

THE EFFECTS OF EXERCISE AND HEAT THERAPY ON THE
AMBULATORY BLOOD PRESSURE OF ADULTS WITH
UNTREATED HYPERTENSION

by

MADISON SERRANO

A THESIS

Presented to the Department of Human Physiology
and the Robert D. Clark Honors College
in partial fulfillment of the requirements for the degree of
Bachelor of Science

March 2023

An Abstract of the Thesis of

Madison Serrano for the degree of Bachelor of Science
in the Department of Human Physiology to be taken June 2024

Title: The Effects of Exercise and Heat Therapy on the Ambulatory Blood Pressure of Adults
with Untreated Hypertension

Approved: Christopher Minson, Ph.D.
Primary Thesis Advisor

BACKGROUND: Cardiovascular disease (CVD) remains a leading cause of death both within the United States as well as worldwide. Hypertension (HTN), or high blood pressure, is a primary yet modifiable risk factor for cardiovascular disease. Exercise (EX) is considered the gold-standard lifestyle intervention for improving blood pressure, but many people are unable or unwilling to engage in traditional exercise training. Heat therapy (HT) represents a potential alternative to exercise for its ability to improve blood pressure and reduce cardiovascular disease risk. **PURPOSE:** This study was completed to compare the efficacy of heat water immersion (HWI) to the gold-standard EX in improving high blood pressure in adults with untreated hypertension. **METHODS:** Forty-one adults with HTN were block randomized between two intervention groups; HWI and EX. Subjects completed 24-hour ambulatory blood pressure monitoring before intervention, after 15 sessions, and at the conclusion of 30 sessions of their given intervention. Statistical analysis included a series of two-way repeated measures analysis of variance with main effects of group and time ($\alpha=0.05$). **RESULTS:** Total 24-hour ambulatory blood pressure was not significantly different between or within groups over time ($p>0.05$) Despite no significant main or interaction effects, these interventions appear to have disparate effects on nighttime blood pressure. SBP was reduced to a lesser extent from waking to

sleeping following EX in post measurements in comparison to mid-point measurements ($p < 0.05$). The mid-point awake SBP of dippers in the EX intervention were higher than the mid-point measurements of the HWI group. Asleep SBP of non-dippers were significantly higher in post measurements in comparison to pre-measurements ($p < 0.01$). Similarly, Asleep DBP of non-dippers were significantly higher in post measurements in comparison to pre-measurements ($p < 0.05$). CONCLUSION: Neither EX nor HWI proved to be statistically significant interventions for lowering blood pressure in adults with untreated hypertension.

Acknowledgements

I would like to extend my sincerest gratitude to Dr. Christopher Minson for welcoming me into the Cardiovascular and Environmental Physiology Lab at the beginning of my sophomore year. It has been an honor to be part of his research process and I look forward to reading about his groundbreaking findings in upcoming years.

Thank you to all of the graduate and undergraduate students within the lab who have supported me throughout this process. Specifically, Emma, Brandon, and Kieran, thank you for always offering your help and making lab such a welcoming place. Most importantly, a special thank you to Dr. Brendan Kaiser who has mentored me since I first joined the lab. This research would not have been possible without him, and I am forever grateful for his guidance throughout every piece of this process. My undergraduate experience at UO would not be as special as it has been without all of the time and teaching Brendan has shared with me throughout the years.

Thank you to Dr. Daphne Gallagher for all your guidance through the Clark Honors College and the thesis process. You helped me hit every milestone with grace and positivity which has allowed me to learn a lot from this opportunity that I will carry onto my future academic and career endeavors. I appreciate you for listening to my non-constructive stories during our meetings and humoring me by laughing at my jokes.

I would also like to thank my family and friends for their support and constant words of encouragement. I do not know any other group of people who were willing to critique several draft presentations and papers having not been studying this research for years. Mom and dad, we did it!

Finally, thank you to the Human Physiology Department for funding of this research through the UO Human Physiology Research Assistant Stipend.

Table of Contents

Introduction	8
Purpose and Hypothesis	8
Research Question	9
Literature Review	10
Exercise Training	11
Passive Heat Therapy – Hot Water Immersion	13
Ambulatory Blood Pressure Monitoring	14
Dipper and Non-Dipper	14
Methods	16
Participants	16
Study Design	16
24 Hour Blood Pressure Monitoring Procedure	17
Exercise Training Intervention	17
Hot Water Immersion	18
Data and Statistical Analysis	19
Results	20
24 Hour Ambulatory Blood Pressure	20
Dipper and Non-dipper	23
Discussion	27
The Effect of Aerobic EX and HWI on Ambulatory Blood Pressure	27
Dipper and Non-dipper Effects on Ambulatory Blood Pressure	28
Limitations and Future Directions	30
References	32
Supporting Materials	
Document: Overview of 24-hour ambulatory blood pressure monitoring	

List of Figures

Figure 1: Current thresholds for hypertension set by the American Heart Association (4)	10
Figure 2: Schematic of timing of 24-hour ambulatory blood pressure monitoring in the study	17
Figure 3: Schematic of the aerobic exercise protocol for one session	18
Figure 4: Schematic of the heat therapy protocol for one session	19
Figure 5.1A: SBP Compared Between Intervention and Time	20
Figure 5.1B: DBP Compared Between Intervention and Time	20
Figure 5.2A: Awake SBP Compared Between Intervention and Time	21
Figure 5.2B: Awake DBP Compared Between Intervention and Time	21
Figure 5.3A: Asleep SBP Compared Between Intervention and Time	21
Figure 5.3B: Asleep DBP Compared Between Intervention and Time	21
Figure 5.4A: SBP Comparisons Between Sex and Time	22
Figure 5.4B: DBP Comparisons Between Sex and Time	22
Figure 6.2C: Asleep Dipper SBP Comparison between Intervention and Time	25
Figure 6.2D: Asleep Dipper DBP Comparison between Intervention and Time	25
Figure 6.3A: Awake Non-Dipper SBP Comparison between Intervention and Time	26
Figure 6.3B: Awake Non-Dipper DBP Comparison between Intervention and Time	26
Figure 6.3C: Asleep Non-Dipper SBP Comparison between Intervention and Time	26
Figure 6.3D: Asleep Non-Dipper DBP Comparisons Between Intervention and Time	26

List of Tables

Table 1: Subject Demographics. Data are presented as means \pm SD.	16
Table 2: Mean values of SBP and DBP over Time	22
Table 3: Change in SBP and DBP over Time	23
Table 4: Number of volunteers with clinically significant change (≥ 2 mmHg)	23
Table 5: Number of volunteers with clinically significant change (≥ 10 mmHg)	23
Table 6: Subjects categorized as dipper and non-dippers	24

Introduction

Cardiovascular disease (CVD) continues to be one of the leading causes of death worldwide. Researching ways to control risk factors of cardiovascular disease is crucial in order to alleviate the mortality rate of CVD. One primary modifiable risk factor for cardiovascular disease is hypertension (HTN), also known as high blood pressure. Clinically significant methods of reducing high blood pressure include lifestyle changes such as physical activity and nutrition, and blood pressure-lowering medication. Specifically, exercise training is considered the gold standard intervention for those willing and able to make this lifestyle change. Despite a plethora of research on interventions for improving blood pressure and cardiovascular disease risk, increasing prevalence of CVD demonstrates the need for different methods of lowering hypertension (1, 2). Although not a novel lifestyle modification, there has been renewed interest within cardiovascular disease research in using hot water immersion as an alternative lifestyle intervention, especially for those who are unable or unwilling to commit to other methods of relieving high blood pressure.

Purpose and Hypothesis

The purpose of this study is to compare the efficacy of the gold standard exercise training and hot water immersion on improving 24-hour ambulatory blood pressure. We hypothesize that hot water immersion will be more effective than aerobic exercise training for lowering ambulatory blood pressure in adults with untreated hypertension.

Research Question


Is passive heat therapy in the form of hot water immersion more effective than the gold standard exercise training for improving ambulatory blood pressure? Is exercise training or heat therapy more effective at expanding the physiological reduction in nighttime blood pressure of adults with hypertension?

Literature Review

Hypertension

Based on data from 2015 to 2018, about 121.5 million or 47% of US adults have hypertension, with high blood pressure being attributed to 11.7% of cardiovascular deaths in 2019 (3). Hypertension (HTN) is a primary yet modifiable risk factor for cardiovascular disease (CVD), heart failure, and strokes (3). Overall, data has shown an 18.7% increase in deaths attributed to CVD since 2010 and about 19 million deaths in 2020 globally (3).

Blood Pressure Categories



BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120-129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130-139	or	80-89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

heart.org/bplevels

Figure 1: Current thresholds for hypertension set by the American Heart Association (4)

There are two types of hypertension, primary and secondary, that are diagnosed based on cause. Primary hypertension refers to high blood pressure with no known or underlying cause whereas secondary hypertension has a defined cause related to another medical condition (5). Diagnosis related to pathologies in the renal (kidney), cardiovascular, endocrine, and neurogenic systems can lead to secondary hypertension (which is beyond the scope of this study) (5). Causes of primary hypertension vary extensively including salt sensitivity related to lower salt production in urine which can be related to abnormalities in electrochemical gradients across

plasma membrane, overconsumption of salt, underconsumption of foods high in potassium and calcium, impaired ability to vasodilate, and malfunctioning of the hypothalamus (5).

No matter the type of hypertension, increased blood pressure or the inability of the body to control blood pressure contributes to blood vessel damage. This is an indicator for multitude of cardiovascular diseases such as coronary or peripheral artery disease, congestive heart failure, atrial fibrillation (an irregular heart rhythm), and chronic kidney disease (6). Overall, hypertension places an unhealthy amount of stress on the heart and its related blood vessels.

Extensive research on lifestyle changes and pharmaceutical treatment for hypertension aim to identify methods for mitigating the long-term effects of high blood pressure. Pharmaceutical treatments (the mechanisms of which are beyond the scope of this review) include diuretics, beta-blockers, ACE inhibitors, angiotensin II receptor blockers, calcium channel blockers, alpha blockers, alpha-2receptor blockers, and vasodilators (7, 8). For those who prefer to mitigate, avoid, or delay intaking antihypertensive drugs, there are a multitude of lifestyle changes that can be made to combat high blood pressure such as exercise training, weight reduction, and lowering salt intake. Out of these three lifestyle changes, physical activity is considered the gold standard lifestyle change, making it the optimal intervention to compare to new methods.

Exercise Training

The American Heart Association and American College of Sports Medicine recommend 150 minutes of moderate-intensity aerobic activity or 75 minutes of vigorous aerobic activity per week for good health in adults but finds that only about one in five adults and teens meet this recommendation (9). Many studies have found that in both medicated and non-medicated

populations aged ≥ 18 who live relatively sedentary lifestyles, exercise training is a safe and effective method of lowering blood pressure (10, 11).

Repeated bouts of exercise are associated with several beneficial physiological adaptations, primarily related to a reduction in systemic vascular resistance which leads to a decrease in blood pressure (12). Although the specific physiological adaptations that occur from exercise are still being explored, chronic exercise most notably increases shear stress, endothelial nitric oxide synthase (eNOS) expression, and nitric oxide (NO) availability within blood vessels which is associated with improved vessel health and beneficial vascular remodeling, reducing CVD risk (12). Shear stress is a longitudinal force created from blood flowing along endothelial cells (5). An increase in shear stress will increase NO release from the endothelial cells leading to vasodilation which can lower blood pressure over time. Overall, there is a wealth of evidence that physical activity can improve other physiological factors associated with reduced CVD risk such as improving endothelial function, mediated by transient increases in cardiac output, blood flow, and shear stress during exercise (13–16).

Despite the vast benefits of exercise therapy on adults with hypertension, many adults are unwilling or unable to participate in this lifestyle intervention. In 2020, the CDC reported that 46.3% of adults aged 18 and over did not meet either the aerobic nor muscle strengthening guidelines as mentioned above (17). People may be unable to meet these guidelines due to several reasons including a disability, acute or chronic pain, or lack of access to exercise equipment that would allow them to complete these guidelines safely. Knowing that many adults are not achieving the recommended amount of physical activity a week, research should and has been looking into alternative interventions that will elicit the same benefits seen from exercise therapy.

Passive Heat Therapy – Hot Water Immersion

Passive heat therapy has been used for spirituality, healing, and as a social outlet for centuries. Common examples include Japanese Onsens, Finnish sauna bathing, and Korean jjimjilbang which all aim to promote good health and improve quality of life (18). Due to the extensive history of reported healing and benefits of passive heat therapy, research on the effects of this type of treatment has increased in recent years. Specifically, a large prospective cohort study from Laukkanen et al, reports that individuals that engage in sauna bathing with the greatest frequency and duration experience the greatest reduction in the risk for sudden cardiac death and all-cause mortality (19).

While exercise training is commonly recommended for improving cardiovascular health, studies have found that heat therapy, in the form of saunas or hot water immersion, can be effective at reducing blood pressure (20, 21). Hot water immersion has been associated with reduced mean arterial and systolic pressure, and improved measurements associated with reduced cardiovascular disease risk such as improved endothelial lining, arterial stiffness, and blood pressure (22–25). Previous research demonstrates that hot water immersion, similar to exercise training, is correlated with improved endothelial function, blood flow, and shear stress in young, sedentary subjects and women with polycystic ovary syndrome (23, 24). Others report that hot spring bathing and feet soaking in warm water is associated with lowering the prevalence of hypertension in older adults and the elderly (20, 26). Overall, hot water immersion has been found to improve symptoms related to high blood pressure and cardiovascular disease in a similar manner as exercise training. Further research needs to be done to compare the two interventions and their effects on ambulatory blood pressure.

Ambulatory Blood Pressure Monitoring

Ambulatory blood pressure monitoring (ABPM) has been demonstrated to be an accurate and useful tool for diagnosing high blood pressure (27, 28). ABPM is recognized as a superior tool for diagnosing hypertension because it takes into account normal stress levels, average daytime BP, average nighttime BP, and the possible effects of other external factors on BP within a 24 hour period (27). For instance, ABPM is a practical method for identifying individuals with white coat hypertension (29–32). White coat hypertension describes a person with an elevated blood pressure in clinic and a normal blood pressure at home (33). Indeed, ABPM allows researchers to see an accurate representation of a person's BP throughout their daily lives. Therefore, it enables researchers to identify individuals with masked hypertension, or a normal BP in clinic and an elevated BP out of clinic (34).

Dipper and Non-Dipper

A helpful feature of ABPM is that it is capable of measuring the circadian changes in blood pressure. In healthy individuals, nocturnal blood pressure is $\geq 10\%$ lower than their waking BP values. Broadly, individuals can be classified as a “dipper” or a “non-dipper” depending on if they experience the nighttime reduction in BP $\geq 10\%$ (35). Studies have found that there is a higher cardiovascular morbidity rate in people diagnosed with non-dipper hypertension in comparison to those with dipper hypertension (36).

Using ABPM, Park et al. found that non-dipper and dipper BP respond to exercise differently depending on the time of day they exercise (37). They had three key findings: 1) non-dippers will respond to exercise despite time of day 2) non-dippers had a greater reduction in SBP with evening exercise compared to dippers 3) exercise at any time of the day exhibited similar 24-hour SBP reduction in dippers and non-dippers (37). According to the study, non-

dippers seemed to benefit most from exercise therapy. Overall, there has been a depth of research on improving the ABP of dippers and non-dippers using the gold standard EX intervention, but more research needs to be done regarding nighttime reduction following heat therapy.

Methods

Participants

Forty-one subjects participated in this study (19 EX & 21 HT; age range: 35-60). Volunteers were pre-screened to confirm eligibility for the study. Elevated or high blood pressure was confirmed by averaging the values of ≥ 2 blood pressure measurements on ≥ 2 separate days. Measurements were taken following 5 minutes of seated rest, with one measurement per arm separate by one minute, as set forth by American Heart Association guidelines. Participants presented with primary hypertension but were free from other cardiorespiratory or metabolic diseases and were not currently taking any variation of blood pressure medication. Female participants were not pregnant or breast-feeding during the intervention.

	Age	Height	Weight	BMI
Exercise	48 \pm 7	172 \pm 9	90 \pm 9	30 \pm 2
Heat Therapy	47 \pm 7	175 \pm 8	94 \pm 18	30 \pm 3

Table 1: Subject Demographics. Data are presented as means \pm SD.

Study Design

This study was a block randomized controlled trial. After pre-screening to confirm eligibility for the study and a battery of pre-intervention baseline testing, volunteers were randomly assigned to either heat therapy or exercise training using a randomized module within our data capture system (REDCap, Nashville, TN, USA). All procedures in this study were approved by the Institutional Review Board at the University of Oregon. All subjects have provided their written and verbal consent to participate in the study as set forth by the Declaration of Helsinki.

24 Hour Blood Pressure Monitoring Procedure

24-hour ambulatory blood pressure monitoring (ABPM) was completed prior to randomization, after 15 sessions of either hot water immersion or exercise, and after the completion of all 30 sessions of assigned intervention. Each ABPM measurement was initiated at the same time of day within participants. Volunteers were fitted with a portable blood pressure cuff on the upper portion of their non-dominant arm and an ambulatory blood pressure monitor (Oscar 2, SunTech Medical, Morrisville, NC, USA).

The blood pressure monitor was calibrated in clinic and programmed with each subject's self-reported awake and sleep time for the 24 hours of ABPM. These times were replicated for mid- and post-intervention assessments. Blood pressure (BP) was measured every 20 minutes during waking hours and every 60 minutes when asleep for the 24-hour period. The subject was asked to go about their normal daily activities and keep their arm relaxed when their BP was being monitored. Volunteers completed an hourly log with their activities and meals throughout the 24-hour period. Subjects refrained from all over the counter medication, alcohol, caffeine, exercise or heat therapy, and prolonged time in a motorized vehicle during their 24-hour monitoring period.

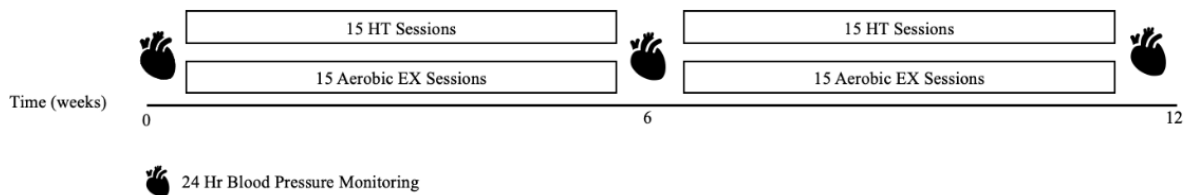


Figure 2: Schematic of timing of 24-hour ambulatory blood pressure monitoring in the study

Exercise Training Intervention

Subjects completed 30 exercise training sessions in total, at a frequency of 3-4 sessions per week. Each session totaled 50 minutes, consisting of a 5-minute warm-up, 40 minutes at a

suggested workload, and a 5-minute cool-down. Suggested workload and target intensities were calculated using the Karvonen method. Warm-up and cool-down were completed at a target intensity at 30% of each subjects' heart rate reserve (HRR).

$$\% HRR = [(MHR - RHR) \times Training \%] + RHR$$

Resistance was adjusted to elicit 30% of HRR during warm-up and cool-down, and 60% of HRR during 40 minutes at target workload. Participants were equipped with a Polar Heart Rate Monitor (Polar Team Pro, Polar Electro, Lake Success, NY, USA). Heart rate was recorded at baseline and then every 5 minutes during the session. For the first and last session only, core temperature via a rectal thermistor or core temp pill was recorded every 5 minutes.

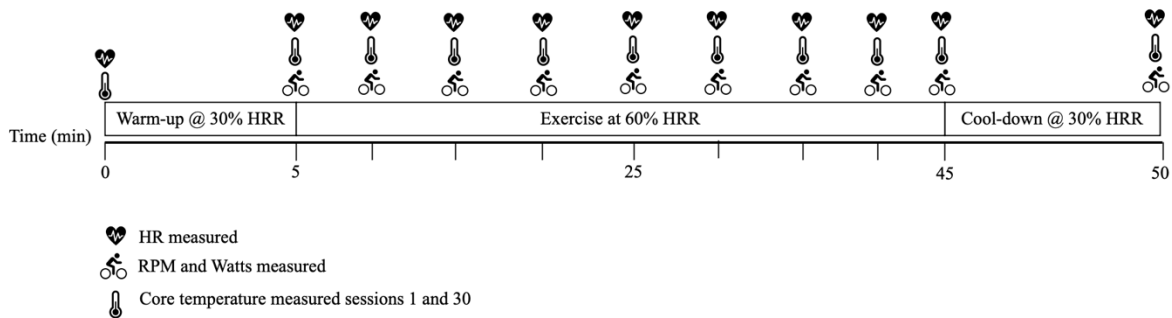


Figure 3: Schematic of the aerobic exercise protocol for one session

Hot Water Immersion

Most subjects completed 30 sessions in total at about 3-4 sessions a week. The sessions consisted of 45 minutes of immersion to mid-sternum in a hot tub at 104°F (40°C) followed by 5 minutes of recovery seated outside of the hot tub. Volunteers were equipped with a polar Heart Rate Monitor (Polar Team Pro, Polar Electro, Lake Success, NY, USA) for all sessions. Heart rate was measured at baseline (0 minutes) and every 5 minutes throughout the 50-minute session. In sessions 1-5 and 30, subjects were also provided a core temp pill (HQ Inc., palmetto, FL, USA) for the measurement of body core temperature or if contraindicated they were provided

with a rectal thermistor (YSI Model 800, Yellow Springs Instruments, Yellow Springs, OH, USA). Core temperature was recorded every 5 minutes for only sessions 1-5 and 30. When core temperature reaches 38.5°C, a fan was turned on if requested by the volunteer and subjects remained immersed to mid-sternum.

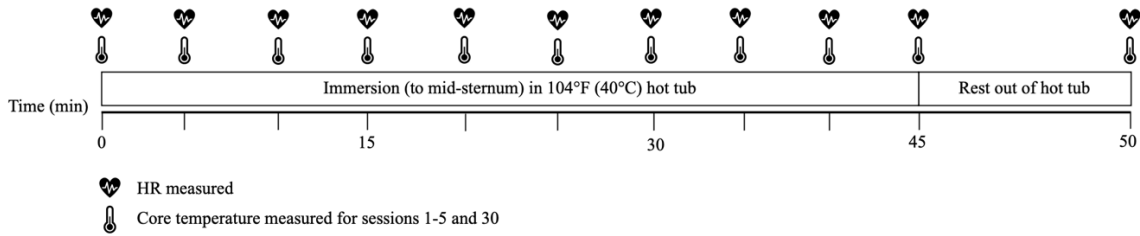


Figure 4: Schematic of the heat therapy protocol for one session

Data and Statistical Analysis

Subject SBP and DBP characteristics were compared using an unpaired two-tailed student's t-test ($\alpha=0.05$). Mean data for all ambulatory blood pressure variables of interest were analyzed using a two-way repeated measures analysis of variance with main effects of group and time. Significance was accepted at $p<0.05$. In the event of a significant main effect, pairwise comparisons were conducted using the Sidak analysis.

Comparisons between subject nighttime blood pressure reduction and ambulatory blood pressure were compared using two-way repeated measures analysis of variance with main effects of group and time ($\alpha=0.05$). Subject nighttime blood pressure reduction was used to split them into groups of dipper and non-dippers for analysis. Female and male comparisons were made with combined HT and EX groups due to limited sample size allowing us to find sex-wise comparisons despite the intervention. Significance was accepted at $p<0.05$. In the event of a significant main effect, pairwise comparisons were conducted using the Sidak analysis.

Results

24 Hour Ambulatory Blood Pressure

There were no significant differences between the mean 24-hour ambulatory blood pressure measurements across time and interventions. Total 24-hour SBP and DBP were not significantly different between intervention groups or compared to different time points throughout the study ($p>0.05$) (Figures 5.1A and 5.1B). Awake 24-hour SBP and DBP were not significantly different between intervention groups or compared to different time points throughout the study ($p>0.05$) (Figures 5.2A and 5.2B). Asleep 24-hour SBP and DBP were not significantly different between intervention groups or compared to different time points throughout the study ($p>0.05$) (Figures 5.3A and 5.3B).

Also, we were interested in sex wise comparisons regardless of the intervention. Male and female participants did not experience any significant changes in 24-hour total ambulatory blood pressure throughout the study ($p>0.05$) (Figure 5.4A and 5.4B).

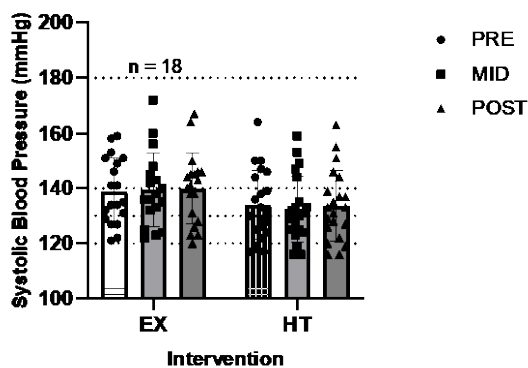


Figure 5.1A: SBP Compared Between Intervention and Time

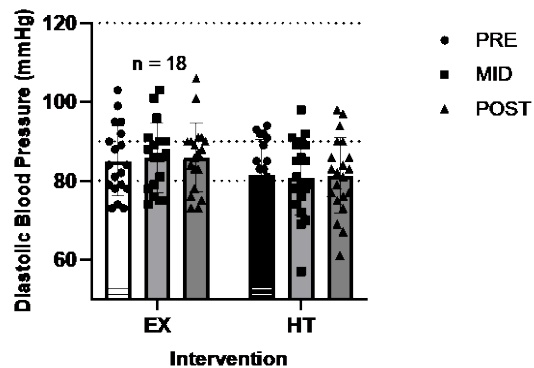


Figure 5.1B: DBP Compared Between Intervention and Time

SBP and DBP Data is represented as mean \pm SD of 24-hour total ambulatory blood pressure. Dotted lines represent current thresholds for hypertension as shown in **Figure 1**.

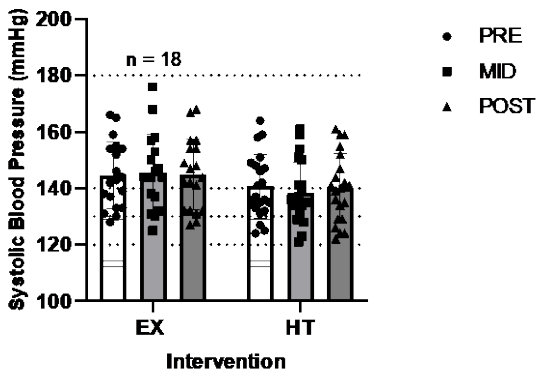


Figure 5.2A: Awake SBP Compared Between Intervention and Time

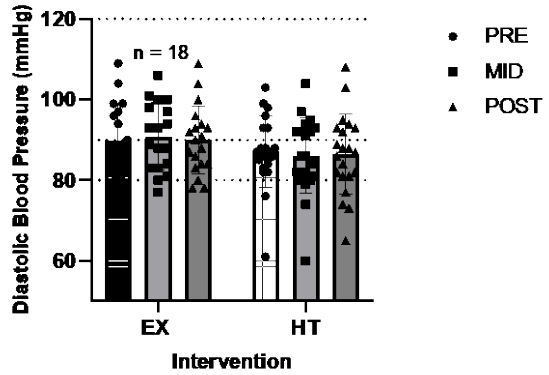


Figure 5.2B: Awake DBP Compared Between Intervention and Time

SBP and DBP Data is represented as mean \pm SD of awake ambulatory blood pressure. Dotted lines represent current thresholds for hypertension as shown in **Figure 1**.

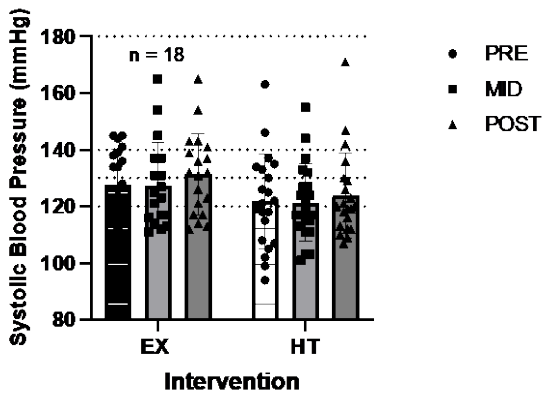


Figure 5.3A: Asleep SBP Compared Between Intervention and Time

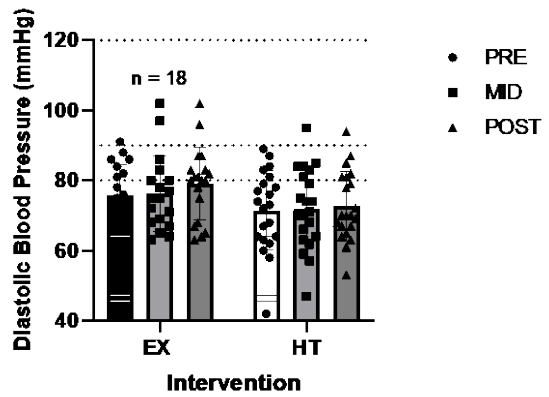


Figure 5.3B: Asleep DBP Compared Between Intervention and Time

SBP and DBP Data is represented as mean \pm SD of total asleep ambulatory blood pressure. Dotted lines represent current thresholds for hypertension as shown in **Figure 1**.

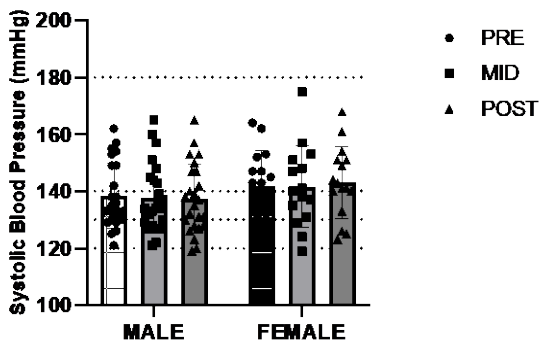


Figure 5.4A: SBP Comparisons Between Sex and Time

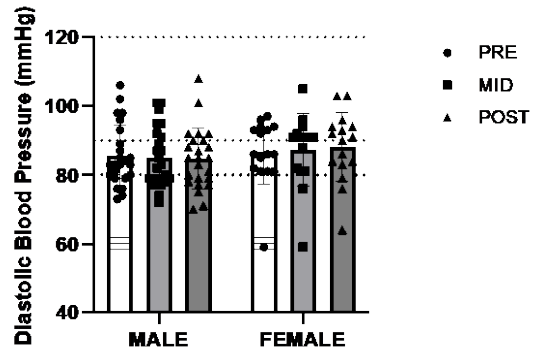


Figure 5.4B: DBP Comparisons Between Sex and Time

Male and female comparisons were made for 24-hour total ambulatory blood pressure. Exercise and hot tub groups were combined for the sex-wise comparisons. Data is represented as mean \pm SD of total 24-hour ambulatory blood pressure. Dotted lines represent current thresholds for hypertension.

	PRE SBP/DBP	MID SBP/DBP	POST SBP/DBP
Total EX	139 \pm 12	139 \pm 13	140 \pm 13
	85 \pm 9	86 \pm 9	86 \pm 9
Total HT	134 \pm 13	132 \pm 12	134 \pm 13
	81 \pm 9	81 \pm 10	81 \pm 10
Awake EX	145 \pm 12	146 \pm 13	145 \pm 13
	90 \pm 9	91 \pm 8	90 \pm 8
Awake HT	141 \pm 11	138 \pm 11	140 \pm 12
	87 \pm 9	86 \pm 9	86 \pm 10
Asleep EX	128 \pm 13	128 \pm 15	131 \pm 14
	76 \pm 9	76 \pm 11	79 \pm 10
Asleep HT	122 \pm 17	121 \pm 14	124 \pm 15
	71 \pm 11	72 \pm 11	73 \pm 10

Table 2: Mean values of SBP and DBP over Time

Data is shown as the mean \pm SD of the raw SBP and DBP. Total data is from the 24-hour total ABPM (Figure 5.1A & 5.1B), awake is from the total awake ABPM (Figure 5.2A & 5.3B), asleep is from the total asleep ABPM (Figure 5.3A & 5.3B).

		Total ABP	Awake	Asleep
EX	SBP	1 ± 7	0 ± 8	4 ± 9
	DBP	1 ± 4	0 ± 6	3 ± 6
HT	SBP	0 ± 9	-1 ± 9	2 ± 11
	DBP	0 ± 5	-1 ± 6	1 ± 6

Table 3: Change in SBP and DBP over Time

Data is shown as the mean ± SD of the change from Pre to Post for both SBP and DBP.

		Total ABP	Awake	Asleep
EX	SBP	6/19	9/19	4/19
	DBP	4/19	7/19	5/19
HT	SBP	9/21	10/21	7/21
	DBP	6/21	9/21	6/21

Table 4: Number of volunteers with clinically significant change (≥ 2 mmHg)

Data is shown as number of subjects of the specific intervention and BP measurement. A threshold of 2 mmHg was considered clinically meaningful by Makai, et al. (38) and Hess et al., (39) .

		Total	Awake	Asleep
EX	SBP	1/19	2/19	2/19
	DBP	1/19	1/19	0/19
HT	SBP	2/21	3/21	3/21
	DBP	1/21	2/21	0/21

Table 5: Number of volunteers with clinically significant change (≥ 10 mmHg)

Data is shown as number of subjects of the specific intervention and BP measurement. The clinically significant criteria of a change ≥ 10 mmHg was investigated by Canoy et al., (40) and Guzman et al., (41).

Dipper and Non-dipper

The mean reduction from waking to sleeping was significantly different from mid ABPM measurements to post ABP measurements in the exercise training group ($p < 0.05$) (Figure 6.1A).

Awake mean SBP midpoint ABPM measurements were significantly different between interventions for dippers ($p < 0.05$) (Figure 6.2A). Asleep mean SBP and DBP of non-dippers in the exercise intervention group had a significant difference between pre and post BP

measurements ($p < 0.001$ and $p < 0.05$, respectively) (Figure 6.3C and 6.3D). True dippers/non-dippers remained dippers/non-dippers throughout the study (Table 6).

Group	EX	HT	MALE	FEMALE
TRUE D	6	9	9	6
TRUE ND	3	3	5	1
ND \rightarrow D	2	2	1	3
D \rightarrow ND	5	5	8	2

Table 6: Subjects categorized as dipper and non-dippers

D denotes dipper and ND refers to non-dippers. Dippers are defined as subjects that had a greater than 10% asleep dip in both SBP and DBP. Some subjects are not included in this table due to the small sample size. Two of these subjects went from D to ND to D and two subjects were ND to D to ND throughout the study.

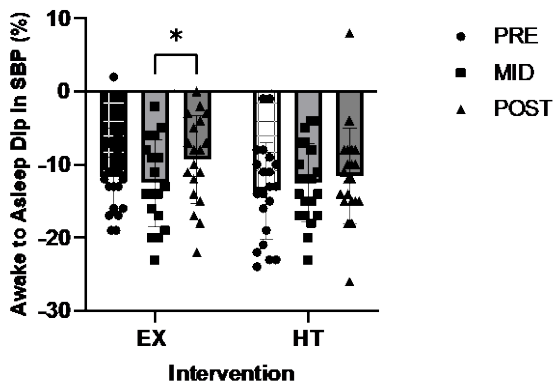


Figure 6.1A: SBP reduction from waking to sleeping

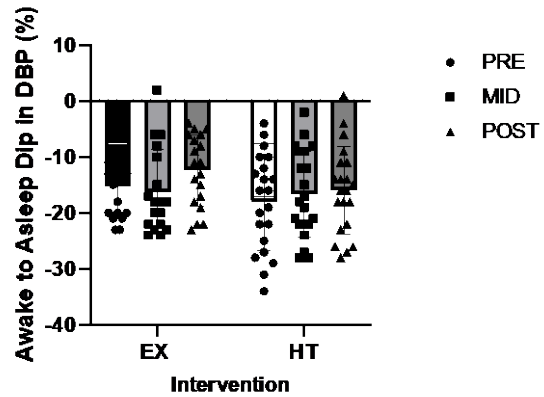


Figure 6.1B: DBP reduction from waking to sleeping

Data is represented as mean \pm SD. Dotted lines represent current thresholds for hypertension.

*Denotes statistical significance ($p < 0.05$)

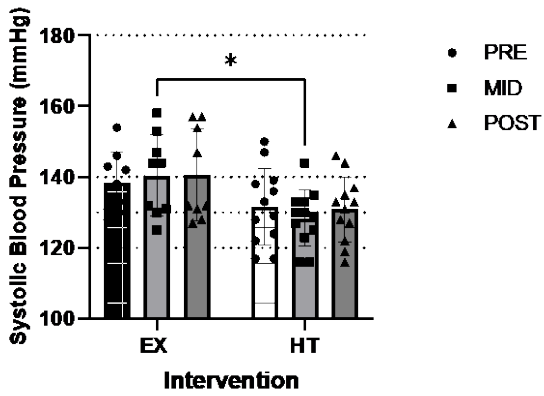


Figure 6.2A: Awake Dipper SBP Comparison between Intervention and Time

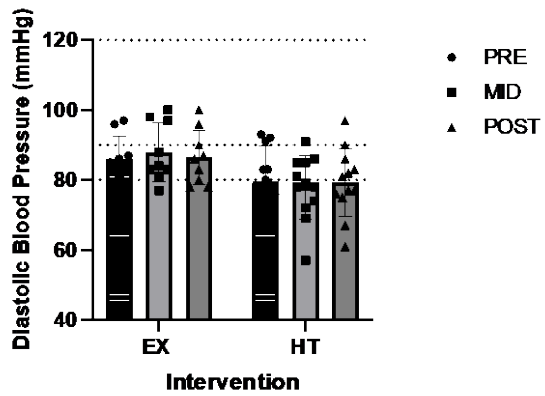


Figure 6.2B: Awake Dipper DBP Comparison between Intervention and Time

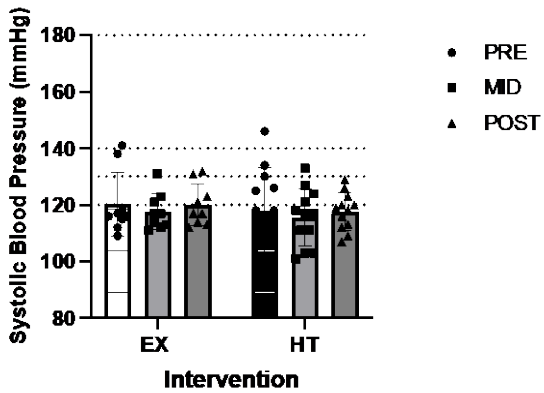


Figure 6.2C: Asleep Dipper SBP Comparison between Intervention and Time

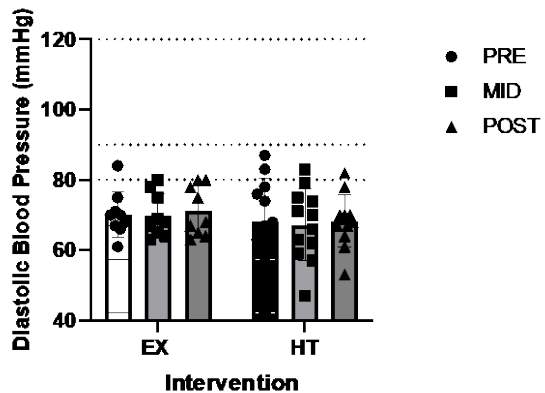


Figure 6.2D: Asleep Dipper DBP Comparison between Intervention and Time

Top row is awake blood pressure measurements and bottom row is asleep blood pressure measurements for only dippers. Data is represented as mean \pm SD. Dotted lines represent current thresholds for hypertension as shown in **Figure 1**. *Denotes statistical significance ($p < 0.05$)

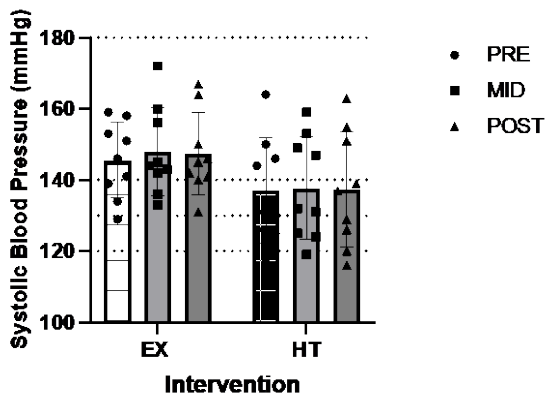


Figure 6.3A: Awake Non-Dipper SBP Comparison between Intervention and Time

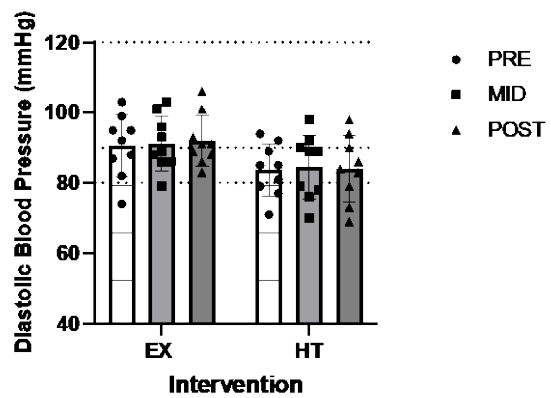


Figure 6.3B: Awake Non-Dipper DBP Comparison between Intervention and Time

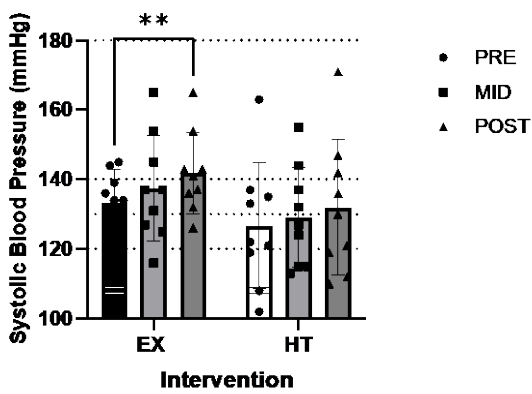


Figure 6.3C: Asleep Non-Dipper SBP Comparison between Intervention and Time

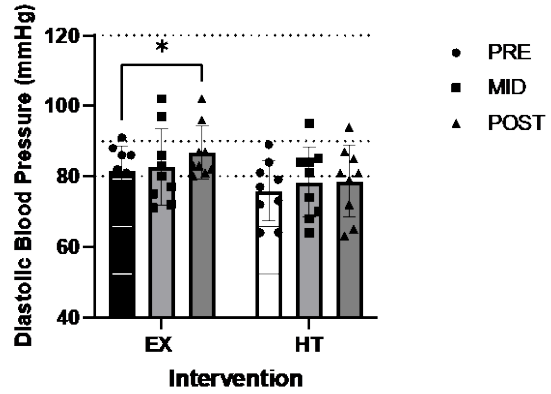


Figure 6.3D: Asleep Non-Dipper DBP Comparisons Between Intervention and Time

Top row is awake blood pressure measurements and bottom row is asleep blood pressure measurements for only non-dippers. Data is represented as mean \pm SD. Dotted lines represent current thresholds for hypertension as shown in **Figure 1**. *Denotes statistical significance ($p < 0.05$) and ** denotes a strong statistical significance ($p < 0.01$)

Discussion

This study examined the effects of exercise therapy and hot water immersion on the ambulatory blood pressure of hypertensive adults. Key findings of the study include: 1) No difference for either HWI or EX for improving total, awake, and asleep ABP 2) Mean reduction from waking to sleeping was significantly different between mid and post ABP for the EX group 3) Awake midpoint SBP of dippers was significantly different between interventions 4) Asleep SBP and DBP in the EX group were significantly different between pre and post measurements of non-dippers.

The Effect of Aerobic EX and HWI on Ambulatory Blood Pressure

The null hypothesis that hot water immersion would not be as effective as exercise therapy in lowering the ambulatory blood pressure of adults with untreated hypertension was not rejected. Furthermore, our data did not support the findings of previous investigations concerning the viability of physical activity and hot water immersion for improving blood pressure. There is a vast amount of evidence for aerobic exercise benefits on lowering blood pressure in both medicated and nonmedicated adults with various degrees of hypertension (42–44). Similarly, many studies have found heat therapy to produce similar effectiveness in lowering cardiovascular risk and improving blood pressure (22–25, 45, 46).

However, the difference between statistically significant and clinically significant changes following an intervention is important to consider when looking at the effectiveness of a treatment. Clinical significance indicates dissimilarity between two different modalities whereas statistical significance is a mathematically significant analysis between treatments (47). Both measures are important within clinical studies but are independent of each other. In other words, a treatment could have clinically meaningful effects but not be statistically significant. Clinical

significance alone in our study can be related to a decrease in risk for CVD when compared to pre-intervention. When looking at clinical studies, clinical significance can support the hypothesis of the researchers that an intervention may be effective, but the limitations of the study may have led to a lack of statistical significance.

Within this study, some volunteers did experience clinically significant reductions in their blood pressure when comparing their pre and post ABP measurements. There are several clinical studies and meta-analysis with varying definitions of clinically meaningful reductions in blood pressure ranging from ≥ 2 mmHg to ≥ 10 mmHg (38–41). **Table 3** and **Table 4** summarizes how many subjects within this study had clinically significant differences between their pre and post ABP measurements. This data shows that there could have been some effectiveness of our interventions as some volunteers did find a benefit to their blood pressure overall. Therefore, a lack of statistical significance does not mean that our interventions did not work at all, but it can indicate a need to reassess our methods for future research.

Dipper and Non-dipper Effects on Ambulatory Blood Pressure

One of the research questions for this study was to examine the benefits of exercise training and heat therapy more closely on dipper and non-dipper HTN. There was an interaction effect between EX mid and HT mid and a main effect of time within the EX group where SBP post was significantly greater than SBP premeasurements.

In **Figures 6.2A-6.2D**, there is a trend of the dipper hot water immersion group at all time points having generally lower SBP than exercise group. This trend means that the hot tub group started with dippers that on average had a lower blood pressure than the exercise group coincidentally, making the statistical difference between the midpoint data questionable in the context of it being due to one of our interventions (**Figure 6.12A**). Therefore, this one

comparison is insufficient to conclude that hot water immersion is a more beneficial modality for those with dipper hypertension.

Unlike the hot water immersion groups for both non-dipper and dippers, there was a main effect of time within the exercise group for SBP nighttime reduction, asleep non-dipper SBP, and asleep non-dipper DBP. **Figure 6.1A** depicts a smaller nighttime reduction in SBP. In other words, our data shows that from mid to post ABPM measurements, subjects in the exercise group on average went from dippers ($> 10\%$ drop) to non-dippers ($< 10\%$ drop). **Figure 6.3C** and **Figure 6.3D** display a significant difference between the pre and post SBP and DBP for asleep non-dippers. On average, both SBP and DBP were higher than pre ABPM data which could contribute to the results seen in **Figure 6.1A**.

Overall, the exercise group data for dippers and non-dippers do not support previous research. As mentioned above there are several studies that attribute aerobic exercise to healthy decreases in blood pressure (42–44). Our results may have occurred due to volunteers scheduling their in-clinic visits for intervention without consideration for their status as dipper or non-dipper. Park et al., found that dippers and non-dipper respond differently to exercise depending on time of day (37). Similarly, Brito et al., found that evening training led to a wider reduction in ambulatory BP in comparison to morning training in men with treated hypertension (48). Although volunteers generally completed all 30 sessions of their intervention and ABPM at the same time, they were able to choose any time of the day that would work for their schedules so long as it could be consistent throughout the study. Therefore, time of day could have led to the discrepancy between our data and previous literature.

Limitations and Future Directions

We encountered some limitations in this study that may have contributed to our unexpected results. The hot water immersion stimulus used in this study is informed by previous research. Brunt et al, (2016) and Ely et al., (2019) found significant differences in their subject groups with a longer time immersed and a similar temperature which indicates that our timing could have been a limiting factor (22, 24). Future research should continue to assess the most accurate temperature and time for effective usage of hot water immersion.

Another limitation could be that exercise did not match the circadian rhythms of our volunteers. Subjects were welcomed to schedule their visits at times that were most convenient for them so long as they completed the protocol. As spoken about above with dipper and non-dipper hypertension, exercising at different time of the day could have an impact on how effective exercise is on lowering blood pressure. Thus, taking into consideration circadian rhythm may be beneficial for future research.

The AHA exercise guideline recommends both aerobic exercise and weight training to combat raising blood pressure. In the present study, only aerobic exercise was compared to heat therapy, but future research should include a combination of aerobic and resistance training against different heating modalities such as hot water immersion in commercial hot tubs or natural hot springs or various saunas.

Although estimated sodium intake was measured during the ABPM sessions, greater nutrition interventions should be explored more to prove the viability of heat therapy. Sodium intake in this study was calculated using the dietary logs from each volunteer and MyFitnessPal (MyFitnessPal Inc, San Francisco, CA, USA). Therefore, our estimated dietary sodium can be deceiving since we assume that volunteers are giving us an accurate recording of the food that

they consume throughout their 24-hour measurement period and that MyFitnessPal, which database relies on its users, presents precise measurements. Future research should consider more strict interventions for nutrition or measure urinary sodium excretion in order to assess if heat therapy alone makes an impact or if nutrition plays a part in the results seen within this study.

Conclusion

Overall, our results suggest that HWI and EX did not have an effect on the ABP of adults with untreated hypertension. However, we found that many of the subjects were able to achieve a clinically significant change in their ABP in both HWI and EX. Although there were some significant findings when comparing nighttime blood pressure reduction in dipper and non-dippers, we were unable to make a conclusive observation that one intervention was more effective at expanding the reduction. Future research should consider nutrition, circadian rhythm, and length of interventions when studying the effects of HWI and EX on the ABP of adults with untreated hypertension.

References

1. **Kodela P, Okeke M, Guntuku S, Lingamsetty SSP, Slonovschi E.** Management of Hypertension With Non-pharmacological Interventions: A Narrative Review. *Cureus* 15: e43022, [date unknown]. doi: 10.7759/cureus.43022.
2. **Dhungana RR, Pedisic Z, De Courten M.** Implementation of non-pharmacological interventions for the treatment of hypertension in primary care: a narrative review of effectiveness, cost-effectiveness, barriers, and facilitators. *BMC Prim Care* 23: 298, 2022. doi: 10.1186/s12875-022-01884-8.
3. Heart Disease and Stroke Statistics—2022 Update: A Report From the American Heart Association [Online]. [date unknown]. <https://www.ahajournals.org/action/showCitFormats?doi=10.1161%2FCIR.0000000000001052> [7 Feb. 2023].
4. Understanding Blood Pressure Readings [Online]. *www.heart.org*: [date unknown]. <https://www.heart.org/en/health-topics/high-blood-pressure/understanding-blood-pressure-readings> [1 Jan. 2024].
5. **Sherwood, Lauralee.** *Human Physiology: From Cells to Systems*. 9th edition. Boston, MA: Cengage Learning, 2016.
6. **Tackling G, Borhade MB.** Hypertensive Heart Disease [Online]. In: *StatPearls*. StatPearls Publishing <http://www.ncbi.nlm.nih.gov/books/NBK539800/> [2 Oct. 2023].
7. **Heidari B, Avenatti E, Nasir K.** Pharmacotherapy for Essential Hypertension: A Brief Review. *Methodist DeBakey Cardiovasc J* 18: 5–16, [date unknown]. doi: 10.14797/mdcvj.1175.
8. **Carey RM, Moran AE, Whelton PK.** Treatment of Hypertension: A Review. *JAMA* 328: 1849–1861, 2022. doi: 10.1001/jama.2022.19590.
9. American Heart Association Recommendations for Physical Activity in Adults and Kids [Online]. *www.heart.org*: [date unknown]. <https://www.heart.org/en/healthy-living/fitness/fitness-basics/aha-recs-for-physical-activity-in-adults> [30 Dec. 2023].
10. **Pescatello LS, Kulikowich JM.** The aftereffects of dynamic exercise on ambulatory blood pressure: *Med Sci Sports Exerc* 33: 1855–1861, 2001. doi: 10.1097/00005768-200111000-00009.
11. **Saco-Ledo G, Valenzuela PL, Ruiz-Hurtado G, Ruilope LM, Lucia A.** Exercise Reduces Ambulatory Blood Pressure in Patients With Hypertension: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *J Am Heart Assoc* 9: e018487, 2020. doi: 10.1161/JAHA.120.018487.
12. **Nystoriak MA, Bhatnagar A.** Cardiovascular Effects and Benefits of Exercise. *Front Cardiovasc Med* 5: 135, 2018. doi: 10.3389/fcvm.2018.00135.

13. **Young DB.** Control of Cardiac Output [Online]. Morgan & Claypool Life Sciences. <http://www.ncbi.nlm.nih.gov/books/NBK54469/> [17 Mar. 2023].
14. **Tinken TM, Thijssen DHJ, Hopkins N, Black MA, Dawson EA, Minson CT, Newcomer SC, Laughlin MH, Cable NT, Green DJ.** Impact of shear rate modulation on vascular function in humans. *Hypertension* 54: 278–285, 2009. doi: 10.1161/HYPERTENSIONAHA.109.134361.
15. **Tinken TM, Thijssen DHJ, Hopkins N, Dawson EA, Cable NT, Green DJ.** Shear stress mediates endothelial adaptations to exercise training in humans. *Hypertens Dallas Tex 1979* 55: 312–318, 2010. doi: 10.1161/HYPERTENSIONAHA.109.146282.
16. **Palmefors H, DuttaRoy S, Rundqvist B, Börjesson M.** The effect of physical activity or exercise on key biomarkers in atherosclerosis--a systematic review. *Atherosclerosis* 235: 150–161, 2014. doi: 10.1016/j.atherosclerosis.2014.04.026.
17. **Elgaddal N.** Physical Activity Among Adults Aged 18 and Over: United States, 2020. , 2022.
18. **Coombs GB, Tremblay JC.** Passive heat therapy for cerebral protection: new ideas of age-old concepts. *J Physiol* 597: 371–372, 2019. doi: 10.1113/JP277314.
19. **Laukkanen T, Khan H, Zaccardi F, Laukkanen JA.** Association between sauna bathing and fatal cardiovascular and all-cause mortality events. *JAMA Intern Med* 175: 542–548, 2015. doi: 10.1001/jamainternmed.2014.8187.
20. **Yamasaki S, Tokunou T, Maeda T, Horiuchi T.** Hot spring bathing is associated with a lower prevalence of hypertension among Japanese older adults: a cross-sectional study in Beppu. *Sci Rep* 12: 19462, 2022. doi: 10.1038/s41598-022-24062-3.
22. **Brunt VE, Eymann TM, Francisco MA, Howard MJ, Minson CT.** Passive heat therapy improves cutaneous microvascular function in sedentary humans via improved nitric oxide-dependent dilation. *J Appl Physiol Bethesda Md 1985* 121: 716–723, 2016. doi: 10.1152/jappphysiol.00424.2016.
23. **Brunt VE, Howard MJ, Francisco MA, Ely BR, Minson CT.** Passive heat therapy improves endothelial function, arterial stiffness and blood pressure in sedentary humans. *J Physiol* 594: 5329–5342, 2016. doi: 10.1113/JP272453.
24. **Ely BR, Francisco MA, Halliwill JR, Bryan SD, Comrada LN, Larson EA, Brunt VE, Minson CT.** Heat therapy reduces sympathetic activity and improves cardiovascular risk profile in women who are obese with polycystic ovary syndrome. *Am J Physiol-Regul Integr Comp Physiol* 317: R630–R640, 2019. doi: 10.1152/ajpregu.00078.2019.
25. **Pizzey FK, Smith EC, Ruediger SL, Keating SE, Askew CD, Coombes JS, Bailey TG.** The effect of heat therapy on blood pressure and peripheral vascular function: A systematic review and meta-analysis. *Exp Physiol* 106: 1317–1334, 2021. doi: 10.1113/EP089424.

26. **Fadlilah S, Erwanto R, Sucipto A, Anita DC, Aminah S.** Soak feet with warm water and progressive muscle relaxation therapy on blood pressure in hypertension elderly. *Pak J Med Heal Sci* 14: 1444–8, 2020.
27. **Pena-Hernandez C, Nugent K, Tuncel M.** Twenty-Four-Hour Ambulatory Blood Pressure Monitoring. *J Prim Care Community Health* 11: 2150132720940519, 2020. doi: 10.1177/2150132720940519.
28. **Isselbacher EM, Preventza O, Hamilton Black J, Augoustides JG, Beck AW, Bolen MA, Braverman AC, Bray BE, Brown-Zimmerman MM, Chen EP, Collins TJ, DeAnda A, Fanola CL, Girardi LN, Hicks CW, Hui DS, Schuyler Jones W, Kalahasti V, Kim KM, Milewicz DM, Oderich GS, Ogbechie L, Promes SB, Gyang Ross E, Schermerhorn ML, Singleton Times S, Tseng EE, Wang GJ, Woo YJ.** 2022 ACC/AHA Guideline for the Diagnosis and Management of Aortic Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation* 146: e334–e482, 2022. doi: 10.1161/CIR.0000000000001106.
29. Measurement of Blood Pressure in Humans: A Scientific Statement From the American Heart Association. [date unknown].
30. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines | Hypertension [Online]. [date unknown]. https://www.ahajournals.org/doi/full/10.1161/HYP.000000000000065?rfr_dat=cr_pub++0pubmed&url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org [19 Feb. 2023].
31. **Siu AL.** Screening for High Blood Pressure in Adults: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med* 163: 778–786, 2015. doi: 10.7326/M15-2223.
32. **Piper MA, Evans CV, Burda BU, Margolis KL, O'Connor E, Whitlock EP.** Diagnostic and Predictive Accuracy of Blood Pressure Screening Methods With Consideration of Rescreening Intervals: A Systematic Review for the U.S. Preventive Services Task Force. *Ann Intern Med* 162: 192–204, 2015. doi: 10.7326/M14-1539.
33. **Nuredini G, Saunders A, Rajkumar C, Okorie M.** Current status of white coat hypertension: where are we? *Ther Adv Cardiovasc Dis* 14: 1753944720931637, 2020. doi: 10.1177/1753944720931637.
34. **Pickering TG, Eguchi K, Kario K.** Masked hypertension: a review. *Hypertens Res Off J Jpn Soc Hypertens* 30: 479–488, 2007. doi: 10.1291/hypres.30.479.
35. **Aksit E, Gursul E, Aydin F, Samsa M, Ozcelik F.** Non-dipper hypertension is associated with slow coronary flow among hypertensives with normal coronary angiogram. *Cardiovasc J Afr* 28: 14–18, 2017. doi: 10.5830/CVJA-2016-045.

36. **Verdecchia P, Schillaci G, Borgioni C, Ciucci A, Gattobigio R, Guerrieri M, Comparato E, Benemio G, Porcellati C.** Altered circadian blood pressure profile and prognosis. *Blood Press Monit* 2: 347–352, 1997.
37. **Park S, Jastremski CA, Wallace JP.** Time of day for exercise on blood pressure reduction in dipping and nondipping hypertension. *J Hum Hypertens* 19: 597–605, 2005. doi: 10.1038/sj.jhh.1001901.
38. **Makai P, IntHout J, Deinum J, Jenniskens K, Wilt GJ van der.** A Network Meta-Analysis of Clinical Management Strategies for Treatment-Resistant Hypertension: Making Optimal Use of the Evidence. *J Gen Intern Med* 32: 921–930, 2017. doi: 10.1007/s11606-017-4000-7.
39. **Hess NCL, Carlson DJ, Inder JD, Jesulola E, Mcfarlane JR, Smart NA.** Clinically Meaningful Blood Pressure Reductions With Low Intensity Isometric Handgrip Exercise. A Randomized Trial. .
40. **Canoy D, Nazarzadeh M, Copland E, Bidel Z, Rao S, Li Y, Rahimi K.** How Much Lowering of Blood Pressure Is Required to Prevent Cardiovascular Disease in Patients With and Without Previous Cardiovascular Disease? *Curr Cardiol Rep* 24: 851–860, 2022. doi: 10.1007/s11886-022-01706-4.
41. **Guzman H, Rouseff M, Tran T, Nasir K, Bou-Khalil J, Mora J, Das S, Brown D, Santiago-Charles J, Ochoa TC, Gilliam C, Lehn V, Aneni E, Oni E, Robertson L, Veledar E, Post J, Castillo B.** Abstract P391: Clinically Significant Blood Pressure Reduction Among Participants of a Lifestyle intervention Improvement Program strongly associated with Reduced Systemic Inflammation in a High Risk Working Population. *Circulation* 129: AP391–AP391, 2014. doi: 10.1161/circ.129.suppl_1.p391.
42. **Dimeo F, Pagonas N, Seibert F, Arndt R, Zidek W, Westhoff TH.** Aerobic Exercise Reduces Blood Pressure in Resistant Hypertension. *Hypertension* 60: 653–658, 2012. doi: 10.1161/HYPERTENSIONAHA.112.197780.
43. **Wen H, Wang L.** Reducing effect of aerobic exercise on blood pressure of essential hypertensive patients. *Medicine (Baltimore)* 96: e6150, 2017. doi: 10.1097/MD.00000000000006150.
44. **Martin JE, Dubbert PM, Cushman WC.** Controlled trial of aerobic exercise in hypertension. *Circulation* 81: 1560–1567, 1990. doi: 10.1161/01.CIR.81.5.1560.
45. **Hesketh K, Shepherd SO, Strauss JA, Low DA, Cooper RJ, Wagenmakers AJM, Cocks M.** Passive heat therapy in sedentary humans increases skeletal muscle capillarization and eNOS content but not mitochondrial density or GLUT4 content. *Am J Physiol-Heart Circ Physiol* 317: H114–H123, 2019. doi: 10.1152/ajpheart.00816.2018.
46. **Cheng JL, MacDonald MJ.** Effect of heat stress on vascular outcomes in humans. *J Appl Physiol* 126: 771–781, 2019. doi: 10.1152/jappphysiol.00682.2018.

47. **Sharma H.** Statistical significance or clinical significance? A researcher's dilemma for appropriate interpretation of research results. *Saudi J Anaesth* 15: 431–434, 2021. doi: 10.4103/sja.sja_158_21.
48. **Brito LC, Peçanha T, Fecchio RY, Rezende RA, Sousa P, Da Silva-Júnior N, Abreu A, Silva G, Mion-Junior D, Halliwill JR, Forjaz CLM.** Morning versus Evening Aerobic Training Effects on Blood Pressure in Treated Hypertension. *Med Sci Sports Exerc* 51: 653–662, 2019.