

IMPACT OF AEROBIC EXERCISE ON BLOOD PRESSURE

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Abstract

Nearly half of American adults have hypertension, the most significant risk factor for cardiovascular disease. With 60% of hypertensive individuals also having high cholesterol, it is of interest whether an exercise prescription can successfully manage both conditions and to examine the impact of atorvastatin medication on blood pressure. In this study, obese, sedentary participants are recruited with the requirement of a $>5\%$ risk for cardiovascular events within the next 10 years or having 2 out of the 5 metabolic risk factors. Participants follow a 12-week exercise prescription designed for high cholesterol consisting of 5 aerobic exercise sessions a week, each 45 minutes long at a 60-75% heart rate reserve. The baseline and post-intervention blood pressure readings of participants were analyzed to determine whether this exercise prescription can also help manage hypertension. Major findings include that an exercise prescription following the guidelines for high cholesterol also elicited reductions in resting, peak exercise, and recovery blood pressure. The greatest reductions were seen in individuals with $>80\%$ compliance in attendance and those with baseline untreated hypertension stage I or II. Atorvastatin medication does not appear to impact blood pressure response to exercise when the participant is already on blood pressure medication. However, in participants that are not on blood pressure medication, atorvastatin treatment elicited greater blood pressure reductions compared to the placebo. Further research is needed to determine whether the addition of resistance exercise, which is recommended by the ACSM for hypertension, would elicit further reductions in blood pressure.

Chapter 1: Introduction

Hypertension is one of the most common chronic diseases in the United States, impacting nearly half of American adults. Hypertension is defined as a consistently elevated blood pressure, in which the systolic pressure is greater than or equal to 130 mmHg and the diastolic pressure is greater than 80 mmHg. As of 2017-2018, 45.5% of adults in the United States or roughly 122 million Americans are estimated to have hypertension. This is an increase from 2013-2014, in which 41.7% of adults in the United States were estimated to have the condition. Significant disparities in the prevalence of hypertension are observed by sex, race, and education [1]. These disparities make hypertension a key concern among the public health field.

With hypertension accounting for 47% of coronary heart disease cases and 54% of strokes in the United States, it is considered the most significant risk factor for cardiovascular disease [2]. As of 2019, hypertension contributes to 1 out of 3 deaths in America, a 34% increase within the last 10 years [3]. Additionally, hypertension is the most expensive cardiovascular condition costing the United States between \$131-\$198 billion a year in the cost of healthcare services, medication, and loss of productivity. Individuals with hypertension are also economically burdened, spending about \$2000 more on health costs a year compared to normotensive individuals [4].

While hypertension poses a major health risk to individuals, it is also the most modifiable risk factor for cardiovascular disease. The treatment of hypertension through lifestyle changes and medication can significantly reduce the risk of developing complications. Evidence supports increasing physical activity as an essential step in treating hypertension and reducing the risk of complications. Physical activity decreases the risk of developing cardiovascular disease in hypertensive patients by 21% and decreases the risk of cardiovascular mortality by 36% [5]. With

hypertension impacting nearly half of the United States population, it is important to analyze the impact of exercise prescription as a method to manage hypertension and reduce complications. With exercise being a cost-effective and accessible lifestyle modification, it is also a promising option for groups that face disparities in hypertension prevalence.

Purpose

This thesis will use data from the *Impact of statin therapy on muscle mitochondrial function and cardiorespiratory adaptations to aerobic exercise training* study led by Dr. Neuffer at East Carolina University. This study aims to evaluate the exercise to varying levels of atorvastatin medication in participants with high cholesterol levels. Therefore, the study uses an exercise prescription that complies with the exercise recommendations for managing high cholesterol. The exercise prescription consists of 5 aerobic exercise sessions a week, each lasting 45 minutes with intensity ranging from 60-75%. Participants exercise for 12 weeks, completing 225 minutes of exercise each week. Within the study, 69% of participants with high cholesterol also experience hypertension. As the exercise prescription used in the study complies with both recommendations for managing high cholesterol and hypertension, there is also an opportunity to analyze exercise response in terms of blood pressure. The purpose of this thesis is to investigate the impact of aerobic exercise on blood pressure response, as well as analyze how compliance, medications, and baseline hypertension classification influence this response.

Research Question & Hypothesis

The research question that this thesis will seek to answer is “Does moderate intensity aerobic exercise elicit a reduction in the blood pressure of hypertensive participants?”.

According to ACSM and AHA recommendations, compliant participants are expected to experience a decrease in blood pressure. Hypertensive participants are expected to experience a

decrease of 5-7 mmHg in systolic blood pressure. Participants with a higher baseline blood pressure are expected to experience the greatest reductions.

Significance

An exercise prescription effective in producing reductions in both blood pressure and cholesterol would have significant benefits on cardiovascular health. Reducing blood pressure helps arteries regain elasticity and become more flexible, while reducing cholesterol prevents plaque buildup in artery walls. Together, this allows more blood flow to the heart, and reduces the likelihood of cardiac events ^[6]. An exercise prescription that is successfully manages both hypertension and cholesterol levels can benefit individuals suffering from these conditions by reducing the risk of developing adverse cardiovascular complications. However, if the exercise prescription is not effective in reducing blood pressure of hypertensive patients, further research is required. This may call for increasing the intensity or frequency of the aerobic exercise prescription, increasing the length of the exercise prescription, or the addition of resistance training. This research will be valuable to individuals with hypertension seeking to manage their hypertension through exercise.

Chapter 2: Review of Literature

Hypertension

Hypertension refers to elevated blood pressure, or the pressure exerted by blood against the walls of arteries. Blood pressure measurements are displayed as systolic blood pressure over diastolic blood pressure. Systolic blood pressure measures the pressure exerted on arteries when the heart contracts and diastolic blood pressure measures the pressure exerted on arteries in between contractions ^[7]. According to the 2017 updated guidelines published by the American Heart Association and American College of Cardiology (Table 1), normal blood pressure is defined as a systolic blood pressure less than 120 mmHg and a diastolic blood pressure less than 80 mmHg. Elevated blood pressure is described as systolic blood pressure between 120-129 mmHg and diastolic blood pressure less than 80 mmHg. Hypertension is classified by a systolic blood pressure value greater than 130 mmHg or a diastolic blood pressure greater than 80 mmHg. Hypertension is further categorized into stages based on the severity of the condition. Stage 1 hypertension is characterized by either a systolic blood pressure between 130 to 139 mmHg or a diastolic blood pressure between 80 to 89 mmHg. Stage 2 hypertension is classified as either a systolic blood pressure greater than 140 mmHg or a diastolic blood pressure greater than 90 mmHg. A systolic blood pressure higher than 180 mmHg or diastolic blood pressure higher than 120 mmHg is considered a hypertensive crisis, requiring immediate medical attention ^[8].

Blood Pressure Category	Systolic Blood Pressure (mmHg)	and/or	Diastolic Blood Pressure (mmHg)
Normal	<120	and	<80
Elevated	120-129	and	<80
Hypertension Stage 1	130-139	or	80-89
Hypertension Stage 2	≥ 140	or	≥ 90
Hypertensive Crisis	>180	and/or	>120

Table 1: American Heart Association Blood Pressure Ranges (American Heart Association) ^[8]

Accurate blood pressure readings are essential to diagnose hypertension and assess the influence of intervention and treatment strategies. It is recommended that caffeine, smoking, and exercise should be avoided 24 hours before blood pressure assessment. Before taking blood pressure readings, individuals should be seated upright quietly for 5 minutes prior with legs uncrossed, flat on the floor. The arm should be supported at heart level and readings should be taken with an appropriately sized blood pressure cuff. The American Heart Association recommends that blood pressure be measured three times in each arm, with each measurement separated by at least a minute, and then averaged. It is necessary to be mindful of “white-coat hypertension” in which blood pressure readings in the presence of a healthcare provider are elevated. This is experienced by approximately 25% of patients ^[9].

Several factors contribute to an increased risk of hypertension, both modifiable and non-modifiable. As individuals age, their blood pressure tends to increase as arteries naturally thicken and stiffen. The Centers for Disease Control and Prevention [CDC] reports that 22.4% of 18-39 year olds, 54.5% of 40-59 year olds, and 74.5% of those older than 60 are hypertensive ^[1]. Individuals with a family history of hypertension are also prone to developing the condition themselves. This is attributed to several genes that increase the risk of high blood pressure and

sensitivity to salt. Underlying medical conditions that impact fluid, sodium, and hormonal control may also raise blood pressure. These conditions include certain tumors, chronic kidney disease, metabolic syndrome, obesity, sleep apnea, and thyroid conditions. Lifestyle factors can significantly increase the risk of hypertension and are the most modifiable risk factors. These include consuming an unhealthy diet with high sodium levels and low potassium levels, drinking too much alcohol or caffeine, lack of physical activity, low quality sleep, smoking, and the use of illegal drugs ^[10].

The Centers for Disease Control and Prevention has also reported significant demographic differences in prevalence of hypertension using data from the National Health and Nutrition Examination Surveys. This data was based upon the most recent 2-year survey cycle from 2017 to 2018. This study reports that the prevalence of hypertension among US adults was 45.4%, with 51% of men affected and 39.7% of women affected. Hypertension prevalence is highest among non-Hispanic blacks (57.1%) compared to non-Hispanic whites (43.6%) and Hispanic adults (43.7%). Hypertension prevalence was lowest in college graduates (38.5%) compared to adults with a high school education or less (47%) and those who had completed some education beyond high school (50.5%). Hypertension prevalence increased from 41.7% in 2013-24 to 45.4% in the 2017-18 survey cycle. This may be attributed to the updated 2017 definition of hypertension, which redefined hypertension guidelines for systolic blood pressure from 140 mmHg to 130 mmHg, and for diastolic blood pressure from 90 mmHg to 80 mmHg^[11]. Of those with hypertension, only 39.64% are considered to have well-controlled hypertension ^[11].

Significant complications are associated with undetected or uncontrolled complications. Hypertension is attributable to 47% of coronary heart disease cases and 54% of strokes in the

United States, making it the most significant risk factor for cardiovascular disease ^[2]. The damage that hypertension inflicts on arteries over time can also result in heart attack, heart failure, kidney disease, vision loss, sexual dysfunction, and peripheral artery disease. Between 2009 and 2019, the death rate attributable to hypertension increased by 34.2% ^[3]. Additionally, hypertension places significant economic burdens on the individual and the United States. Individuals with hypertension are subject to \$1920 higher annual adjusted incremental expenditure, in comparison to non-hypertensive individuals. In addition, they pay 2.5 times the inpatient cost, almost 2 times the outpatient cost, and 3 times the prescription medication expenditure compared to non-hypertensive individuals. The estimated annual incremental cost to the United States is \$131 billion higher annually for the hypertensive population than the non-hypertensive population ^[4].

The first-line treatment recommended for hypertension, especially those classified as elevated blood pressure or Stage 1 hypertension, is lifestyle modifications. Recommended modifications include weight loss, physical activity, healthy dietary pattern, and moderation or elimination of alcohol consumption. Antihypertensive medication may be recommended by providers based on the level of blood pressure and presence of high atherosclerotic cardiovascular disease risk. When antihypertensive medication is required, the individual is commonly prescribed a thiazide diuretic, angiotensin-converting enzyme inhibitor, and calcium channel blocker. Clinical trials have supported that lowering blood pressure through lifestyle modifications or medication lowers the risk of cardiovascular disease morbidity and mortality ^[12].

High Cholesterol

Cholesterol is a type of lipid that is important for the body to perform many functions, however, high levels can cause damage to artery walls and lead to heart disease. Cholesterol levels are measured through a blood test called a lipid panel. This panel provides HDL cholesterol levels, LDL cholesterol levels, and triglyceride levels. HDL cholesterol, or high-density lipoprotein, is beneficial and moves extra cholesterol from the bloodstream to the liver. This helps to keep arteries clear of excess cholesterol. LDL cholesterol, or low-density lipoprotein, can contribute to plaque buildup in arteries when levels are too high. High levels of triglycerides can also increase the risk of atherosclerosis. Total cholesterol can be calculated with these values using the following formula:

$$\text{HDL} + \text{LDL} + 20\% \text{ Triglycerides} = \text{Total Cholesterol}$$

Total cholesterol values provide insight on the total amount of cholesterol circulating in the blood. In healthy cholesterol readings, total cholesterol is under 200 mg/dL, LDL cholesterol is under 100 mg/dL, and HDL cholesterol is greater than or equal to 60 mg/dL. In at-risk cholesterol readings, total cholesterol is between 200-239 mg/dL, LDL cholesterol is between 100-159 mg/dL, and HDL cholesterol is between 40-59 mg/dL (males) or 50-59 mg/dL (females). Cholesterol levels become dangerous, placing individuals at risk for cardiovascular damage, when total cholesterol is over 240 mg/dL, LDL cholesterol is over 160 mg/dL, and HDL cholesterol is under 40 mg/dL (male) or 50 mg/dL (female) ^[13]. These categorization values are displayed in Table 2.

Cholesterol Levels	Total Cholesterol	LDL Cholesterol	HDL Cholesterol
Healthy	< 200 mg/dL	< 100 mg/dL	≥ 60 mg/dL
At-Risk	200-239 mg/dL	100-159 mg/dL	40-59 mg/dL (male) 50-59 mg/dL (female)
Dangerous	≥ 240 mg/dL	≥ 160 mg/dL	< 40 mg/dL (male) < 50 mg/dL (female)

Table 2: Cholesterol Level Ranges ^[13]

Like hypertension, risk factors for high cholesterol also include modifiable and non-modifiable factors. Familial hypercholesterolemia can be passed from parent to child and make it more difficult for the body to remove LDL cholesterol from the blood or break it down into the liver. With age, the risk for high cholesterol also increases as the body's metabolism changes and LDL cholesterol is less efficiently removed by the liver. High cholesterol is commonly diagnosed in individuals between the ages of 40-59. Underlying medical conditions and some medications can also raise LDL cholesterol levels and decrease HDL levels. Lifestyle habits are also a significant contributor to high cholesterol levels and are modifiable. Unhealthy lifestyle habits include eating foods high in saturated fats, lack of physical activity, smoking, high stress levels, and drinking too much alcohol ^[14].

Data published by the Centers for Disease Control and Prevention also reveals demographic disparities in high cholesterol levels. From 2017-2020, 10% of US adults had high total cholesterol levels, above 240 mg/dL. This translates to approximately 25 million adults. Additionally, another 86 million adults have total cholesterol levels above 200 mg/dL, placing them at risk for developing high cholesterol. 17% of US adults were reported to have low HDL levels, below 40 mg/dL ^[15].

High cholesterol levels, or hypercholesterolemia, are a major risk factor in the formation of atherosclerotic plaques. High levels of LDL cholesterol are believed to increase the risk of atherosclerotic lesion formation, while elevated HDL levels have been shown to decrease the risk. The formation of these plaques increases the risk of coronary artery disease, peripheral artery disease, aortic aneurysms, and stroke. High cholesterol levels increase the risk of morbidity and mortality from cardiovascular conditions ^[16].

The National Cholesterol Education Program (NCEP) guidelines recommend that lifestyle changes be implemented for all patients with high cholesterol levels placing them at risk for cardiovascular disease. Changes recommended include reducing intake of saturated fats and cholesterol, increasing soluble fiber intake, physical activity, moderation of alcohol, smoking cessation. Addition of drug therapy is evaluated based on level of cardiovascular risk and assessment of levels after initiating lifestyle changes. In high-risk patients or patients not responding to lifestyle changes, statin therapy is initiated ^[17].

Correlation between hypertension and high cholesterol

Both hypertension and high cholesterol have significant impacts on arteries and the cardiovascular system, increasing the risk of cardiovascular complications. Hypertension damages arteries by causing them to lose elasticity and become stiff and brittle, while high cholesterol leads to plaque buildup in the walls of arteries ^[6]. A study in the Journal Hypertension suggests that diagnosis with both high LDL cholesterol levels and hypertension further increases the risk of developing cardiovascular disease. This study reports that high levels of lipoprotein (a), a type of LDL cholesterol, are associated with a 24% higher risk of cardiovascular disease among people who have hypertension. In this study, 18.8% of participants

with both high cholesterol and hypertension experienced cardiovascular disease events. This was higher than participants that were only diagnosed with either hypertension or high cholesterol^[18]. Additionally, diagnosis with both high cholesterol and hypertension increases the risk of developing peripheral artery disease. This condition is associated with a further increased risk of heart attack, stroke, and death^[6].

Exercise Prescriptions for Hypertension and High Cholesterol

The American Heart Association and American College of Cardiology recommend lifestyle approaches to prevent and treat elevated blood pressure and cholesterol. For mild or moderate hypertension and high cholesterol, lifestyle changes are the first line of treatment. Medications are only implemented in these patients if lifestyle changes are unsuccessful. This applies to 21% of US adults with mild risk hypertension or cholesterol and 28-37% of adults with moderate risk hypertension or cholesterol. Of the recommended lifestyle changes, increasing physical activity is recommended to lower both blood pressure and blood cholesterol.

The American College of Sports Medicine recommends that individuals with hypertension engage in aerobic exercise 5-7 days a week. Exercise should be moderate intensity, meaning 40-60% of VO₂ max or 11-14 on the RPE scale. This should cause noticeable increases in heart rate and breathing. Each exercise session should consist of 30-60 minutes of continuous or accumulated aerobic exercise with emphasis placed on prolonged, rhythmic activities using large muscle groups. Recommended activities include walking, cycling, and swimming. Additionally, The American College of Sports Medicine recommends supplementing aerobic exercise with resistance exercise and flexibility exercises 2-3 days a week^[9].

Research suggests that an effective exercise prescription for lowering hypertension results in acute physiologic responses, post-exercise physiological responses, and chronic physiological responses. During the acute physiologic response, aerobic exercise increases and redistributes cardiac output to active muscles. This process causes systolic blood pressure to rise as cardiac output increases, while diastolic blood pressure falls. The post-exercise physiological response leads to hypotension, with immediate blood pressure reductions of 5-7 mmHg. Due to this benefit, it is recommended that hypertensive individuals maintain a high exercise frequency. This antihypertensive effect of exercise is attributed to vascular changes including increased vascular length, increased lumen diameter, and increased number of precapillary sphincters. Increased baroreceptor sensitivity, decreased norepinephrine level, and alterations in expression of vasodilator and vasoconstrictor factors also contribute to decreased blood pressure ^[9].

To manage high cholesterol, the 2017 Hypertension Clinical Practice Guidelines recommend 3-4 sessions of moderate to vigorous intensity exercise per week, with each exercise session lasting 40 minutes. Intensity of exercise should range between 40-84% of VO₂ max. There are no specific recommendations for resistance exercise to manage cholesterol ^[5]. The mechanisms of how exercise decreases cholesterol levels are unclear, however, it seems to increase skeletal muscle's ability to use lipids instead of glycogen. This appears to reduce cholesterol levels in blood ^[19].

There is strong evidence that physical activity decreases both blood pressure and cholesterol. Research indicates a dose-response relationship, in which increased intensity and frequency of exercise results in greater reductions of blood pressure and cholesterol levels. Additionally, research has indicated a “floor effect”, in which individuals with higher baseline blood pressure and cholesterol values experienced the greatest reductions. The 2018 Physical

Activity Guidelines Committee reported these findings in regard to hypertension following a meta-analysis. Normotensive participants experienced a systemic blood pressure reduction of 2 mmHg, participants with elevated or stage 1 hypertension experienced a systemic blood pressure reduction of 4 mmHg, and participants with stage 2 or higher hypertension experienced a systemic blood pressure reduction of 5-9 mmHg. The average effects of exercise reported in the meta-analysis were a systolic blood pressure reduction of 4 mmHg and a diastolic blood pressure reduction of 3 mmHg. Blood pressure reductions from exercise lower overall cardiovascular disease risk by 20-30%. A similar “floor effect” is seen in the relationship between exercise and blood cholesterol. A 2006 meta-regression across aerobic exercise trials reported that greater improvements were observed with lower baseline levels of HDL cholesterol and higher baseline levels of LDL and triglycerides. Research indicates that aerobic exercise tends to increase HDL cholesterol levels and decrease triglyceride levels, however, there is less consistent evidence that aerobic exercise decreases LDL cholesterol levels ^[5].

Chapter 3: Methodology

The methodology and data used for this thesis originates from the *Impact of statin therapy on muscle mitochondrial function and cardiorespiratory adaptations to aerobic exercise training* study led by Dr. Neufer in the ECU Diabetes & Obesity Institute. The primary aim of the study is to investigate exercise response among patients with high cholesterol receiving one of three atorvastatin medication treatments. As the exercise recommendations for high cholesterol and hypertension align, I will be using the data from this study to analyze the impact of aerobic exercise on blood pressure. This study began in April 2019 and the final participant completed the study in October 2023. Between June 2022 and May 2023, I assisted with data collection for this study as an undergraduate research assistant.

Participant Selection Criteria

The primary study recruited obese, sedentary participants between the ages of 35-65 years. Inclusion criteria to determine study eligibility included BMI between 25-43 kg/m², sedentary lifestyle, stable weight, and stable medication doses for 90 days. Additionally, potential participants were required to have either a >5% risk for a cardiovascular event in the next 10 years and/or LDL > 120 and/or 2 out of 5 metabolic syndrome risk factors. Metabolic syndrome risk factors include triglycerides ≥ 150 mg/dl, HDL ≤ 40 mg/dl, glucose ≥ 100 mg/dl, waist circumference > 102 cm for males and 88 cm for females, blood pressure > 130 mmHg systolic and/or 85 mmHg for diastolic or being treated for hypertension. Study exclusion criteria included smoking, use of statins or other medications that affect lipid profiles within the last 6 months, diagnosis of chronic diseases (CVD, diabetes, other metabolic diseases, cancer, HIV, AIDS), individuals taking cyclosporine or strong CYP3A4 inhibitors, history of abnormal

bleeding problems, anti-platelet medication, women who are pregnant or breastfeeding, and individuals with polymorphisms (SLCO1B1 and GATM).

Potential participants first completed a telephone screen, during which data was collected on health history, medications and physical activity levels. The second screening took place in-person and measured height and weight, blood pressure, a fasting blood draw (glucose, lipids, complete metabolic panel, and creatine kinase). These screening visits were used to determine the potential participant's eligibility. 100 potential participants were screened for the study. Of the participants screened, 55 participants were eligible and started the study. The study was completed by 42 participants.

Randomization

The present study used a double-blind, randomized, placebo-controlled design. Eligible participants were randomly assigned to one of three treatment groups: (1) exercise prescription plus placebo; (2) exercise prescription plus 20 mg/day atorvastatin; (3) exercise prescription plus 80 mg/day atorvastatin. As this was a double-blind study, neither the study coordinators nor participants were aware of which treatment they were receiving. The randomization of the treatment group was carried out by a biostatistician using a computer-based random number generator at a 1:1:1 ratio.

Procedure

After confirming eligibility, participants completed three visits to collect baseline measurements. During these visits, the following tests and measurements were performed: blood pressure (resting, peak exercise, recovery), DEXA scan, exercise test, NIRS, physical

performance assessment, pain assessment, muscle strength, muscle biopsy and IVGTT, and blood draw. Upon completion of baseline visits, participants received compensation of \$100.

Following baseline visits, participants began the 12-week exercise prescription. After 1-month of exercise; a blood draw, muscle biopsy, and IVGTT were completed. Blood draw results were used to detect abnormal myopathy and changes in liver function which may result from statin use to ensure participant safety. Upon completion of the 1-month visit, participants received \$100.

Upon completion of the 12-month exercise prescription, post-intervention data was collected over the course of three visits. The following tests and measurements were performed: blood pressure (resting, peak exercise, recovery), DEXA scan, exercise test, NIRS, physical performance assessment, pain assessment, muscle strength, IVGTT, and blood draw. Participants received \$300 compensation following completion of the 12-week exercise prescription with compliance $\geq 80\%$ and an additional \$300 following completion of post-intervention visits. In total, participants with $\geq 80\%$ compliance received \$800, participants with compliance of 65-79% received \$700, and participants with compliance below 65% received \$600.

Exercise Prescription

The 12-week exercise prescription consisted of aerobic exercise sessions 5 days each week at 60-75% intensity, determined by participant's $VO_{2\max}$. The exercise prescription followed a three-stage progression: (1) Week 1 = 30 min, 3 days/week, 60% $VO_{2\max}$; (2) Week 2 = 30 min, 5 days/week, 60% $VO_{2\max}$; (3) Week 3-12 = 45 min, 5 days/week, 60-75% $VO_{2\max}$. To determine appropriate intensity for each participant, participants complete a $VO_{2\max}$ test during their baseline visits. This is used to calculate heart rate ranges corresponding to prescribed

intensity. All exercise sessions were completed within the ECDOI or FITT Building exercise facilities. These sessions were supervised by research staff and intensity was monitored and recorded every five minutes.

Data Analysis

Data collected throughout the course of the study was entered and stored in a RedCap database. To ensure confidentiality, each participant was assigned a code, under which their data is stored. Additionally, access to the database is restricted and password protected.

The following participant measurements from RedCap were used in data analysis: demographic information, compliance, resting blood pressure, peak exercise blood pressure, recovery blood pressure, blood pressure medication, and LDL cholesterol. Baseline resting blood pressure was used to classify participants as normal blood pressure, elevated blood pressure, hypertension stage I, and hypertension stage II. As this is a double-blind study, it cannot be identified whether or not the participant was receiving the atorvastatin or placebo treatment. However, this can be estimated by comparing baseline and post-intervention LDL cholesterol levels. If LDL cholesterol decreased significantly ($<40\%$) from baseline to post-intervention and the post-intervention LDL cholesterol reading is within normal range, it is estimated that the participant was receiving either the 20 mg/day or 80 mg/day atorvastatin treatment. This estimation is used to analyze the impact of atorvastatin medication on blood pressure response to exercise.

A demographic analysis was performed by age, race, and sex of participants and represented as percentages. The remainder of data analysis focused on blood pressure response to exercise. Mean blood pressure difference was calculated for each participant and averaged. Mean

blood pressure difference was calculated by subtracting the respective post-intervention blood pressure value from the baseline value. This allowed standard deviation to be calculated. Paired T-tests were used to calculate the T-value and P-value. Results were considered significant if the P-value was less than 0.05.

Chapter 4: Results

Demographics

After screening, 55 participants began the study, and 42 participants completed the study. The average participant was white (71.4%), female (76.2%), and between the ages of 50-59 years (50%) (Table 3).

Descriptor	# of Participants	% of Participants
Race		
White	30	71.40%
Black or African American	9	21.40%
Asian	3	0.07%
Sex		
Male	10	23.80%
Female	32	76.20%
Age		
30-39	7	12.70%
40-49	8	19.00%
50-59	21	50.00%
60+	6	14.30%

Table 3: Demographic Descriptors of Participants that Completed Intervention. Presented as percentage of total population. $N=42$.

Overall Analysis

A complete analysis of blood pressure response was performed including all participants. This analysis found a negative mean blood pressure difference for most participants, as expected from prior research. According to prior research, systolic and diastolic blood pressure was expected to decrease 5-7 mmHg in response to exercise. Peak exercise systolic blood pressure saw a slightly higher decrease (-8.28 mmHg), while a less significant decrease was seen in resting systolic blood pressure (+0.36 mmHg) and recovery blood pressure (-3.51). The mean

increase in resting systolic blood pressure can be explained by a significant outlier in the data set. Diastolic blood pressure saw consistent reductions across measurements. However, reductions were slightly less significant than predicted resting diastolic (-3.76 mmHg) and recovery diastolic (-3.14 mmHg), while a larger reduction was observed for peak exercise diastolic (-5.92 mmHg).

Blood Pressure Value	Mean Blood Pressure Difference
Systolic Blood Pressure	
Resting	+0.36 ± 2.31
Peak Exercise	-8.28 ± 5.61
Recovery	-3.51 ± 5.05
Diastolic Blood Pressure	
Resting	-3.76 ± 1.93
Peak Exercise	-5.92 ± 1.41*
Recovery	-3.14 ± 1.91

Table 4: Mean Blood Pressure Difference - All Participants. Presented as mean ± SD. Mean blood pressure difference calculated by subtracting post-intervention blood pressure by baseline blood pressure. Paired T-test analysis was performed to determine significance of results.

*Indicates finding is significantly different from the control ($p < 0.05$).

Analysis of Variables Impacting Blood Pressure Response to Exercise

Exercise compliance, medications, and baseline hypertension classification were analyzed as possible variables influencing blood pressure response to exercise. The calculation of mean blood pressure difference from baseline to post-intervention allowed analysis of how certain factors enhanced or decreased blood pressure reductions. A negative mean blood pressure difference indicates a decrease in blood pressure, while a positive mean blood pressure difference indicates an increase in blood pressure.

The present study identified adequate attendance to exercise sessions by a compliance $\geq 80\%$. Of the participants that completed the study, 32 (76.2%) had a compliance rate $\geq 80\%$. 10 participants (23.7%) had a compliance rate between 65-79%, and no participants had a compliance rate below 65%. Results indicate that the group of participants with compliance rates $\geq 80\%$ experienced greater mean reductions for most blood pressure measurements, with the exception of peak diastolic and recovery systolic blood pressure. Participants with a $\geq 80\%$ compliance rate experienced a decrease of approximately 5 mmHg for resting diastolic, peak diastolic, and recovery diastolic blood pressure. These findings were significant at a <0.05 significance level (Table 5).

Compliance	Resting BP		Peak Exercise BP		Recovery BP	
	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
>80%	-0.03 $\pm$ 2.48	-5.28 $\pm$ 2.43*	-10.83 $\pm$ 5.94	-5.53 $\pm$ 1.76*	-3.26 $\pm$ 6.45	-4.67 $\pm$ 2.20*
65-79%	+1.60 $\pm$ 4.62	+1.10 $\pm$ 3.59	+0.22 $\pm$ 14.49	-7.38 $\pm$ 4.17	-5.71 $\pm$ 4.97	+2.43 $\pm$ 3.99

Table 5: Mean Blood Pressure Difference – Categorized by Compliance. Presented as mean $\pm$ SD. Mean blood pressure difference calculated by subtracting post-intervention blood pressure by baseline blood pressure. Paired T-test analysis was performed to determine significance of results. *Indicates finding is significantly different from the control ($p < 0.05$).

Variations were observed when comparing participants that were on blood pressure medication to those not on blood pressure medication. For almost all blood pressure measurements, significantly greater reductions were observed in those not taking blood pressure medications. In addition to blood pressure medication, analysis was performed to determine if there was a difference between participants who received the atorvastatin and placebo treatments in the primary study. In the participant group on blood pressure medication, there was no clear trend to indicate that blood pressure response was impacted by atorvastatin treatment when

compared to the placebo. However, within the participant group not on blood pressure medications, greater reductions were seen in those receiving atorvastatin treatment compared to those on the placebo treatment (Table 6).

Medications	Resting BP		Peak Exercise BP		Recovery BP	
	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
BP Meds	+3.31 ± 2.31	+1.71 ± 2.71	+6.44 ± 8.68	-6.19 ± 2.40*	-2.87 ± 7.06	-2.60 ± 3.30
Atorvastatin	+2.15 ± 5.79	+2.15 ± 3.29	+3.77 ± 9.97	-5.08 ± 2.24*	-6.08 ± 8.45	-4.25 ± 3.46
Placebo	+0.75	+0.25	+18.00	-11.00	+10.00	+11.00
No BP Meds	-1.46 ± 2.48	-7.48 ± 2.43*	-18.52 ± 6.70*	-5.73 ± 1.76*	-4.00 ± 7.23	-3.55 ± 2.32
Atorvastatin	-1.40 ± 3.14	-8.00 ± 3.21*	-18.53 ± 8.02*	-5.21 ± 2.17*	-11.08 ± 8.34	-5.23 ± 1.66*
Placebo	+0.50 ± 4.01	-6.70 ± 3.92	-18.50 ± 12.81	-6.63 ± 3.16	+9.14 ± 13.04	-1.63 ± 5.33

Table 6: Mean Blood Pressure Difference – Categorized by Medications. Presented as mean ± SD. . SD not represented when sample size is too small to calculate. Mean blood pressure difference calculated by subtracting post-intervention blood pressure by baseline blood pressure. Paired T-test analysis was performed to determine significance of results. *Indicates finding is significantly different from the control (p<0.05).

The final variable analyzed was baseline hypertension classification. Baseline hypertension classification was determined by using the AHA's blood pressure categorizations (Table 1) for each participant's baseline resting blood pressure. At baseline, 40.5% of participants had treated hypertension, 28.6% had normal blood pressure, 4.8% had elevated blood pressure, 19% had untreated hypertension stage I, and 9.5% had untreated hypertension stage II. Analysis indicated that participants with baseline treated hypertension and normal blood pressure experienced little, if any, reductions in blood pressure. However, participants with untreated hypertension stage I or II experienced significant reductions in blood pressure. A trend is observed that participants with higher baseline blood pressure experience greater reductions (Table 7).

Baseline Hypertension Classification	Mean Difference in Resting Blood Pressure	
	Systolic	Diastolic
Treated Hypertension (BP Meds)	+3.31 ± 4.54	+1.71 ± 2.71
Normal Blood Pressure	+5.83 ± 3.44	-1.00 ± 2.87
Elevated Blood Pressure	-7.00	-3.00
Hypertension Stage I	-3.75 ± 3.24	-15.25 ± 4.57*
Hypertension Stage II	-16.00	-14.00

Table 7: Mean Blood Pressure Difference – Categorized by Baseline Hypertension Classification. Presented as mean ± SD. SD not represented when sample size is too small to calculate. Mean blood pressure difference calculated by subtracting post-intervention blood pressure by baseline blood pressure. Paired T-test analysis was performed to determine significance of results. *Indicates finding is significantly different from the control (p<0.05).

Chapter 5: Discussion

Major Findings

This research indicates that an exercise prescription that follows guidelines for high cholesterol is also effective in managing hypertension. A negative mean difference was observed overall for all blood pressure measurements, except resting systolic blood pressure. Overall reductions in diastolic blood pressure ranged between -3.14 and -5.92 mmHg. Overall reductions in systolic blood pressure were more varied and slightly less significant than proposed by prior research. However, these reductions translate to a reduced risk of heart disease and mortality.

This research indicates that compliance, medications, and baseline hypertension classification influence blood pressure response to exercise. The analysis of compliance shows that participants with >80% compliance experienced more significant blood pressure reductions when compared to the 65-79% compliance range. This finding can be explained by the fact that participants with higher compliance attended more exercise sessions and remained within the prescribed exercise intensity range.

The impact of blood pressure medication and atorvastatin medication on blood pressure response to exercise was also measured. Participants not taking blood pressure medications experienced more significant reductions in blood pressure compared to those taking medications. This finding can be explained by previous research that found that the effects of exercise and blood pressure medication are not additive, rather exercise slightly strengthens the effect of medication on blood pressure ^[20]. Therefore, because blood pressure medication is already regulating blood pressure, the impact of exercise is less significant in blood pressure response. However, exercise is still beneficial to individuals on blood pressure medications as it

strengthens muscles and bones, lowers cholesterol and blood sugar, and improves the heart's efficiency ^[21]. The impact of atorvastatin medication was also analyzed in comparison to the placebo treatment. Within the group of participants on blood pressure medication, there is no clear trend that indicates atorvastatin impacts blood pressure response in comparison to the placebo. However, when analyzing the group of participants not on blood pressure medication, it appears that those receiving the atorvastatin treatment experienced more significant blood pressure reductions than those receiving the placebo. Previous research supports this finding, indicating that statins may act as an antihypertensive agent in individuals with higher baseline blood pressure and low HDL-C levels. Therefore, statins do not significantly lower blood pressure in participants with treated hypertension or normal blood pressure. Literature suggests that this effect is possibly due to the inhibition of 3-hydroxyl-3-methylglutaryl coenzyme A reductase or the reversal of endothelial dysfunction, decreased arterial compliance, and activation of inflammatory pathways ^[22].

Analysis of baseline hypertension classification on blood pressure response found that participants with higher baseline blood pressure experienced greater reductions as a result of exercise. Participants with baseline normal blood pressure or treated hypertension exhibited little to no reductions in blood pressure. Participants with baseline untreated hypertension stage I or II experienced much more significant reductions in blood pressure. This finding supports previous research on the “floor effect” or “law of initial values”, in which those with the highest baseline values benefit the most from exercise ^[9].

Strengths and Limitations

A strength of this study design was that all exercise sessions were monitored by a research assistant in either the ECDOI gym or FITT building. This ensured participants complied

with the exercise prescription. During monitored sessions, research assistants checked participants heart rate every 5 minutes to ensure it was within the correct intensity range. This allowed research assistants to modify intensity as needed by increasing the speed, incline, or resistance of machinery. Additionally, this ensured that exercise was taking place in a safe manner. The randomized, double-blinded study design prevented bias within the research.

Although the double-blinded nature of the study prevented bias, it is also a limitation as it prevented a definitive determination of treatment groups during data analysis for this specific project. The primary investigators and biostatistician were unblinded prior to the completion of the study to examine if the trial was finding more or less significant effects for outcome measures. Although treatment group can be estimated by analyzing baseline and post-intervention cholesterol levels, this factor must be considered as a potential source of error. Additionally, there is a possibility that some participants blood pressure readings may be impacted by “white-coat hypertension” or anxiety. These factors may cause a participant’s blood pressure reading to appear more elevated than usual. As this research uses data from the primary study, there is also a limitation due to only one fasting blood pressure measurement being taken at each timepoint. In future studies, it is recommended that blood pressure readings be repeated several times at each timepoint to prevent such errors. Finally, participants in this study were monitored to ensure correct intensity throughout exercise sessions, and assistants were present to modify intensity as needed. This may make this exercise prescription difficult for the average individual to replicate. However, the average individual may be able to use technology such as a watch with a heart rate monitoring function to achieve similar results.

Suggestions for Future Research

Future research may further explore the impact of atorvastatin treatment on blood pressure response to exercise. Additionally, future research may examine the impact of various exercise types on blood pressure response to exercise. As the ACSM has added resistance exercise to hypertension guidelines, future studies may analyze the impact of resistance and a combination of resistance and aerobic exercise on blood pressure response.

Conclusion

An exercise prescription designed for the management of high cholesterol is also effective in reducing blood pressure. The most significant blood pressure reductions are seen in participants with >80% compliance that are not on blood pressure medication but are receiving the atorvastatin treatment. Additionally, previous research is supported that participants with higher baseline blood pressure experience greater reductions as a result of exercise. These blood pressure reductions are associated with a decreased risk for cardiovascular events and mortality, especially in participants with baseline untreated hypertension. Further research is needed to replicate the study in a single-blind study setting and to analyze the impact of resistance exercise on blood pressure response.

Chapter 6: References

- [1] Centers for Disease Control and Prevention. (2020). Hypertension prevalence among adults aged 18 and over: United States, 2017-2018. National Center for Health Statistics.
<https://www.cdc.gov/nchs/products/databriefs/db364.htm>
- [2] Wu, C., Hu. H., Chou, Y., Huang, N., Li, C. (2015, November). High blood pressure and all-cause and cardiovascular disease mortalities in community-dwelling older adults. *Medicine (Baltimore)*, 94(47). Doi: 10.1097/MD.00000000000002160
- [3] Tsao, C., et al. (2022, January 26). Heart disease and stroke statistics – 2022 update: A report from the American Heart Association. Doi: <https://doi.org/10.1161/CIR.0000000000001052>
- [4] Kirkland, E., Heincelman, M., Bishu, K., Schumann, S. Schreiner, A., Axon, R., Mauldin, P., Moran, W. (2018, May 30). Trends in healthcare expenditures among US adults with hypertension: National estimates, 2003-2014. *Journal of the American Heart Association*, 7(11). <https://pubmed.ncbi.nlm.nih.gov/29848493/>
- [5] Gibbs, B., et al. (2021, June 2). Physical activity as a critical component of firstline treatment for elevated blood pressure or cholesterol: Who, what, and how?: A scientific statement from the American Heart Association. *Journal of the American Heart Association*.
<https://doi.org/10.1161/HYP.0000000000000196>
- [6] Manhattan Cardiology. High cholesterol & high blood pressure can increase your risk for PAD. <https://manhattancardiology.com/high-cholesterol-high-blood-pressure-canincrease-your-risk-for-pad/>
- [7] Centers for Disease Prevention and Control. (2021). High blood pressure.
<https://www.cdc.gov/bloodpressure/index.htm>
- [8] American Heart Association. (2023). Understanding blood pressure readings.

<https://www.heart.org/en/health-topics/high-blood-pressure/understanding-bloodpressure-readings>

- [9] Zaleski, A. (2019, February 27). Exercise for the prevention and treatment of hypertension – Implications and application. American College of Sports Medicine.

<https://www.acsm.org/blog-detail/acsm-certified-blog/2019/02/27/exercise-hypertensionprevention-treatment>

- [10] National Heart, Lung, and Blood Institute. (2022, March 24). High blood pressure - Cause and risk factors. <https://www.nhlbi.nih.gov/health/high-blood-pressure/causes>

- [11] Cobufo, M., Gayam, V., Soluny, J., Rahman, E., Enoru, S. Foryoung, J. Agbor, V., Durfresne, A., Nfor, T. (2020, September 6). Prevalence and control rates of hypertension in the USA: 2017-2018. International Journal of Cardiology Hypertension. doi: 10.1016/j.ijchy.2020.100044

- [12] Carey, R., Moran, A., Whelton, P. (2022, November 8). Treatment of hypertension: A review. Journal of American Medical Association, 328 (18), 1849-1861. Doi: 10.1001/jama.2022.19590

- [13] Cleveland Clinic. (2022, July 28). Cholesterol numbers and what they mean. <https://my.clevelandclinic.org/health/articles/11920-cholesterol-numbers-what-do-they-mean>

- [14] National Heart, Lung, and Blood Institute. (2022, March 24). Blood cholesterol - Causes and risk factors. <https://www.nhlbi.nih.gov/health/blood-cholesterol/causes>

- [15] Centers for Disease Control and Prevention. (2023, May 15). High Cholesterol Facts. <https://www.cdc.gov/cholesterol/facts.htm>

- [16] Huff, T., Boyd, B., Jialal, I. (2023, March 6). Physiology, cholesterol. <https://www.ncbi.nlm.nih.gov/books/NBK470561/>

- [17] Schaiff, R., Moe, R., Krichaum, D. (2008, November-December). An overview of cholesterol management. *American Health & Drug Benefits*, 1(9).
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4106545/>
- [18] American Heart Association. (2022, December 13). Combo of bad cholesterol and high blood pressure may increase heart attack or stroke risk.
<https://newsroom.heart.org/news/combo-of-bad-cholesterol-and-high-blood-pressure-may-increase-heart-attack-or-stroke-risk>
- [19] Mann, S., Beedie, C., Jimenez, A. (2014). Differential effects of aerobic exercise, resistance exercise, and combined exercise modalities on cholesterol and the lipid profile: Review, synthesis, and recommendations. *Journal of Sport Medicine*, 44(2), 211-221.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3906547/>
- [20] Pescatello, L., Wu, Y., Gao, S., Livingston, J., Sheppard, B., Chen, M. (2021, January 20). Do the combined blood pressure effects of exercise and antihypertensive medications add up to the sum of their parts? A systematic meta-review. *British Journal of Sports and Exercise Medicine*, 7(1). doi: 10.1136/bmjsem-2020-000895
- [21] LeWine, H. (2024, February 16). Do beta blockers interfere with exercise?. Harvard Medical School Exercise & Fitness. <https://www.health.harvard.edu/exercise-and-fitness/do-beta-blockers-interfere-with-exercise#:~:text=So%2C%20your%20beta%20blocker%20won,your%20heart's%20efficiency%20and%20endurance.>
- [22] Liu, H., Deng, N., Wu, Z., Zhou, Z., Tian, Z., Liu, Z., Wang, Y., Zheng, H., Ou, Y., Jiang, Z. (2023, March). Statin's role on blood pressure levels: Meta-analysis based on randomized controlled trials. *The Journal of Clinical Hypertension*, 25(3), 238-250.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9994171/>