risk factors compared to aerobic exercise (Table 1). Partaking in resistance exercise mitigates a decline in muscle mass by increasing fat-free mass, but also decreasing percent body fat, which is rarely seen with aerobic training (Banz et al., 2003; Braith & Stewart, 2006; Cornelissen et al., 2011; Garber et al., 2011). Resistance exercise can also increase bone mass and strength in the bones stressed (Kohrt, Bloomfield, Little, Nelson, & Yingling, 2004). Aside from body composition improvements, plasma triglycerides, blood glucose levels, insulin sensitivity, and blood pressure have improved in normotensive, pre-hypertensive and stage-1 hypertensive individuals (Braith & Stewart, 2006; Cornelissen et al., 2011; Garber et al., 2011). Little evidence exists that resistance training improves lipoprotein-lipid profiles (Braith & Stewart, 2006).

Table 1. *Comparison of Effects Between Aerobic Exercise (AE) & Resistance Exercise (RE) on Health*

Variable	AE	RE
Total body fat	↓↓	↓
Intra-abdominal fat	↓↓	↓↔
Lean body mass	↔	↑↑
Resting metabolic rate	↑	↑↑
Muscular strength	↔	↑↑↑
Muscular mass	↔	↑↑
Capillary density	↑	↔
Mitochondrial volume	↑↑	↓↔
Insulin sensitivity	↑↑	↑↑
Insulin response to glucose challenge	↓↓	↓↓
Resting heart rate	↓↓	↔
Peak VO2	↑↑↑	↑↔
Submaximal exercise rate-pressure product	↓↓↓	↓↓

↑ Indicates increased; ↓, decreased; ↔, negligible effect; 1 arrow, small effect; 2 arrows, moderate effect; 3 arrows, large effect.

Adapted from Braith & Stewart, 2006

In healthy, normotensive individuals, blood pressure reductions of about 3 mmHg are seen for both DBP and SBP with resistance exercise, with no evidence that resistance exercise increases central arterial stiffness (Braith & Stewart, 2006).

During a 20-week study in men and women performing resistance exercise, a significant reduction in central SBP and DBP was found of 6 and 3 mm Hg, respectively, with little change to arterial stiffness (Taaffe, Galvão, Sharman, & Coombes, 2007). Not all studies conducted agree that central arterial stiffness is not affected with resistance exercise. Although there may be an increase in central arterial stiffness, a greater increase was also seen in vasodilatory capacity compared to aerobic exercise (Collier et al., 2008). This vasodilation may be a compensatory increase to offset the arterial stiffness.

Looking more into the mechanisms of blood pressure reduction by resistance exercise, an increase in left ventricular wall thickness has been seen, which may be a response to the pressure load and serves to reduce the systolic burden per myofiber, therefore preserving normal left ventricular stress (Artero et al., 2012; Pluim, Zwinderman, van der Laarse, & van der Wall, 2000; Williams et al., 2007). Other improvements have been seen in autonomic and endothelial function (Braith & Stewart, 2006; Collier et al., 2009; Maeda et al., 2004). Endothelin-1 reduction is important since it is a potent vasoconstrictor and also has atherosclerotic effects, meaning that the decrease with chronic exercise may result in beneficial effects on the cardiovascular system (Maeda et al., 2004).

Physical Activity and Blood Pressure

Aerobic Exercise

Most research on physical activity and blood pressure has been done using aerobic exercise. A meta-analysis by Fagard (2006) examining dynamic aerobic endurance training found a significant reduction in resting blood pressure ($P<0.001$) in both SBP and DBP (-3.0 [95% CI, -4.0,-2.0]/-2.4 [95%CI -3.1,-1.7] mm Hg). This reduction became more pronounced when groups studied were divided into hypertensive (-6.9 [95% CI, -9.1,-4.6]/ -4.9 [95% CI, -6.5,-3.3] mm Hg) and normotensive (-1.9 [95% CI, -3.0,-0.9]/-1.6 [95% CI, -2.3,-1.0] mm Hg) (Fagard, 2006). In a meta-analysis of 53 trials on SBP and 50 trials on DBP, an overall pooled net effect of aerobic exercise indicated a SBP reduction of -3.8 mm Hg (95% CI, -5.0, -2.7; $p <0.001$) and DBP reduction of -2.6 (95% CI, -3.4, 1.8; $p <0.001$) (Whelton et al., 2002). Aerobic exercise has a slightly greater effect on hypertensive than normotensive individuals (Whelton et al., 2002). With this, aerobic exercise clearly provides a reduction in blood pressure in subjects, with a greater effect seen in those with elevated blood pressure (pre- or stage I hypertensives), but the parameters to maximize these effects are not known (Cardoso et al., 2010; Semlitsch et al., 2013; Whelton et al., 2002).

Fitness and physical activity levels also affect the risk of developing hypertension. When comparing white men in the Atherosclerosis Risk in Communities Study, being in the highest quartile of leisure physical activity was associated with lower odds of developing hypertension ($p=0.01$) compared to those in the lowest quartile of physical activity (Pereira et al., 1999). A prospective study conducted in Finland also found a dose-response relationship between the amount of physical activity reported by self-report questionnaire and risk of hypertension in both men ($P<0.001$) and women ($P=0.005$) (Hu et al., 2004).

When using cardiorespiratory fitness, divided into 3 groups (lowest 20%, middle 40%, and upper 40%), similar results were found as high cardiorespiratory fitness was associated with a 25% reduction in risk compared to low cardiorespiratory fitness (Shook et al., 2012). Additionally, of 3,148 healthy participants, those who maintained or improved their fitness levels had a 26% and 28% lower risk of incident hypertension compared with those who lost fitness (Lee et al., 2012). For the total population, approximately 34% of hypertension incidence could theoretically be prevented if individuals increase their fitness from low to moderate or moderate to high, with a calculated prevented fraction of 0.34 (Carnethon et al., 2010).

Resistance Exercise

The American Heart Association (Williams et al., 2007) and American College of Sports Medicine (Ratamess et al., 2009) have both included resistance exercise in their recommendations for individuals with and without cardiovascular disease, although the literature is sparse compared to what is already known about aerobic exercise.

In a review of 12 resistance exercise study groups, a significant reduction in DBP of -3.5 mm Hg (95% CI, -6.1,-0.9) was noted (P<0.01), but there was no significant reduction in SBP (P=0.10) with a reduction of -3.2 mm Hg (95% CI, -7.1, 0.7) (Fagard, 2006). Kelley and Kelley (2000) also found resistance exercise reduced SBP -3 mm Hg (95% CI, -4, -1) and DBP -3 mm Hg (95% CI, -4, -1), showing an approximately 2-4% decrease. In a more recent meta-analysis, 33 study groups were utilized resulting in similar reductions, but both were significant ($p<0.01$) (Cornelissen et al., 2011). Overall, with weighted net changes, resistance exercise reduced SBP 3.5 mm Hg (95% CI, -5.6,-1.3) and DBP 3.2 mm Hg (95% CI, -4.4,-1.9) (Cornelissen et al., 2011). When further divided into dynamic resistance training (30 study groups) and isometric handgrip training (3 study groups), there was a more dramatic decrease in SBP of -2.6 mm Hg ($p=0.015$) for dynamic training and -11.8 mm Hg ($p=0.01$) for isometric handgrip training (Cornelissen et al., 2011).

These meta-analyses are supported by an individual study conducted by Moraes et al (2012). After 12 weeks of resistance exercise by 15 Stage 1 hypertensive volunteer men without medication, SBP and DBP were both significantly reduced (SBP 150 ± 3 mm Hg to 134 ± 4 mm Hg, $p<0.001$; DBP 93 ± 2 mm Hg to 81 ± 1 mm Hg, $p<0.01$) (Moraes et al., 2012). Detraining effects were also taken into consideration, in which the participants were asked to not exercise for 4 weeks following the training period. All values remained similar to those seen immediately after ending the training program (Moraes et al., 2012).

Resistance exercise appears to not be as strong a predictor for the risk of hypertension as aerobic exercise. However, most of the randomized controlled trials have had limitations such as small sample size around 30 participants in studies over a wide range of intervention periods from 6 to 52 weeks (Blumenthal, Siegel, & Appelbaum, 1991; Cornelissen et al., 2011; Sillanpää et al., 2009; Yoshizawa et al., 2009). A majority of the studies utilized weight machines, in which there was a range of 6 to 16 machines or exercises performed, 1-5 sets with 3 being the most common, and a range of 6 to 30 repetitions with most studies using

8-12 repetitions per set (Cornelissen et al., 2011). When assessing strength from an upper body chest press and lower body leg press in men (n=4147), the risk of hypertension in the highest tertile compared to the lowest tertile was reduced 25% (HR 0.75 [95% CI, 0.61-0.93]) (Maslow et al., 2010). Of note, this dose-response relationship was no longer significant after controlling for cardiorespiratory fitness.

Combination Exercise

The use of combination exercise (aerobic and resistance exercise) in research for blood pressure compared to aerobic or resistance exercise alone or a control has had many different outcomes (Table 2). These differences are often due to inconsistent methods, different populations, or a lack of appropriate stimulus to observe an effect.

In studies with a sample size smaller than 100, the intervention period has varied from 4 weeks to 9 months, with most studies using 12 weeks of intervention. Many of these studies have approximately 15 participants per group and the population varies from apparently healthy individuals (Sillanpää et al., 2009; N Sousa, Mendes, Abrantes, Sampaio, & Oliveira, 2014; Wood et al., 2001; Yoshizawa et al., 2009) to diabetics (Jorge et al., 2011) to those who are inactive (Bateman et al., 2011; Ho, Dhaliwal, Hills, & Pal, 2012; Stewart et al., 2005; Wanderley et al., 2013). Some of these study groups were also normotensive individuals (Bateman et al., 2011; Laoutaris et al., 2013; Yoshizawa et al., 2009), which would explain why there were not significant reductions in blood pressure.

As seen in research not utilizing combination exercise, most studies with an aerobic only group saw significant reductions in systolic blood pressure for those participants (Calders et al., 2011; Collier et al., 2008; Jorge et al., 2011; Sousa, Mendes, Abrantes, Sampaio, & Oliveira, 2013; Wanderley et al., 2013; Wood et al., 2001). The resistance exercise only groups did not have as pronounced results, with only three studies seeing blood pressure improvements (Collier et al., 2008; Jorge et al., 2011; Sillanpää et al., 2009). All but two of the studies that utilized combination training saw significant improvements in either SBP or DBP (Bateman et al., 2011; Calders et al., 2011; Ho, Dhaliwal, et al., 2012; Jorge et al., 2011; Nelson Sousa et al., 2013; Stewart et al., 2005). Unfortunately, there is a mix in the exercise prescription for combination training in which some studies have doubled the total intervention time compared to the allotted time for either aerobic or resistance exercise alone. This does not allow one to differentiate between whether the change in blood pressure was due to the extended time or the benefits of the combination (Bateman et al., 2011; Sillanpää et al., 2009).

Looking a little deeper into the studies, there may have been flaws in the methods. For example, some studies did not exclude individuals on hypertensive medications (Ho, Radavelli-Bagatini, Dhaliwal, Hills, & Pal, 2012; Jorge et al., 2011; Laoutaris et al., 2013; Sillanpää et al., 2009) or did not consider it in their analyses, which could affect the exercise effect on blood pressure. Other issues arising were training the control group about diet and exercise, in which they may have been more health conscious and increased their adherence to a healthy diet (Jorge et al., 2011; Stewart et al., 2005).

Table 2. *Chart of Studies*

Author (year)	Study Sample			Intervention Period	Intervention Group				Results	
	Size	**Health Status**	**Age (Sex)**		**AT**	**RT**	**AT+RT**	**Control**	**Within (pre-post)**	**Between**
Blumenthal (1991)	99	non-obese, hypertensive	(M & F)	4-months	X	X		X	--	--
Bateman (2011)	86	sedentary; BMI 25-35; mild-mod dyslipidemia; normotensive	18-70 (M & F)	8 months	X	X	X		DBP of Comb	--
Calders (2011)	45	IQ between 45-70; pre-hypertensive	18-60 (M & F)	20 weeks	X		X	X	--	SBP: Comb vs. Con; AE vs Con; AE vs Comb(comb>AE)
Collier (2008)	30	post-menopausal women; pre- & stage-1 hypertensives	30-60 (M & F)	4 weeks	X	X			sign difference for both groups, SBP & DBP	
Jorge (2011)	48	type 2 diabetics, BMI 25-40; pre-hypertensive (29 on meds)	30-70 (M & F)	12 weeks	X	X	X	X	sign difference for all 4 groups, SBP & DBP	--
Sillanpaa (2009)	62	healthy; pre-hypertensive	39-64 (F)	21 weeks	X	X	X	X	SBP for RT	--
Sousa (2013)	48	apparently healthy; pre- & stage-1 hypertensives	65-75 (M)	32 weeks	X		X	X	SBP AE & Comb	--
Ho (2012)	64	BMI 25-40, sedentary (<1 hr of mod PA/wk for past 3 months); 10 hypertensives at beginning of study	40-66 (M & F)	12 weeks	X	X	X	X	SBP: Con & Comb; DBP: Control	--
Wanderley (2013)	50	inactive pre-hypertensive	> 60 (M & F)	8 months	X	X		X	SBP & DBP of AT	--
Yoshizawa (2009)	35	healthy, sedentary; normotensive	32-59 (F)	12 weeks	X	X		X	--	--
Laoutaris (2013)	27	patients with chronic heart failure; ~70% on beta blockers; normotensive	57 +/- 11 (M & F)	12 week	X		X		--	--
Stewart (2005)	104	inactive (<90 min/wk); SBP 130-159, DBP 85-99	55-75 (M & F)	26 weeks			X	X	SBP & DBP for Comb & Con	DBP: Comb > Con
Wood (2001)	36	pre-hypertensive	60-84 (M & F)	12 weeks	X	X	X	X	SBP of AE	

Conclusion

Since combination training may have more benefits than either resistance or aerobic exercise alone on different health outcomes, such as HbA1c levels for diabetics, looking into the effects on blood pressure is warranted (Church et al., 2010; Sigal et al., 2007). However, as seen in the previous section on combination exercise, there is a lack of consistency in the results produced by combination exercise. This is mainly due to faulty methods or a lack of adequate sample size. In a couple of the studies, combination training had double the exercise time (performing both the complete aerobic and resistance exercise protocols), which resulted in longer exercise duration (Bateman et al., 2011; Sigal et al., 2007). This makes it difficult to determine whether the results were due to the extended time of performing exercise or the different mechanisms of both aerobic and resistance training having an additive effect. Small issues in methods arise with the Calders et al (2011) study where true randomization was not performed; there was low power; and no resistance exercise only comparison group. Replication of the aforementioned studies, with control of the inconsistent methods, is therefore necessary.

Along with the small pool of data on combination training, there is also a scarcity of data on the effect of resistance exercise in hypertensives. This warrants more randomized control trials assessing the effects of resistance exercise on blood pressure, CVD risk factors and blood pressure regulating mechanisms (Cornelissen et al., 2011).

CHAPTER 3

METHODOLOGY

Participants

This study consisted of 69 adults, 45 to 74 years of age, who had stage 1 hypertension or pre-hypertension, were overweight or obese, and sedentary. Stage 1 hypertension and pre-hypertension were defined as having a blood pressure (systolic/diastolic) of 140-149/90-99 and 120-139/80-89 mmHg (Chobanian et al., 2003), respectively, without taking any anti-hypertensive medications. Overweight and obese (class 1 or 2) were quantified by having a body mass index of 25-40 kg/m^2 (NHLBI Obesity Education Initiative Expert Panel, 1998). Sedentary was defined as not meeting the aerobic and resistance exercise guidelines: <150 minutes/week of moderate intensity aerobic exercise, <75 minutes of vigorous intensity aerobic exercise, or the combination of the two, and <2 days/week of resistance exercise over the last 3 months (U.S. Department of Health and Human Services, 2008). Participants were limited to non-smokers due to the strong effect of smoking on the study outcomes of blood pressure and other cardiovascular disease risk factors (Go et al., 2014).

Exclusion criteria included any serious medical problem that prevented participants from exercising according to the American College of Sports Medicine and American Heart Association guidelines for contraindications to exercise (American College of Sports Medicine, 2013; Williams et al., 2007). They include: unstable coronary heart disease or decompensated heart failure; severe pulmonary hypertension or aortic stenosis; acute myocarditis, endocarditis, pericarditis, or aortic dissection; and other medical conditions that were life threatening or that could interfere with or be aggravated by exercise training. Other exclusions included pregnant women or women anticipating pregnancy during the course of the intervention, and those who planned on being away for more than 2 weeks in the 2 month intervention period. Table 3 shows the recruitment plan utilized.

Table 3. *Recruitment Plan* – Steps taken to recruit participants

Actions	Info
1. Send email to mailing list (~200 emails) from previous study	Study description, inclusion criteria, exclusion criteria, request phone number and convenient time to receive a phone call for screening
2. Request and send mass email to ISU faculty & staff	Study description, inclusion criteria, exclusion criteria, request phone number and convenient time to receive a phone call for screening
3. Post flyers around ISU and Ames	
4. Phone screening	**<u>Inclusion:</u>** -Age 45-74 -120-159 SBP, 80-99 DBP -Non-smoker -BMI: 25-40 -<150 min/wk moderate-intensity aerobic exercise and <2 days/wk of resistance training **<u>Exclusion:</u>** -Hypertension medication -Heart attack, stroke, cancer or diabetes -Life-threatening conditions that interfere with or are aggravated by exercise -Serious arthritis or joint problem in the ankle, knee, elbow, or shoulder that prevent from doing 1-RM and treadmill tests -Plans to be away for >2 weeks during the 2 month intervention (possibly in September, October, and November) -pregnant women or anticipating pregnancy
5. Schedule Orientation time	Offer the choices of orientation times and schedule participant

As seen in Table 3, participants were phone screened for self-reported blood pressure levels and physical activity. During the orientation session, participants had their blood pressure, height, and weight measured to determine if they met the inclusion criteria. Upon meeting the inclusion criteria, participants participated in 2 education sessions. One session was a presentation on the benefits of exercise and cardiovascular disease, with the second session addressing the equipment to be used for the exercise sessions and testing for familiarity purposes. These sessions were used to minimize dropout and determine a baseline level of physical activity by pedometer step count over 3 days of wear from the orientation session to the second education session.

Of the 69 participants who completed the education sessions, each was randomly assigned to one of four groups: 1) no-training control group, 2) aerobic training only group, 3) resistance training only group, and 4) combination of both aerobic and resistance training group. Randomization was performed based on age, sex, baseline blood pressure, and BMI.

In order to enhance adherence, we used strategies such as behavioral contract signings, flexible scheduling, money incentive, and adherence monitoring (Figure 1).

Management Plan:

All participants:

- If ever a participant misses a session without communication, contact them via phone call or text to try to re-schedule

Exercise participants:

- When each participant enters the lab, take their pedometer and record their daily step count and return it after exercise, not to count walking steps during exercise.
- Participants should check their attendance record form.

Control participants:

- Phone call once per week to receive pedometer information, make sure they keep their normal physical activity levels (should be inactive) and diet, and thank them for their cooperation

Figure 1. *Management Plan* – Strategies used to enhance adherence

The Iowa State University (ISU) Institutional Review Board approved this study, and each participant signed an informed consent document prior to participation.

Data Collection Procedures

Measurements taken at the very beginning of the study and at the end of the 8 week supervised exercise period included peripheral blood pressure, resting heart rate, fasting blood chemistry analysis, sub-maximal treadmill exercise test, 1-repetition maximum strength tests, body composition, anthropometry, a personal and family health history questionnaire including physical activity, and a 3-day diet record. All measures were conducted in the same laboratory and with the time of day standardized.

Peripheral blood pressure and resting heart rate were measured using the Sphygmacor XCEL (AtCor Medical, Itasca, IL, USA) automated device. A brachial pressure cuff was placed on the participant's left arm over the brachial artery with the participant in a seated position, legs uncrossed. The brachial systolic and diastolic blood pressure was measured 3 times by the device, with a two-minute rest period between each measurement. The SphygmaCor XCEL, discarded the first reading and reported the average of the last 2 readings for all measurements.

The fasting blood chemistry analysis measured a lipid profile (total cholesterol, low- and high-density lipoprotein cholesterol, and triglycerides) and glucose, after an overnight fast of at least 12 hours. Approximately 5 mL of blood was taken by a registered nurse to determine these markers via venipuncture from a superficial arm vein.

The submaximal treadmill exercise test was performed using the modified Balke and Ware protocol (Balke & Ware, 1959; Moraes et al., 2012). Participants began walking on the treadmill at 3.3 miles per hour (mph) with a 0% incline for 1 minute, which then increased to a 2% incline. After the first 2 minutes, the incline increased 1% every minute, keeping the speed fixed at 3.3 mph. All participants reached 70% of their heart rate reserve (equivalent to 85% of age-predicted maximal heart rate) prior to ending the submaximal test. No participants complained of chest discomfort or requested to end the protocol following the American College of Sports Medicine guidelines (American College of Sports Medicine, 2013a). Total time on the treadmill was recorded as an indicator of cardiorespiratory fitness.

Maximal contractile strength was assessed using the 1 repetition maximum (RM) technique on a computer controlled integrated training management system (TechnoGym Wellness System, Gambettola, Italy) for the seated chest and leg press. Participants warmed up with a light resistance load and weight was added at approximately 10-20 lbs (or 5-10% of body weight) for upper body and 30-40 lbs (or 10-20% of body weight) until a maximum load was reached. Participants had a resting period of at least 2 minutes between each attempt. An absolute 1 RM was determined when the participant successfully lifted the weight through the entire range of motion but could no longer increase the load (Baechle & Earle, 2000). If a participant could exceed the amount of weight on the machine, the 1 RM was estimated using a training load chart (Landers, 1984).

Body weight and height were measured via a standard stadiometer to calculate body mass index as weight in kilograms divided by height in meters squared. Waist circumference was measured at the level of the umbilicus in centimeters. Body composition was assessed via 2 methods. Each participant's body fat was estimated using a sum of 3 skinfold thicknesses. Three measurements were taken at each site and averaged for use in the prediction equations. Men were measured at the chest, abdomen, and thigh, whereas women were measured at the tricep, thigh, and suprailiac (American College of Sports Medicine, 2013b). All measurements were taken on the right side of the body with the participant standing upright. The following equations were used for calculation (American College of Sports Medicine, 2013b):

Men: body fat density = 1.10938 – 0.0008267 (sum of three skinfolds) + 0.00000016 (sum of three skinfolds)^2 – 0.0002574 (age)[SEE 0.008 or ~3.5% fat]
Women: body fat density = 1.099421 – 0.0009929 (sum of three skinfolds) + 0.00000023 (sum of three skinfolds)^2 – 0.0001392 (age)[SEE 0.009 or ~ 3.9% fat]
Body fat % = (457/body density) – 414.2

Weight, body mass index, body fat percentage, fat mass, and fat free mass were also calculated using bioelectrical impedance analysis (BIA) (InBody 720, Biospace Co, Ltd, Seoul, Korea).

A questionnaire developed from other large cohorts was given to each participant in regards to lifestyle habits, physical activity from all four domains (home, occupation, leisure, & transportation), and personal and family medical history. Participants also completed surveys about social support (Duke-UNC

Functional Social Support Questionnaire) (Broadhead, Gehlbach, de Gruy, & Kaplan, 1988) and a 3-day diet record. Figure 3 below is a breakdown of each stage of the baseline procedures.

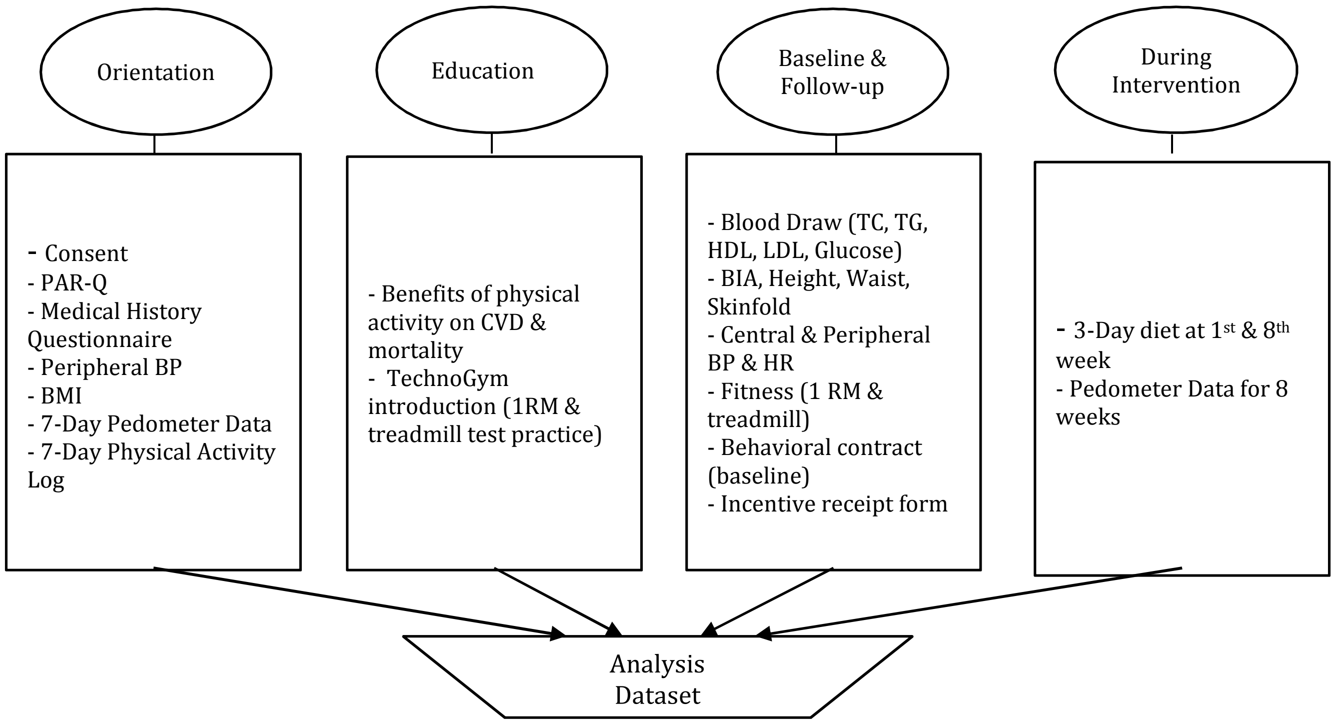

Figure 2*. Measurement Collection* – Visual aid indicating when each measurement was taken throughout the study

Exercise Intervention

Each study group had equal training time that lasted 8 weeks, in which all participants exercised 3 days per week for 60 minutes, except the non-exercise control group. All training sessions were supervised in the Iowa State Forker Building.

The aerobic exercise only group utilized the treadmill or cycle ergometer, starting at 40% of their maximal heart rate, progressing to approximately 70% of their maximal heart rate as the intervention progressed (Table 4). Participants could choose to exercise at a higher intensity, not to exceed 80% of their maximum heart rate, which was recorded via the heart rate monitor worn during all exercise sessions.

Table 4. *– Aerobic Only Exercise Prescription*

Aerobic Training						
	Day 1		Day 2		Day 3	
Week	Time	Intensity	Time	Intensity	Time	Intensity
1	20	40	20	40	30	50
2	30	50	30	50	35	60
3	35	60	40	65	40	65
4	45	65	45	70	45	70
5	50	70	50	70	55	70
6	55	70	60	70	60	70
7	60	70	60	70	60	70
8	60	70	60	70	60	70

The resistance only group performed 12 exercises consisting of: chest press, shoulder press, pull-down, lower-back extension, abdominal crunch, torso rotation, biceps curl, triceps extension, leg press, quadriceps extension, leg curl, and hip abduction. Their program progressed to 3 sets of 10 repetitions for upper body and 14 repetitions for lower body (Table 5). Weight prescriptions were estimated based on age, height, weight, and sex for each machine by the TechnoGym Wellness System. Upon reaching the assigned weight, participants were encouraged to increase weight until reaching exhaustion on the last repetition, indicating the lower the repetitions, the higher the intensity of resistance exercise.

Table 5. *Resistance Only Exercise Prescription*

Resistance Training									
	Day 1			Day 2			Day 3		
		Reps			Reps			Reps	
Week	Sets	Upper	Lower	Sets	Upper	Lower	Sets	Upper	Lower
1	1	18	20	1	18	20	2	18	20
2	2	18	20	2	18	20	2	18	20
3	2	15	18	2	15	18	2	15	18
4	2	15	18	2	15	18	2	15	18
5	2	12	16	2	12	16	2	12	16
6	2	12	16	2	12	16	2	12	16
7	3	10	14	3	10	14	3	10	14
8	3	10	14	3	10	14	3	10	14

The combination group completed 30 minutes of aerobic exercise and 30 minutes of resistance exercise per session (Table 6). These participants followed the same intensity and protocol as the other groups, only reducing their resistance training to 8 exercises instead of 12 (excluding shoulder press, arm curl, arm extension, and leg extension) and 2 sets instead of 3 sets.

Table 6. *Combination Exercise Prescription* - (T: Time, I: Intensity, S: Sets, U: Upper Body, L: Lower Body)

Combination of Aerobic and Resistance Training															
	Day 1					Day 2					Day 3				
	Aerobic		Resistance			Aerobic		Resistance			Aerobic		Resistance		
Week	T	I	S	U	L	T	I	S	U	L	T	I	S	U	L
1	20	40	1	18	20	20	40	1	18	20	20	50	2	18	20
2	20	50	2	18	20	20	50	2	18	20	25	60	2	18	20
3	30	45	2	15	18	30	45	2	15	18	30	50	2	15	18
4	30	50	2	15	18	30	50	2	15	18	30	50	2	15	18
5	30	55	2	12	16	30	55	2	12	16	30	55	2	12	16
6	30	55	2	12	16	30	60	2	12	16	30	60	2	12	16
7	30	60	2	10	14	30	65	2	10	14	30	65	2	10	14
8	30	65	2	10	14	30	70	2	10	14	30	70	2	10	14

All participants were asked to refrain from any moderate or vigorous physical activity outside the intervention. All participants, regardless of group, reported daily steps using a pedometer (OMRON HJ-321, OMRON Healthcare, Hoofddorp, Netherlands), on a weekly basis during the intervention period.

Dietary counseling was implemented for all study groups, guided by the Dietary Approaches to Stop Hypertension (DASH) Diet (Sacks et al., 2001) to minimize dietary variability among groups and avoid weight loss (Sigal et al., 2007). The aim of the DASH diet is to reduce sodium, sweets, added sugars, and red meats. The DASH diet recommendations are grains and grain products (6-8 servings), vegetables (4-5 servings), fruits (4-5 servings), low-fat dairy products (2-3 servings), lean meats, poultry, and fish (≤6 servings), nuts, seeds, & dry beans (4-5 servings per week), fats and oils (2-3 servings), and sweets (≤5 servings per week). A registered dietitian provided the necessary dietary counseling at baseline to help the participants implement the recommended dietary changes. The focus of the dietary counseling was on changing the quality of the diet without changing the amount of energy intake. A 3-day food diary was obtained during the first and eighth week of the intervention and analyzed using The Food Processor Diet and Nutrition Analysis Software (ESHA, Salem, Oregon).

Data Analysis Procedures

The primary outcome variables were peripheral systolic and diastolic blood pressure, measured in millimeters of mercury. Secondary outcomes included BMI, weight, waist circumference, lean body mass, fat mass, body fat percentage, cardiorespiratory fitness, strength, and fasting lipids and glucose. Participants were classified as unhealthy if on the health history questionnaire indication was made of current or previous history of: chronic obstructive pulmonary disorder (COPD), asthma, arthritis, diabetes, hypercholesterolemia, or depression. Heavy alcohol consumption was defined as >14 and >7 drinks per week in men and women, respectively (Willenbring, Massey, & Gardner, 2009).

Statistical Analysis

Descriptive statistics were calculated for each variable in each group, and compared using χ^2 test or ANOVA test. Analyses took into account covariates including age, sex, and baseline values of each outcome measure. Additional analyses controlled for baseline body mass index, change in weight, dietary factors, and average daily steps. A linear-mixed effects model was used with repeated measures for time, group, and time-by-group interaction. Reported are the change values for each outcome measure and 95% confidence intervals, as well as any statistical significance for the 6 inter-group contrasts (aerobic training vs. control; resistance training vs. control; aerobic training vs. resistance training; combination training vs. aerobic training; combination training vs. resistance training, and combination training vs. control) for changes in outcome variables between baseline and 8 weeks. Statistical analyses were performed using the SAS software (SAS Institute, Cary, NC), and all of the *P* values are 2-sided, with an a priori α-level of 0.05 determined to be significant.

CHAPTER 4

RESULTS

From August to October 2014, 206 individuals were screened for study eligibility. The most common reasons for exclusion from randomization were low blood pressure, blood pressure medication, too busy, or no longer interested. Figure 3 shows the flow of participants from recruitment to follow-up. Of the 69 individuals who were randomized, 66 (96%) completed the 8-week intervention. Physician prescription of high blood pressure medication, a case of pneumonia, and muscle discomfort did not allow 3 participants to complete the study. Table 7 shows the participants' baseline characteristics. The groups were randomized and similar in age, sex, BMI, and resting peripheral blood pressure. No significant between-group differences were noted for any baseline measures except blood glucose (higher in resistance training only group compared to other groups).

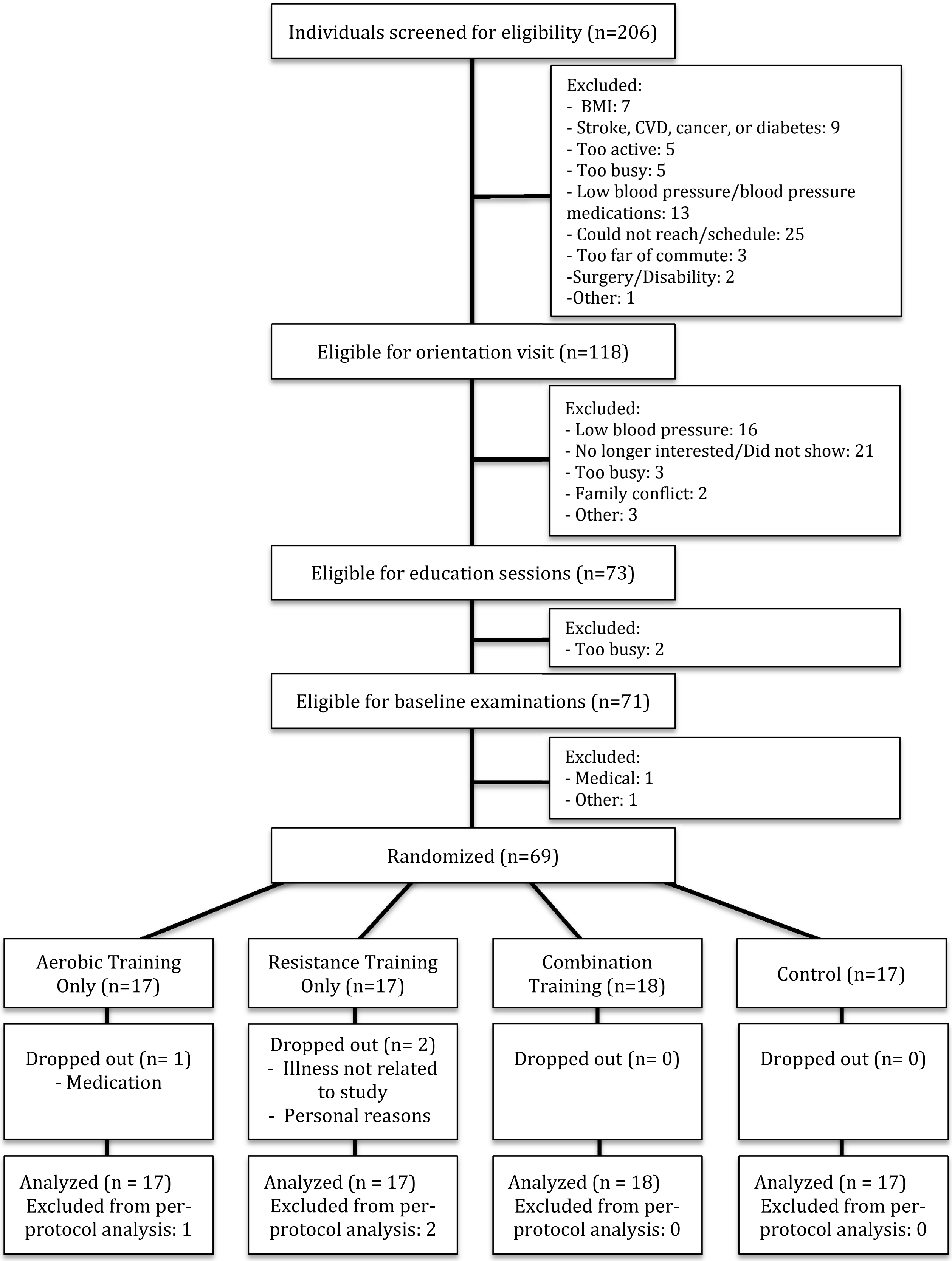

Figure 3. *Study Flow Diagram*

Table 7*. Baseline Characteristics*[a]

	All	AT	RT	Comb	Con	p
n	69	17	17	18	17	
Age, mean (SD), y	58 (7)	58 (7)	57 (9)	58 (7)	58 (6)	0.94
Women, No. (%)	42 (61%)	10 (59%)	10 (59%)	11 (61%)	11 (65%)	0.98
Post-Menopausal, No. (%)	35 (83%)	9 (90%)	7 (70%)	9 (81%)	10 (91%)	0.56
Race/ethnicity, No. (%)						
White, No. (%)	64 (93%)	16 (94%)	16 (94%)	16 (89%)	16 (94%)	0.53
Non-White, No. (%)	5 (75)	1 (6%)	1 (6%)	2 (11%)	1 (6%)	
Education, No. (%)						
High School, No. (%)	11 (16%)	3 (18%)	4 (24%)	2 (11%)	2 (12%)	0.96
College, No. (%)	31 (45%)	7 (41%)	7 (41%)	9 (50%)	8 (47%)	
Graduate School, No. (%)	27 (39%)	7 (41%)	6 (35%)	7 (39%)	7 (41%)	
Body Composition						
BMI, kg/m^2	32.4 (5.2)	32.5 (5.9)	33.1 (5.9)	31.9 (5.5)	32.4 (3.7)	0.93
Weight, kg	94.5 (19.0)	97.1 (20.7)	95.8 (21.2)	93.6 (18.9)	91.4 (16.0)	0.83
Waist circumference, cm	105 (13)	103 (14)	106 (17)	104 (13)	106 (10)	0.91
Lean Body Mass, kg	56.7 (13.2)	59.0 (13.6)	58.1 (14.1)	55.8 (14.1)	54.0 (11.8)	0.69
Fat Mass, kg	38.1 (11.3)	38.6 (13.2)	38.1 (12.7)	38.6 (12.2)	37.6 (7.3)	0.99
Body Fat Percentage, %	40.1 (8.1)	39.1 (8.6)	39.5 (8.0)	40.6 (10.0)	41.4 (5.7)	0.85
Resting Hemodynamics						
Resting Heart Rate, bpm	69 (9)	67 (10)	70 (10)	66 (7)	72 (10)	0.21
Peripheral SBP, mm Hg	131 (13)	131 (10)	131 (14)	131 (16)	129 (12)	0.98
Peripheral DBP, mm Hg	81 (9)	81 (10)	81 (11)	81 (10)	80 (8)	0.99
Cardiorespiratory Fitness						
Time on treadmill, sec	319 (174) [67]	323 (184)	300(167) [16]	338 (211) [17]	313 (142)	0.94
Lower Body Muscular Strength						
1 RM Leg Press, kg	123 (47) [68]	122 (44)	136 (56)	111 (43)	123 (44) [16]	0.50
Upper Body Muscular Strength						
1 RM Bench Press, kg	44 (21)	46 (23)	45 (21)	42 (20)	44 (23)	0.96

(Table 7 continued)

Medical Conditions						
Chronic Obstructive Pulmonary Disease, No. (%)	1 (1.5%)	0	0	1 (6%)	0	0.43
Asthma, No. (%)	9 (13%)	0	2 (12%)	3 (17%)	4 (24%)	0.24
Osteoarthritis, No. (%)	8 (12%)	2 (12%)	2 (12%)	0	4 (24%)	0.19
Rheumatoid Arthritis, No. (%)	4 (6%)	1 (6%)	1 (6%)	1 (6%)	1 (6%)	1.00
Osteoporosis, No. (%)	5 (7%)	3 (18%)	2 (12%)	0	0	0.11
Type 2 Diabetes, No. (%)	2 (3%)	1 (6%)	1 (6%)	0	0	0.55
Hypercholesterolemia , No. (%)	24 (35%)	3 (18%)	6 (35%)	8 (44%)	7 (41%)	0.35
Depression, No. (%)	9 (13%)	3 (18%)	1 (6%)	3 (17%)	2 (12%)	0.72
Smoking History, No. (%)	13 (19%)	2 (12%)	3 (18%)	6 (33%)	2 (12%)	0.31
Parental History of High Blood Pressure, No. (%)	53 (77%)	15 (88%)	12 (71%)	13 (72%)	13 (76%)	0.61
Heavy alcohol drinking, No. (%)+	4 (6%)	0	1 (6%)	1 (6%)	2 (12%)	0.54
Diet	(n = 64)	(n = 15)	(n = 15)	(n = 18)	(n = 16)	
Total Intake, kcal	1882 (473)	1966 (582)	1857 (484)	1842 (465)	1871 (387)	0.89
Fat, g	73 (21)	75 (20)	68 (20)	69 (22)	78 (22)	0.45
Protein, g	79 (22)	77 (21)	80 (24)	80 (26)	79 (16)	0.99
Carbohydrates, g	229 (76)	250 (26)	230 (66)	229 (67)	210 (66)	0.55
Sodium, mg	2952 (1024)	2928 (1036)	2821 (1073)	2959 (1132)	3091 (916)	0.91
Fasting Blood Lipids and Glucose						
Fasting glucose, mg/dL	98 (9)	97 (8)	104 (11)	98 (8)	96 (6)	**0.03**
Total Cholesterol, mg/dL	214 (37)	219 (26)	200 (33)	215 (47)	223 (36)	0.27
High-Density Lipoprotein Cholesterol, mg/dL	53 (15)	55 (13)	49 (12)	56 (21)	54 (13)	0.55
Triglycerides, mg/dL	162 (73)	151 (68)	167 (93)	146 (67)	184 (60)	0.41
Low-Density Lipoprotein Cholesterol, mg/dL	130 (32)*	134 (28)	121 (33)*	130 (37)	133 (28)	0.63

a: Data are means (SD) for continuous variables or number of participants (%) for categorical variables.
* values in brackets are number of individuals with complete data (one participant in RT group had an extreme value for triglycerides, thus low-density lipoprotein cholesterol could not be calculated)
+: >14 drinks/week for men and >7 drinks/week for women
SBP: systolic blood pressure; DBP: diastolic blood pressure; RM: repetition maximum

Adherence to Exercise Training

From baseline to 8 weeks, the mean exercise attendance was 96% in all groups except resistance training (92%) (Table 8). On average, participants doing aerobic exercise did 100 ± 6% of the prescribed exercise amount in minutes, and their average exercise intensity was greater than what was prescribed (119 ± 13%) based on their heart rate measured during each exercise session. On average, resistance training participants completed 100 ± 2% of prescribed sets (exercise amount), and they exercised at the weight prescribed 99 ± 11% of the time based on the weight that they lifted in each exercise session.

Table 8. *Exercise Adherence*

Adherence & Attendance						
	All	AT	RT	Comb	Control	p
Aerobic, % (SE)						
Minutes Completed	100 (6)	101 (7)	-	100 (5)	-	0.42
Intensity	119 (13)	121 (14)	-	117 (12)	-	0.48
Resistance, % (SE)						
Sets Completed	100 (2)	-	99 (2)	100 (2)	-	0.37
Weight	99 (11)	-	96 (10)	101 (11)	-	0.14
Attendance, No. (%)	23/24 (96%)	23/24 (96%)	22/24 (92%)	23/24 (96%)	-	0.17

Outside of ART-B exercise sessions, lifestyle physical activity was recorded with pedometers over the whole 8 weeks of the intervention period and did not change significantly over time ($p = 0.69$). There was a significant difference between groups ($p < 0.01$) with aerobic exercise group recording the most steps, followed by the control, resistance, and combination group (Figure 4). The mean step calculations do not include steps accumulated during the supervised exercise sessions.

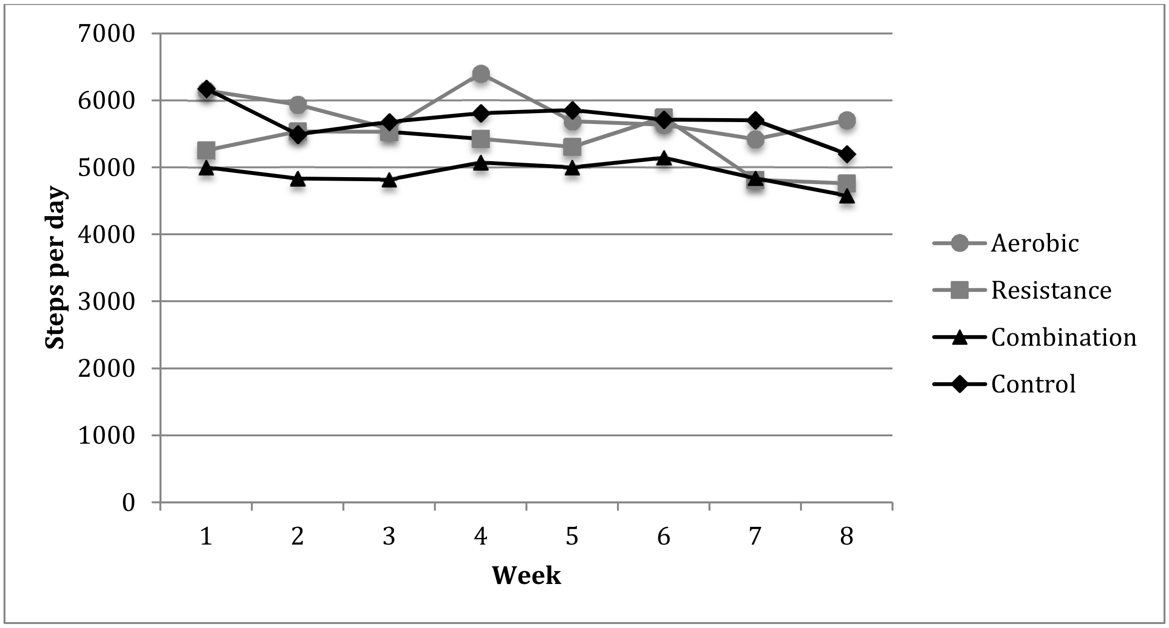

Figure 4. *Weekly Average Daily Step Counts*

Baseline and follow-up 3-day diet records were analyzed for any changes in diet throughout the study period (Figure 5). No significant changes were noted in total calorie, fat, carbohydrate, or sodium intake. There were significant differences between groups for change in protein intake ($p = 0.02$) with a significant group x time interaction ($p = 0.02$).

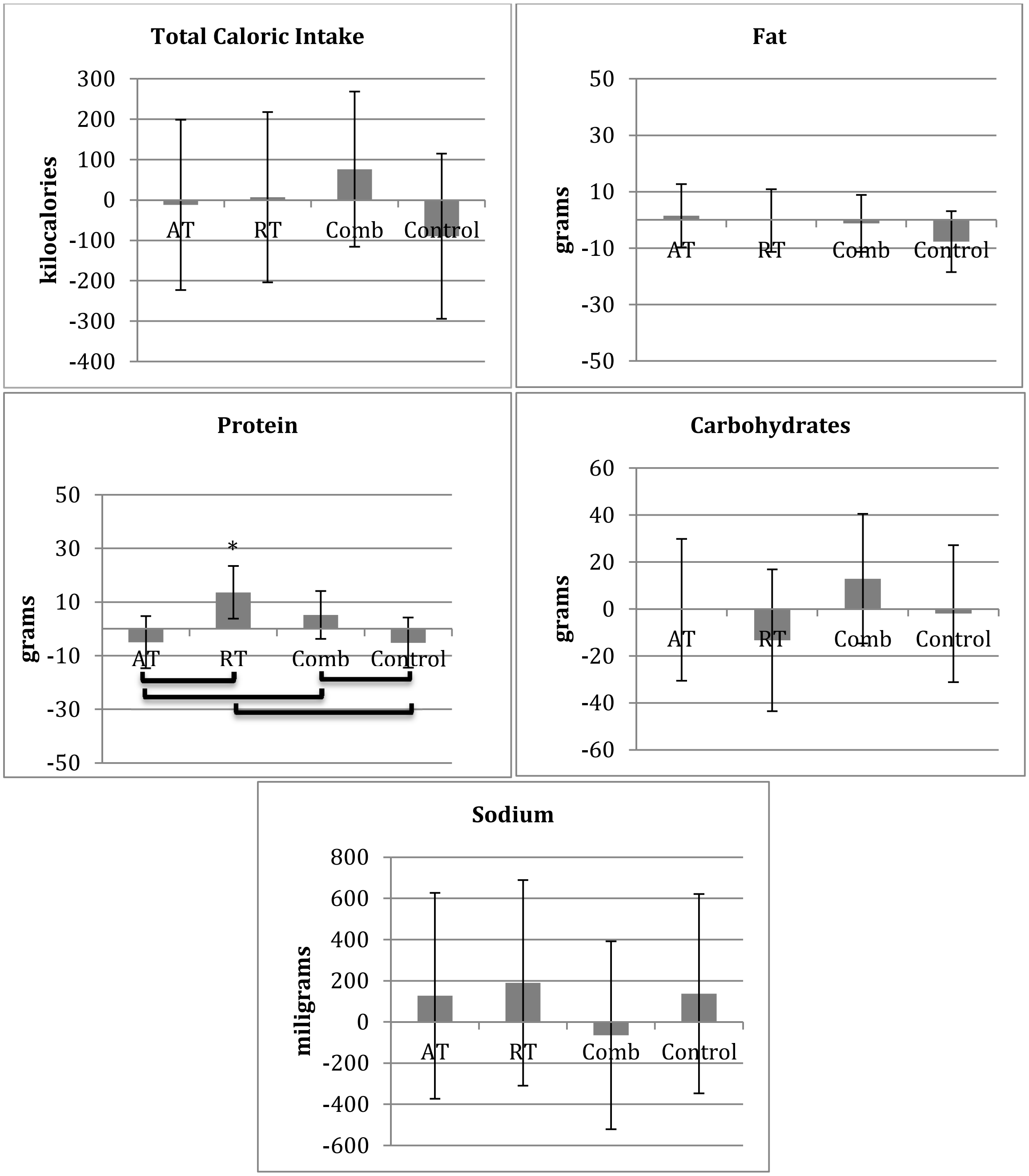

Figure 5. *Change in Baseline and Follow-up Dietary Measures for Total Kilocalories, Fat, Protein, Carbohydrates and Sodium.* Error bars indicate 95% CI. Groups connected by brackets indicate $p < 0.05$ for change between groups; * $p < 0.05$ for change within group from baseline to follow-up

The summary of pre-training and post-training change scores for all outcome variables are presented in Table 9, as well as p-values for the repeated measure ANOVAs. Additionally, more detailed results will be discussed further below. Findings from the intention-to-treat analyses are reported using the last observation carried forward method (if the outcome value was missing for the participant, the baseline value for that outcome was inserted, which is a more conservative method for analysis). However, results from the per protocol analyses, in which the 3 individuals who dropped out of the study were not included, showed similar results (data not shown). Further analyses were individually run with additional covariates of baseline BMI, change in weight, dietary factors (total kilocalories, protein, fat, and sodium), and average daily steps. No significant changes were noted so those results are not included.

Table 9. *Effects of Exercise Modes on Changes in Outcome Variables*. SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; RM: Repetition Maximum; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol

Characteristic	Mean (95% Confidence Interval)				p-value			Significant Differences Between Groups
	Aerobic (AT)	Resistance (RT)	Combination (Comb)	Control (Con)	group	time	interaction	
Body Composition								
BMI, kg/m^2	-0.3 (-0.7, 0.0)	-0.1 (-0.5, 0.3)	0.2 (-0.2, 0.6)	0.0 (-0.3, 0.4)	0.19	0.57	0.18	AT vs. Comb, AT vs. Con
Weight, kg	**-1.0 (-1.9, -0.1)**	-0.19 (-1.09, 0.70)	**0.9 (0.0, 1.8)**	0.1 (-0.8, 1.0)	**0.03**	0.78	**0.03**	AT vs. Comb, AT vs. Con, RT vs. Comb
Waist circumference, cm	0.4 (-1.3, 2.0)	**-1.7 (-3.3, -0.1)**	0.9 (-0.7, 2.5)	0.5 (-1.2, 2.1)	0.11	0.99	0.11	AT vs. RT, RT vs. Comb, RT vs. Con
Lean body mass, kg	-0.3 (-1.0, 0.5)	0.1 (-0.6, 0.9)	**0.8 (0.0, 1.5)**	-0.1 (-0.9, 0.6)	0.17	0.51	0.19	AT vs. Comb, Comb vs. Con
Fat Mass, kg	**-0.9 (-1.5, -0.2)**	-0.3 (-1.0, 0.3)	-0.1 (-0.7, 0.5)	0.2 (-0.5, 0.8)	0.14	0.08	0.15	AT vs. Comb, AT vs. Con
Body Fat Percentage, %	-0.6 (-1.2, 0.0)	-0.2 (-0.8, 0.4)	-0.4 (-1.0, 0.1)	0.1 (-0.5, 0.7)	0.36	**0.047**	0.46	AT vs. Con
Resting Hemodynamics								
Resting Heart Rate, bpm	-2.4 (-5.3, 0.5)	2.1 (-0.8, 5.0)	-1.8 (-4.6, 1.0)	1.9 (-1.0, 4.8)	**0.01**	0.93	**0.048**	AT vs. RT, AT vs. Con, RT vs. Comb, Comb vs. Con
Peripheral SBP, mmHg	0.1 (-3.9, 4.0)	-0.9 (-4.9, 3.0)	-0.2 (-4.0, 3.7)	-0.7 (-4.7, 3.3)	0.98	0.66	0.98	
Peripheral DBP, mmHg	-0.3 (-3.5, 2.9)	0.1 (-3.1, 3.3)	**-3.7 (-6.8, -0.6)**	0.1 (-3.2, 3.3)	0.27	0.24	0.27	AT vs. Comb, RT vs. Comb, Comb vs. Con
Central SBP, mmHg	-0.6 (-4.0, 1.1)	-2.5 (-5.9, 1.0)	-0.7 (-4.1, 2.6)	-0.9 (-4.3, 2.6)	0.9	0.18	0.85	
Central DBP, mmHg	-2.4 (-4.9, 0.1)	-0.1 (-2.6, 2.4)	**-4.4 (-6.8, -1.9)**	-0.8 (-3.3, 1.7)	0.08	**<0.01**	0.08	RT vs. Comb, Comb vs. Con

(Table 9 continued)

Cardiorespiratory Fitness								
Time on treadmill, sec	**72 (38, 107)**	12 (-23, 48)	**51 (17, 86)**	18 (-17, 52)	**0.04**	**<0.01**	0.053	AT vs. RT, AT vs. Con, RT vs. Comb, Comb vs. Con
Lower Body Muscular Strength								
1 RM Leg Press, kg	-1.1 (-10.3, 8.1)	**13.3 (4.1, 22.5)**	**11.1 (2.1, 20.0)**	2.3 (-7.2, 11.7)	0.09	**0.01**	0.09	AT vs. RT, AT vs. Comb, RT vs. Con
Upper Body Muscular Strength								
1 RM Bench Press, kg	**3.6 (1.8, 5.4)**	**4.3 (2.4, 6.1)**	**4.4 (2.6, 6.2)**	**2.0 (0.2, 3.9)**	0.43	**<0.01**	0.24	RT vs. Con, Comb vs. Con
Fasting Blood Lipids and Glucose								
Fasting glucose, mg/dL	0.0 (-3.1, 3.1)	0.1 (-3.0, 3.1)	-1.6 (-4.6, 1.4)	1.7 (-1.4, 4.8)	0.52	0.96	0.5	Comb vs. Con
Total Cholesterol, mg/dL	-3.7 (-11.9, 4.6)	-6.5 (-14.8, 1.8)	-3.1 (-11.2, 4.9)	-2.8 (-11.0, 5.5)	0.61	0.06	0.92	
HDL-C, mg/dL	0.1 (-2.3, 2.4)	0.4 (-2.0, 2.8)	**-2.5 (-4.8, -0.2)**	-1.6 (-4.0, 0.8)	0.34	0.13	0.25	AT vs. Comb, RT vs. Comb
Triglycerides, mg/dL	-11.3 (-31.8, 9.2)	**-26.4 (-46.9, -5.9)**	3.3 (-16.6, 23.3)	**-22.3 (-42.8, -1.8)**	0.38	**0.01**	0.17	RT vs. Comb, Comb vs. Con
LDL-C, mg/dL	-1.5 (-8.6, 5.7)	-0.9 (-8.2, 6.5)	1.8 (-5.3, 8.8)	3.2 (-3.9, 10.4)	0.56	0.71	0.77	

Bolded values indicate statistical significance at the α=0.05 level.

Resting Hemodynamics

Baseline, follow-up, and change values for resting hemodynamics across groups are summarized in Table 10. No significant differences in change in peripheral SBP were seen within or between any of the groups. The significant peripheral DBP reduction of -3.7 mmHg (95% CI -6.8, -0.6) in the combination group was significantly different from all other groups (Figure 6). Change in resting heart rate was significantly different between groups (p = 0.01), with a significant group-by-time interaction (p = 0.048) (Table 9). The aerobic and combination groups showed a decrease in resting heart rate of -2.4 (-5.3, 0.5) and -1.8 (-4.6, 1.0) beats per minute, respectively, which were significantly different from the resting heart rate changes in the resistance [2.1 bpm (-0.8, 5.0)] and control groups [1.9 bpm (-1.0, 4.8)] (Figure 6).

Table 10. *Baseline, Follow-up, and Change in Resting Hemodynamics.*

Intervention Group	No. of Participants	Baseline Value Mean (SE)	Follow-up Value Mean (SE)	Within-Group Changes Change (95% CI)	Comparison Vs. Control Change (95% CI)	p-value
Peripheral Systolic Blood Pressure, mmHg						
Aerobic	17	131 (1.4)	131 (1.4)	0.1 (-3.9, 4.0)	0.9 (-3.1, 4.9)	0.66
Resistance	17	131 (1.4)	130 (1.4)	-0.9 (-4.9, 3.0)	-0.0 (-4.0, 4.0)	0.99
Combination	18	131 (1.4)	130 (1.4)	-0.2 (-4.0, 3.7)	0.7 (-3.2, 4.6)	0.72
Control	17	130 (1.4)	130 (1.4)	-0.7 (-4.7, 3.3)	-	
Peripheral Diastolic Blood Pressure, mmHg						
Aerobic	17	81 (1.1)	80 (1.1)	-0.3 (-3.5, 2.9)	-0.2 (-3.4, 3.0)	0.89
Resistance	17	81 (1.1)	81 (1.1)	0.1 (-3.1, 3.3)	0.2 (-3.0, 3.4)	0.90
Combination	18	81 (1.1)	77 (1.1)	**-3.7 (-6.8, -0.6)**	-3.6 (-6.8, -0.5)	**0.02**
Control	17	80 (1.1)	81 (1.1)	0.1 (-3.2, 3.3)		

(Table 10 continued)

Resting Heart Rate, bpm						
Aerobic	17	69 (1.0)	66 (1.0)	-2.4 (-5.3, 0.5)	**-4.9 (-7.8, -2.0)**	**<0.01**
Resistance	17	69 (1.0)	71 (1.0)	2.1 (-0.8, 5.0)	-0.1 (-3.0, 2.8)	0.94
Combination	18	69 (1.0)	67 (1.0)	-1.8 (-4.6, 1.0)	**-4.4 (-7.3, -1.5)**	**<0.01**
Control	17	69 (1.0)	71 (1.0)	1.9 (-1.0, 4.8)	-	

Bolded values indicate statistical significance at the α=0.05 level.

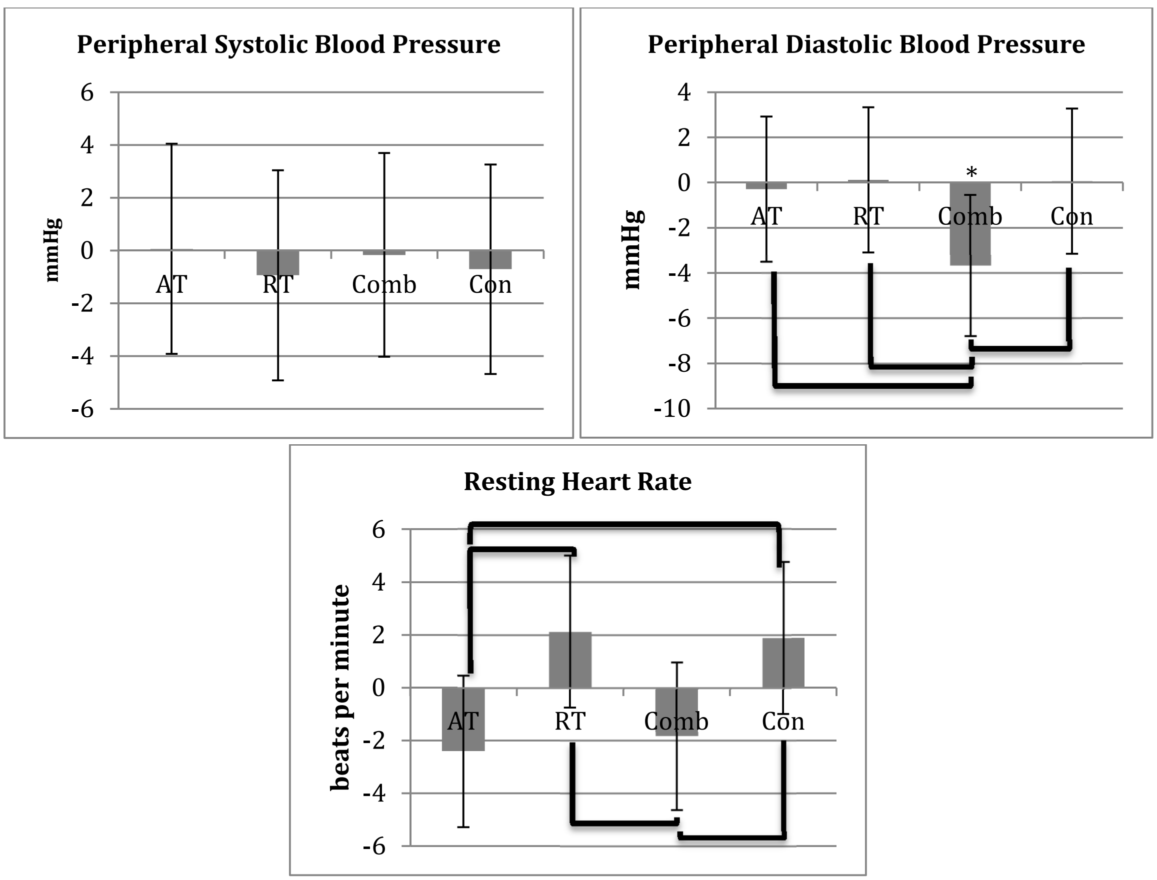

Figure 6*. Effects of Exercise Modes on Change in Peripheral SBP and DBP, Central SBP and DBP, and Resting Heart Rate*. Error bars indicate 95% CI. Groups connected by brackets indicate p <0.05 for change between groups; * p < 0.05 change within group from baseline to follow-up

Body Composition

Baseline, follow-up, and change values for body composition measurements across groups are summarized in Table 11. The aerobic exercise group appeared to receive the greatest benefit in regards to body composition with significant reductions [mean (95% CI)] in weight [-1.0 kg (-1.9, -0.1)] and fat mass [-0.9 kg (-1.5, -0.2)], whereas the resistance training group significantly decreased their waist circumference by -1.7 cm (95% CI -3.3, -0.1) on average. Both lean body mass and weight significantly increased in the combination group. All groups appeared to have a decrease in body fat percentage, compared to the control, with only the aerobic group being significantly different (Table 11).

A significant time-by-group interaction (p=0.03) was seen for change in weight, with the aerobic and combination group showing the greatest, but opposite, changes (Figure 7). The aerobic group reductions in BMI, weight, and fat mass were significantly greater than the change in the combination and control groups, whereas the waist circumference reduction by the resistance training group was significantly different from all other groups. The lean body mass change in the combination group was significantly greater than that of the aerobic or control group, but not resistance group (Figure 7). The change in weight and body fat percentage in the combination training group showed a trend toward significance compared to the control group (p for interaction = 0.07 & 0.09, respectively).

Table 11. *Baseline, Follow-up, and Change in Body Composition.*

Intervention Group	No. of Participants	Baseline Value Mean (SE)	Follow-up Value Mean (SE)	Within-Group Changes Change (95% CI)	Comparison Vs. Control Change (95% CI)	p-value
BMI, kg/m^2						
Aerobic	17	32.4 (0.1)	32.1 (0.1)	-0.3 (-0.7, 0.0)	**-0.4 (-0.8, -0.0)**	**0.04**
Resistance	17	32.4 (0.1)	32.3 (0.1)	-0.1 (-0.5, 0.3)	-0.2 (-0.5, 0.2)	0.39
Combination	18	32.4 (0.1)	32.6 (0.1)	0.2 (-0.2, 0.6)	0.2 (-0.2, 0.5)	0.36
Control	17	32.4 (0.1)	32.5 (0.1)	0.0 (-0.3, 0.4)	-	
Weight, kg						
Aerobic	17	94.5 (0.3)	93.4 (0.3)	**-1.0 (-1.9, -0.1)**	**-1.1 (-2.0, -0.2)**	**0.02**
Resistance	17	94.5 (0.3)	94.3 (0.3)	-0.2 (-1.1, 0.7)	-0.3 (-1.2, 0.6)	0.55
Combination	18	94.5 (0.3)	95.3 (0.3)	**0.9 (0.0, 1.8)**	0.8 (-0.1, 1.7)	0.07
Control	17	94.5 (0.3)	94.5 (0.3)	0.1 (-0.8, 1.8)		
Waist Circumference, cm						
Aerobic	17	105.1 (0.6)	105.4 (0.6)	0.3 (-1.3, 2.0)	0.1 (-1.5, 1.7)	0.87
Resistance	17	105.0 (0.6)	103.3 (0.6)	**-1.7 (-3.3, -0.1)**	**-2.0 (-3.6, -0.4)**	**<0.01**
Combination	18	105.0 (0.6)	105.9 (0.6)	0.9 (-0.7, 2.5)	0.6 (-1.0, 2.2)	0.46
Control	17	104.9 (0.6)	105.3 (0.6)	0.5 (-1.2, 2.1)	-	
Lean Body Mass, kg						
Aerobic	17	56.7 (0.3)	56.5 (0.3)	-0.3 (-1.0, 0.5)	-0.1 (-0.9, 0.6)	0.72
Resistance	17	56.7 (0.3)	56.8 (0.3)	0.1 (-0.6, 0.9)	0.3 (-0.5, 1.0)	0.46
Combination	18	56.7 (0.3)	57.5 (0.3)	**0.8 (0.0, 1.5)**	**0.4 (0.2, 1.6)**	**0.01**
Control	17	56.7 (0.3)	56.6 (0.3)	-0.1 (-.9, 0.6)	-	
Fat Mass, kg						
Aerobic	17	38.2 (0.2)	37.3 (0.2)	**-0.9 (-1.5, -0.2)**	**-1.0 (-1.7, -0.4)**	**<0.01**
Resistance	17	38.2 (0.2)	37.9 (0.2)	-0.3 (-1.0, 0.3)	-0.5 (-1.1, 0.1)	0.13
Combination	18	38.2 (0.2)	38.1 (0.2)	-0.1 (-0.7, 0.5)	-0.3 (-0.9, 0.4)	0.40
Control	17	38.2 (0.2)	38.4 (0.2)	0.2 (-0.5, 0.8)	-	
Body Fat Percentage, %						
Aerobic	17	40.1 (0.2)	39.5 (0.2)	-0.6 (-1.2, 0.01)	**-0.7 (-1.3, -0.1)**	**0.02**
Resistance	17	40.1 (0.2)	39.9 (0.2)	-0.2 (-0.8, 0.4)	-0.3 (-0.9, 0.3)	0.27
Combination	18	40.2 (0.2)	39.7 (0.2)	-0.4 (-1.0, 0.1)	-0.5 (-1.1, 0.1)	0.09
Control	17	40.2 (0.2)	40.2 (0.2)	0.1 (-0.5, 0.7)	-	

Bolded values indicate statistical significance at the α=0.05 level.

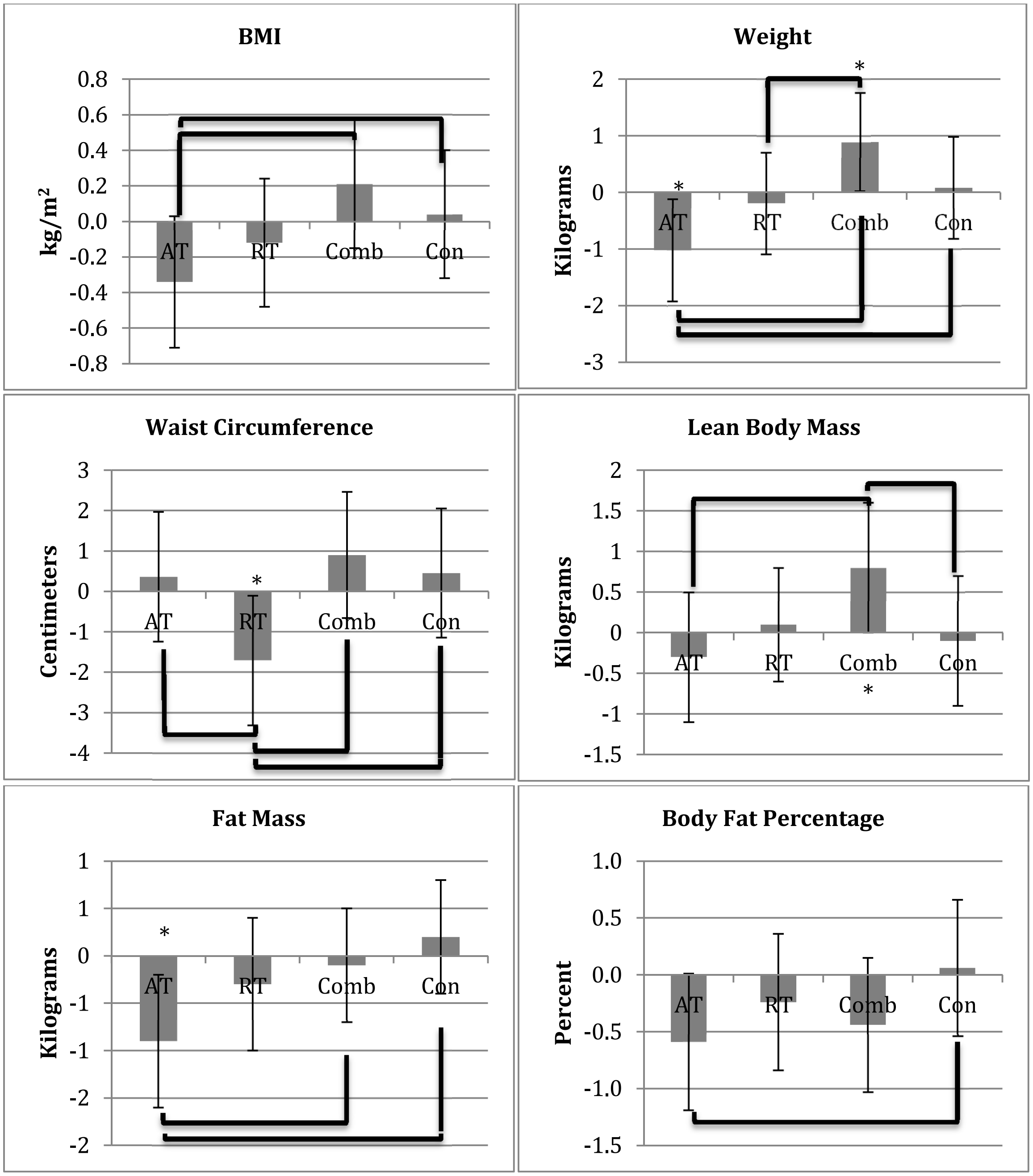

Figure 7. *Effects of Exercise Modes on Change in BMI, Weight, Waist Circumference, Lean Body Mass, Fat Mass, and Body Fat Percentage*. Error bars indicate 95% CI. Groups connected by brackets indicate p <0.05 for change between groups; * p < 0.05 change within group from baseline to follow-up

Cardiorespiratory Fitness and Muscular Strength

Baseline, follow-up, and change values for cardiorespiratory fitness and muscular strength measurements across groups are summarized in Table 12. The effect of the training stimulus was demonstrated with greater significant increases in time on the treadmill during the submaximal test for aerobic exercise and strength for resistance exercise participants over time ($p < 0.01$ for all). Although not significantly greater, the aerobic group increased their time on the treadmill by 72 seconds (95% CI 38, 107) compared to 51 seconds (17, 86) in the combination group, with no significant changes seen in either the resistance or control groups.. Lower body muscular strength increased significantly in both the resistance group [13.3 kg (95% CI, 4.1, 22.5)] and combination group [11.1 kg (2.1, 20.0)]. Upper body muscular strength significantly increased in all exercise groups with 2.0 kg (95% CI 0.2, 3.9) and 2.2 kg (0.4, 4.0) greater increases seen in the resistance and combination groups, respectively, compared with the control.

The changes in treadmill time for the aerobic and combination groups were significantly different from the resistance and control groups (Figure 8). There was a trend indicating that the combination and aerobic groups showed greater improvements over time (p for interaction = 0.05). Participants in the resistance and combination groups saw significant lower body muscular strength increases compared to the aerobic group, and upper body muscular strength compared to the control group (Figure 8). For lower body muscular strength, there was a trend indicating an interaction for group and time ($p = 0.09$).

Table 12. *Baseline, Follow-up, and Change in Treadmill Time and Muscular Strength.*

Intervention Group	No. of Participants	Baseline Value Mean (SE)	Follow-up Value Mean (SE)	Within-Group Changes Change (95% CI)	Comparison Vs. Control Change (95% CI)	p-value
Treadmill Time, seconds						
Aerobic	17	319 (12)	391 (12)	**72 (38, 107)**	55 (20, 89)	<0.01
Resistance	16	318 (13)	330 (13)	12 (-23, 48)	-7 (-42, 28)	0.70
Combination	17	320 (12)	371 (12)	**51 (17, 86)**	34 (0, 69)	0.050
Control	17	319 (12)	337 (12)	18 (-17, 52)	-	-
Leg Press 1 Repetition Maximum, kg						
Aerobic	17	123 (3.3)	122 (3.3)	-1.1 (-10.3, 8.1)	-3.8 (-13.1, 5.6)	0.43
Resistance	17	123 (3.3)	137 (3.3)	**13.3 (4.1, 22.5)**	**11.3 (1.9, 20.6)**	0.02
Combination	17	122 (3.2)	133 (3.2)	**11.1 (2.1, 20.0)**	7.9 (-1.4, 17.2)	0.09
Control	17	123 (3.4)	125 (3.4)	2.3 (-7.2, 11.7)	-	
Chest Press 1 Repetition Maximum, kg						
Aerobic	17	44 (0.6)	48 (0.6)	**3.6 (1.8, 5.4)**	1.5 (-0.4, 3.3)	0.12
Resistance	17	44 (0.6)	49 (0.6)	**4.3 (2.4, 6.1)**	**2.0 (0.2, 3.9)**	**0.03**
Combination	17	44 (0.6)	49 (0.6)	**4.4 (2.6, 6.2)**	**2.2 (0.4, 4.0)**	**0.02**
Control	17	44 (0.6)	46 (0.6)	**2.0 (0.2, 3.9)**	-	

Bolded values indicate statistical significant at the α=0.05 level.

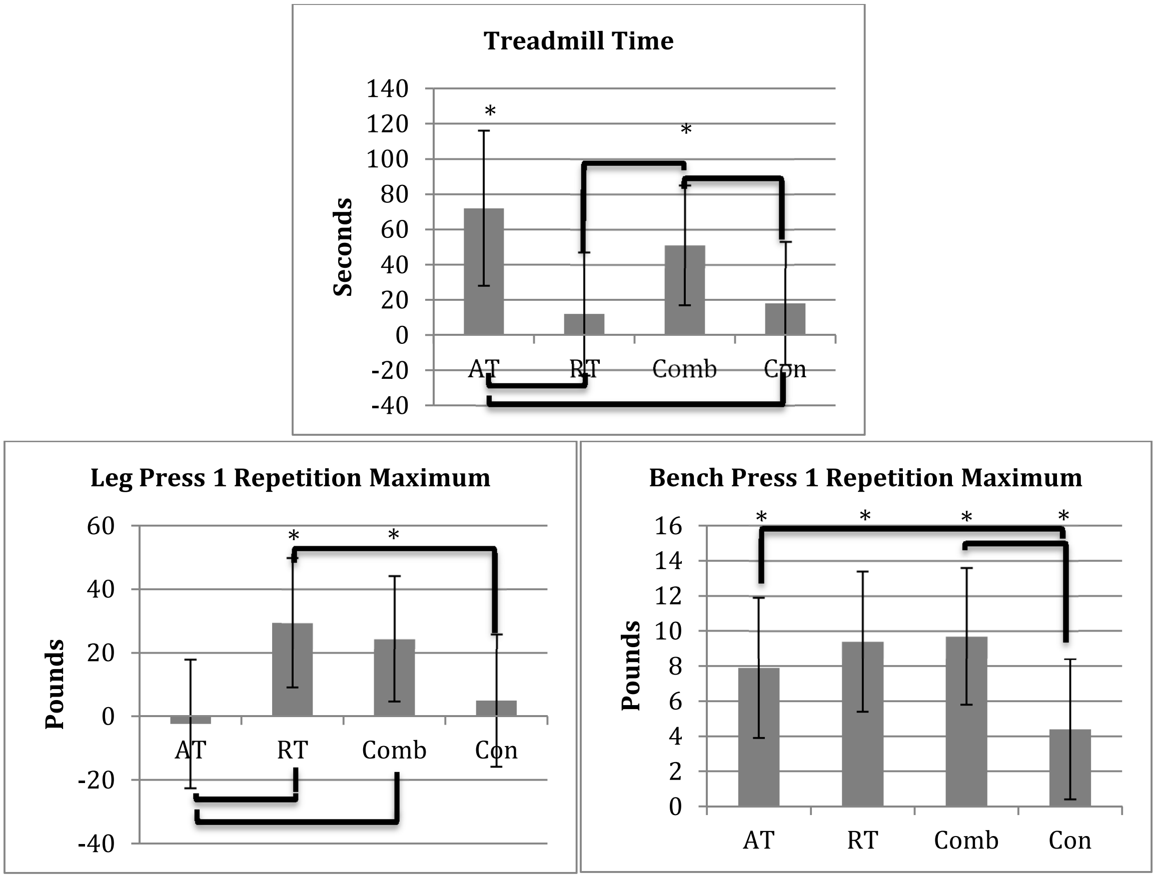

Figure 8*. Effects of Exercise Modes on Change in Treadmill Time, Leg Press 1 RM, and Bench Press 1RM*. Error bars indicate 95% CI. Groups connected by brackets indicate p <0.05 for change between groups; * p < 0.05 change within group from baseline to follow-up

Fasting Blood Lipids and Glucose

Baseline, follow-up, and change values for blood lipids and glucose measurements across groups are summarized in Table 13. Fasting blood glucose, total cholesterol, and low-density lipoprotein cholesterol did not change significantly within any of the training groups. However, high-density lipoprotein cholesterol significantly decreased in the combination group [-2.5 mg/dL (95% CI -4.8, -0.2)], and triglycerides significantly decreased in the resistance and control groups by -26.4 mg/dL (-46.9, -5.9) and -22.3 mg/dL (-42.8, -1.8), respectively.

Change values and between-group comparisons can be seen in Figure 9. Significant between-group comparisons were seen between the combination and control group for fasted glucose and triglycerides with difference being -3.2 mg/dL (95% CI -1.3, -0.2) and 21.9 mg/dL (1.5, 42.4), respectively.

Table 13. *Baseline, Follow-up, and Change in Fasting Blood Lipids and Glucose.*

Intervention Group	No. of Participants	Baseline Value Mean (SE)	Follow-up Value Mean (SE)	Within-Group Changes Change (95% CI)	Comparison Vs. Control Change (95% CI)	p-value
Glucose, mg/dL						
Aerobic	17	98 (1.1)	98 (1.1)	0 (-3.1, 3.1)	-1.6 (-4.7, 1.4)	0.29
Resistance	17	99 (1.1)	99 (1.1)	0.1 (-3.0, 3.1)	-1.3 (-4.5, 1.9)	0.41
Combination	18	98 (1.1)	97 (1.1)	-1.6 (-4.6, 1.4)	**-3.2 (-1.3, -0.2)**	**0.04**
Control	17	98 (1.1)	100 (1.1)	1.7 (-1.4, 4.8)	-	
Triglycerides, mg/dL						
Aerobic	17	161 (7.3)	149 (7.3)	-11.3 (-31.8, 9.2)	7.9 (-12.8, 28.6)	0.45
Resistance	17	163 (7.3)	136 (7.3)	**-26.4 (-46.9, -5.9)**	-5.2 (-25.8, 15.4)	0.61
Combination	18	160 (7.1)	163 (7.1)	3.3 (-16.6, 23.3)	**21.9 (1.5, 42.4)**	**0.04**
Control	17	164 (7.3)	141 (7.3)	**-22.3 (-42.8, -1.8)**	-	
High-Density Lipoprotein Cholesterol, mg/dL						
Aerobic	17	54 (0.8)	54 (0.8)	0.1 (-2.3, 2.4)	1.8 (-0.6, 4.2)	0.14
Resistance	17	53 (0.8)	54 (0.8)	0.4 (-2.0, 2.8)	1.8 (-0.5, 4.2)	0.13
Combination	18	54 (0.8)	51 (0.8)	**-2.5 (-4.8, -0.2)**	1.2 (-3.1, 1.6)	0.51
Control	17	53 (0.8)	52 (0.8)	-1.6 (-4.0, 0.8)	-	
Low-Density Lipoprotein Cholesterol, mg/dL						
Aerobic	17	130 (2.5)	128 (2.5)	-1.5 (-8.6, 5.7)	-4.9 (-12.0, 2.3)	0.18
Resistance	17	129 (2.6)	128 (2.6)	-0.9 (-8.2, 6.5)	-5.5 (-12.8, 1.8)	0.14
Combination	18	130 (2.5)	132 (2.5)	1.8 (-5.3, 8.8)	-1.8 (-8.9, 5.4)	0.62
Control	17	130 (2.5)	133 (2.5)	3.2 (-3.9, 10.4)	-	
Total Cholesterol, mg/dL						
Aerobic	17	215 (3.0)	211 (2.9)	-3.7 (-11.9, 4.6)	-1.3 (-9.6, 7.0)	0.75
Resistance	17	213 (3.0)	207 (3.0)	-6.5 (-14.8, 1.8)	-5.7 (-14.1, 2.7)	0.18
Combination	18	215 (3.0)	211 (2.8)	-3.1 (-11.2, 4.9)	-1.1 (-9.2, 7.1)	0.8
Control	17	215 (2.9)	213 (2.9)	-2.8 (-11.0, 5.5)	-	

Bolded values indicate statistical significance at the α=0.05 level.

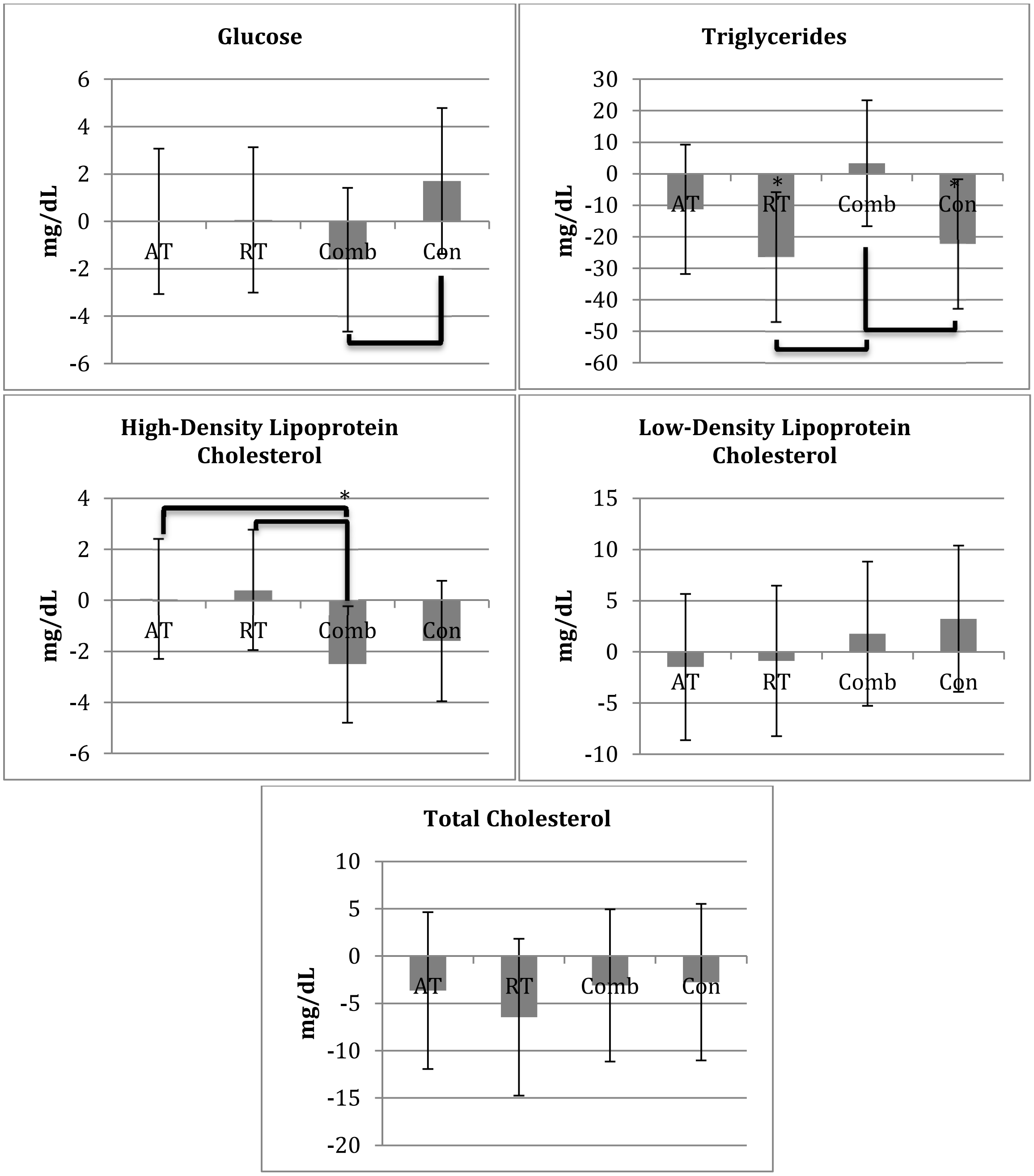

Figure 9*. Effects of Exercise Modes on Change in Glucose, Triglycerides, HDL-C, LDL-C, and Total Cholesterol*. Error bars indicate 95% CI. Groups connected by brackets indicate $p < 0.05$ for change between groups; * $p < 0.05$ change within group from baseline to follow-up

CHAPTER 5

SUMMARY AND CONCLUSIONS

The primary finding from this randomized, controlled exercise trial involving individuals with pre- or stage 1 hypertension is that although resistance and aerobic training provide some benefits on blood pressure reduction, only the combination of the two was significantly associated with reductions in both peripheral and central diastolic blood pressure. Additionally, the combination training group showed greater cumulative benefit across all cardiovascular outcomes compared to either the aerobic or resistance training group alone. One of the main goals when determining the exercise prescription for ART-B was to ensure that the total duration of weekly exercise was similar across groups. This goal was met with each group progressively increasing their exercise time to 60 minutes per session.

Although others (Collier et al., 2008; Cornelissen et al., 2011; Fagard, 2006; Moraes et al., 2012; Whelton et al., 2002) reported decreases in systolic blood pressure following aerobic and/or resistance exercise training, no exercise groups created similar results in the present study. Despite the fact that no significant differences were found in the aerobic, resistance, or combination groups for systolic blood pressure, it is important to refer to the change of about -0.9 mmHg in peripheral SBP in the resistance group and the significant reductions in DBP for the combination group, which were greater than the reduction observed in controls.

Several considerations may contribute to the smaller changes in SBP than expected in the exercisers. As people age, there is a progressive increase in arterial stiffness that contributes to systolic hypertension due to a decrease in elastic fibers, especially in post-menopausal women (Berry et al., 2004; Dart et al., 2004; Ehsani, 2001). With over half of our study population older women and 83% of them post-menopausal (mean age of 61 years), this could be a contributing factor. This increased arterial stiffness in older post-menopausal women may not be amenable by 8 weeks of exercise. Very similar to the current results, the only significant reduction for Bateman et al (2011) was noted in the DBP of the combination group after 8 months of exercise. Their study population was similar in that the participants were sedentary, overweight or obese, not on hypertensive medications, nor stage 2 hypertensives, but with the wide age range from 18 to 70 years (mean age of 50 years). On average, the study population had fairly normal blood pressure at baseline with large standard deviations. In the study by Stewart et al (2005), a combination exercise group was compared to a control group after 26 weeks of exercise in older persons (mean age of 63 years) with untreated SBP/DBP of 130-159/85-99 mmHg at baseline, which is similar to our study participants. Due to both groups seeing a reduction in blood pressure, the only significant between group differences were seen in diastolic blood pressure (p=0.02) (Stewart et al., 2005).

Other studies have also seen no significant SBP changes across aerobic, resistance, or combination groups after exercise interventions in people with elevated blood pressure (Stensvold et al., 2010; Yoshizawa et al., 2009). Most exercise intervention studies that have found significant within and between group differences for blood pressure measurements have been at least 12 weeks long

(Calders et al., 2011; Ho et al., 2012; Sousa et al., 2013; Wood et al., 2001). This could indicate that the 8 week intervention was not long enough to see the expected blood pressure responses to exercise.

Secondly, the control group also saw reductions in their peripheral and central blood pressure. These reductions reduced power to ascertain exercise induced blood pressure changes in the exercise groups compared with the control group. These individuals were also not a true non-treatment group as they received the information regarding diet and education sessions, in an attempt to have a similar control factor across groups. Although their reported steps and diet did not significantly change throughout the study, volunteers for an exercise intervention tend to be a motivated group so they likely made some lifestyle changes that were not detected or completely controlled by our methods. Other studies (Blumenthal et al., 1991; Church, Earnest, Skinner, & Blair, 2007; Stewart et al., 2005) have found similar results in which all groups showed SBP reductions and only exercisers had a significant change in DBP compared to the control group.

Lastly, blood pressure measurements and classifications only took place one day at orientation for inclusion in the study, as well as measured one day for the baseline and follow-up exam, although they were measured a minimum of 2 times on each day. According to the American Heart Association Council on High Blood Pressure Research, being classified as hypertensive should occur with the average of at least 2 office visits on differing days (Pickering et al., 2005). Had blood pressure been measured multiple times over at least two days, some variability in measurements that may have been attributed to stress and other lifestyle factors could have been minimized (Goldenberg, Pines, Baldwin, Greene, & Roh, 1948), although bias was reduced with the current data measurements occurring at the same time of day for baseline and follow-up.

In regards to body composition, the aerobic training group had the most significant changes in comparison to the control group with reductions in BMI, weight, fat mass, and body fat percentage. A recent meta-analysis (Schwingshackl, Dias, Strasser, & Hoffmann, 2013) of randomized controlled trials comparing aerobic, resistance, and combination training also concluded that aerobic training only resulted in more body composition improvements than either combination or resistance training. Although non-significant, all training groups saw a decrease in body fat percentage in comparison to the control group. This has been supported by Wanderley et al. (2013) finding that both regular aerobic and resistance training decrease total body fat, suggesting exercise training is an effective intervention for healthy weight management. Only the resistance-training group had a significant decrease in waist circumference in our study, which may be attributable to the increase in lean body mass, increase in abdominal muscle tone, or may indicate their loss of fat mass was from the abdomen (Choo et al., 2014). The increase in weight in the combination group was achieved by the significant increase in lean body mass and small reduction in fat mass, which is a healthy body composition change. Another possible explanation for the weight gain in the combination group could be related to energy intake compensation (King, Hopkins, Caudwell, Stubbs, & Blundell, 2008).

Training-induced adaptations commonly reported after aerobic and resistance training were observed in the current training program, where aerobic training led to significant increases in cardiorespiratory fitness (Church et al., 2007; Katzmarzyk et al., 2001) and resistance training led to significant increases in maximal strength (Steib, Schoene, & Pfeifer, 2010; Yoshizawa et al., 2009). Non-significant differences in gains by the aerobic and resistance groups alone compared to the combination group are similar to those reported by Karavirta et al (2011). It has previously been shown that a dose-response relationship exists between aerobic exercise and increases in cardiorespiratory fitness in sedentary, overweight or obese women (Church et al., 2007). Although not significant in this study, the aerobic group did have a larger increase in treadmill time and cardiorespiratory fitness than the combination group, probably related to time spent in aerobic exercise per exercise session.

Some synergistic effects may have masked some of the group mean values, as seen with the non-significant increase in cardiorespiratory fitness in the resistance training group and significant upper body muscular strength gains in the aerobic group. Both aerobic and resistance exercise have shown to increase skeletal muscle capillarization (Hepple et al., 2014; Prior, Blumenthal, Katzel, Goldberg, & Ryan, 2014), which could increase the ability of the muscles to utilize oxygen, ultimately both resulting in improved cardiorespiratory fitness. Secondly, neurological improvements (Nishimune, Stanford, & Mori, 2014) and exercising self-efficacy may have improved for those in the aerobic only group, making them feel more confident when preparing to do their 1 RM tests at follow-up. The aerobic and control groups may have also been more familiar with the bench press machine at follow-up after completing the baseline, attributing their increases to a learning effect, but, an attempt to eliminate this bias occurred prior to baseline with the second education session and practice attempts.

Overall, training-induced changes in fasting blood lipids and glucose were small and did not vary much between the training and control groups. Total cholesterol, triglycerides, and low-density lipoprotein cholesterol decreased in both the aerobic and resistance training groups, whereas only total cholesterol decreased in the combination group. Fasting glucose decreased only in the combination group, but most groups were already in the optimal range, so a lack of response to exercise may be expected. High-density lipoprotein cholesterol slightly increased in the aerobic and resistance groups, but significantly decreased in the combination group. The high-density lipoprotein and low-density lipoprotein response in the combination group is opposite of what was expected, with exercise training typically increasing high-density lipoprotein cholesterol levels and decreasing low-density lipoprotein cholesterol. The unusual and lack of blood lipid responses to the exercise intervention may be due to the intervention only lasting 8 weeks as high-density lipoprotein cholesterol is not as sensitive to exercise (Powers & Howley, 2004) and possibly due to non-modifiable risk factors such as sex, age, and genetics. More likely, diet was not strictly controlled in the study, in which dietary composition might be a potential confounder for the changes in lipid profiles. To minimize confounding effects associated with variation in diet, the participants were informed to maintain their usual dietary habits throughout the study period, but we cannot guarantee this occurred as seen in most lifestyle intervention studies. This may also be the main reason why a significant decrease in triglycerides was seen in the control group. Small or non-significant changes in blood lipid profiles and glucose have been reported in several other intervention studies (Bateman et al., 2011; N Sousa et al., 2014; Yoshizawa et al., 2009).

Strengths of the ART-B study include that it was a randomized, run-in design in individuals with untreated pre- or stage-1 hypertension with excellent attendance and adherence. Additionally, all exercise sessions had equal training time with direct verification of the amount and intensity of exercise being completed using heart rate monitors, the TechnoGym Wellness System, and training supervision. Because the TechnoGym Wellness System allows for objective measurement of all physical activity, this allowed assurance that the participants were completing all of the assigned exercise prescription and not reporting physical activity not completed. Furthermore, the exercise prescriptions performed were well tolerated by previously sedentary, overweight and obese individuals, making them easily obtainable by a more general population. Blood pressure measurement bias was also minimized by the utilization of an automated device. Lastly, participants wore a pedometer to track steps throughout the entire 8 week study period. Previous studies typically only have participants track outside physical activity at baseline and follow-up, but with the entire study period documented, this may have influenced participants to not be active outside of the gym, whereas in previous studies, there is uncertainty as to whether participants increased their physical activity levels throughout the intervention period since they were not being monitored.

Although daily steps were tracked throughout the 8-week period and 3-day diet logs were assessed at baseline and follow-up for changes in diet, we were still limited in identifying physical activity other than stepping that may have occurred outside of the structured exercise sessions, as well as changes in caloric intake and diet composition throughout the study period. Another limitation, due to the sedentary and unfit population, is cardiorespiratory fitness was estimated using a submaximal treadmill test instead of a maximal effort. Additionally, the leg press machine utilized had 9 kilogram weight increments, which may have prevented finding true repetition maximum increases due to such a large increase in weight per each attempt. Lastly, the sample size recruited may have not been large enough to account for variation or the intervention period long enough to see significant differences in the main outcomes within and between groups, albeit the control group also seeing a reduction in peripheral and central blood pressure. Future work should include larger randomized, controlled trials with a more strict control of diet and longer intervention period.

Conclusion

Because many adults are at risk for, or have hypertension, these results have broad clinical implications. Among individuals with pre- or stage-1 hypertension, a combination of aerobic and resistance training, compared with a non-exercise control group, resulted in improved peripheral and central diastolic blood pressure even though the exercise intervention was only 8 weeks long. In addition, these data suggest that combination training may be of greater value than either aerobic or resistance training alone as it showed to be the most beneficial, in general, overall. Furthermore, individuals hoping to improve their blood pressure and other cardiovascular disease risk factors through physical activity should be encouraged to perform both aerobic and resistance training.

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