REPEATED INFRARED SAUNA BATHING IN ADULTS WITH OBESITY AND PULSE WAVE VELOCITY

by

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Introduction: Obesity is associated with elevated cardiovascular disease risk due to increased arterial stiffness. Passive heat therapy has been shown to reduce arterial stiffness, which can be determined by pulse wave velocity (PWV). Previous reports have shown that heat therapy can reduce arterial stiffness, however it is unknown whether repeated far-infrared sauna bathing is also effective at targeting arterial stiffness in individuals with obesity. **Purpose:** To test the hypothesis that repeated far-infrared sauna bathing would reduce PWV in individuals with obesity. **Methods:** We recruited 5 individuals (4 men, 1 woman, age: 34±10 years) with obesity (BMI 35.5±3.8 kg/m^2) who were randomly assigned to the heat therapy (n=3) or time control (n=2) groups. The heat therapy group completed 30 far-infrared sauna sessions (54±6°C) for 43±4 minutes within 9 weeks. The time control group maintained activities of daily living. Arterial stiffness as quantified by carotid-femoral PWV via applanation tonometry (SphygmoCor® XCEL). PWV was measured before heating (PRE), after 15 sauna sessions or 4-5 weeks (MID), and after 30 sauna sessions or 9-10 weeks (POST). **Results:** There was no effect of time (p = 0.4605), group (p = 0.3817), or group x time interaction (p = 0.3412) for pulse wave velocity at PRE vs. MID vs. POST for Control (6.7±0.9 vs. 6.2±0.2 vs. 6.5±0.6 m/s) or Heat (7.6±1.5 vs. 7.7±1.6 vs. 8.0±2.1 m/s). **Conclusions:** These data indicate that 30 sessions of far-infrared sauna sessions did not reduce arterial stiffness in individuals with obesity.

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Introduction

Obesity is one of the most prominent and impactful health conditions in the United States. The Centers for Disease Control and Prevention (CDC) found that 41.9% of Americans were obese in 2020, constituting an 11.4% increase in obesity and a 4.4% increase in severe obesity compared to 2000, and this number is projected to continue to climb (*National Health Statistics Reports, Number 158, June 14, 2021*, 2021). It is known that excess adiposity impacts many aspects of an individual's health such as glucose regulation, inflammation, and a buildup of fatty deposits in non-adipose tissue regions such as the liver. The most notable health detriment correlated with obesity, however, is damage to the heart and blood vessels of the cardiovascular system. The 2015 Global Burden of Disease Study reported that obesity led to 4 million deaths worldwide with over two-thirds due to cardiovascular disease. The strong association between obesity and poor cardiovascular health is a major contributor to why cardiovascular disease is the leading cause of death both in the United States and worldwide (Powell-Wiley et al., 2021).

The development of a cardiovascular condition or cardiac event can be attributed in part to an increase in arterial stiffness (Aroor et al., 2018). Arterial stiffness refers to the thickening or hardening of the walls of the arteries (Boutouyrie et al., 2021). The gold standard method of measuring arterial stiffness is pulse wave velocity (PWV), or the rate at which a pulse wave travels through the arterial tree (Gurovich & Braith, 2011). PWV is calculated by dividing the total distance that the blood travels between two anatomical positions (i.e. the carotid artery in the neck to the femoral artery in the thigh) by the amount of time it took to do so (Van Bortel et al., 2012). A high PWV is associated with increased arterial stiffness as it takes a pulse wave less time to reach a given area of the body, but increasing the demand on the heart to maintain blood

flow to the systemic circulation (Gurovich & Braith, 2011). Since PWV is the most widely used measure of arterial stiffness, it can be used to predict the risk of developing a cardiovascular disease or experiencing a cardiovascular event (Sabatine et al., 2018).

Frequent bouts of physical activity are one way to reduce excess weight and improve cardiovascular parameters including arterial stiffness. Modalities of exercise can vary from sports to strength training to aerobic training and much more. Unfortunately, not all individuals are capable of or desire to participate in typical forms of exercise to benefit from the metabolic and cardiovascular adaptations associated with regular exercise. An alternative or addition to exercise is heat therapy, defined as the repeated exposure to a hot stimulus such as a sauna, steam room, or hot tub. Heat therapy shows similar benefits to exercise such as improved vascular function and reducing inflammation, both of which have an effect on arterial stiffness (Brunt et al., 2016; Brunt & Minson, 2021; Carter et al., 2014; Cullen et al., 2020; Ely et al., 2018; Lee et al., 2018). Additionally, heat therapy may be a promising option for individuals with obesity because it is less taxing on the joints which may be reason to limit participation in regular exercise (Nguyen et al., 2021).

Previous research has shown a link between heat therapy and improved cardiovascular health (Brunt et al., 2016; Ely et al., 2019; Lee et al., 2018; Nguyen et al., 2021; Sugawara & Tomoto, 2020). The majority of these studies utilize hot water immersion, water-perfused suits, or Finnish sauna bathing. Despite increasing popularity and accessibility of far-infrared saunas to the general public, there is a lack of evidence for the use of this sauna as a form of heat therapy outside of inpatient cardiac patients. Additionally, there is limited research on the implications for far-infrared sauna therapy on PWV or for individuals with obesity. Thus, the purpose of our study was to investigate the effects of repeated far-infrared sauna therapy on arterial stiffness in

individuals with obesity. We hypothesized that repeated far infrared sauna therapy will reduce arterial stiffness, marked by a reduction in PWV.

Literature Review

Obesity

According to the American Heart Association, 2.4 million worldwide deaths were attributed to a high body mass index (BMI) in 2020 (Tsao et al., 2023), which is triple that of 1975 (Koenen et al., 2021). BMI is calculated as an individual's weight in kilograms divided by the square of their height in meters and is one cost-effective way to classify body composition. A BMI greater than or equal to 30 kg/m^2 is classified as obese, a category that 50% of Americans will fall into by 2030 (Ward et al., 2019). Obesity is caused by an excess amount of white adipose tissue. Adipose tissue serves as both storage and endocrine tissue. For the function of storage, the two main locations of adipose tissue are 1) surrounding the major organs and blood vessels within the abdomen (visceral), and 2) below the skin (subcutaneous) (Koenen et al., 2021). An excess of visceral adipose tissue carries cardiovascular and metabolic disease risk due to the greater secretion of pro-inflammatory markers (i.e., tumor necrosis factor alpha, interleukin-6, interleukin-1beta) (Ely et al., 2018). Individuals with obesity have a shift to a higher population of M1-macrophages (pro-inflammatory) relative to M2-macrophages (anti-inflammatory) (Koenen et al., 2021). The inflammatory response is triggered due to the accumulation and expansion of adipocytes. This expansion compresses the blood vessels and diminishes the blood supply to adipocytes, which decreases the oxygen delivery, and results in hypoxia which can lead to cell death (Ely et al., 2018). In addition to the chronic low-grade inflammation from adipose tissue, and due to the finite storage capacity of adipocytes, excess triglycerides begin to accumulate in non-adipose tissue, such as such as the liver, heart, and

vessels. This is defined as lipotoxicity. Lipotoxicity exacerbates the pro-inflammatory state, as there are more adipokines secreted locally, such as in the peripheral vasculature, that alter the signaling pathways in these locations (Koenen et al., 2021).

Cardiovascular Disease

Cardiovascular disease is the leading cause of death worldwide (Aroor et al., 2018). Cardiovascular disease includes any condition that results in diseased vessels, structural damage, and blood clots (i.e., coronary artery disease, high blood pressure, stroke, etc.). Despite being preventable in many cases, heart diseases were responsible for taking the lives of 20 million people, including 700,000 (one in five) Americans during 2020 (Tsao et al., 2023). The biggest risk factor for developing a cardiovascular disease is aging, however, there are increasing amounts of middle aged and younger individuals being diagnosed (Brunt & Minson, 2021). A large contributor to this trend is the rising rates of individuals with obesity. Cardiovascular risk factors such as an inactive or sedentary lifestyle, poor diet, high low-density lipoprotein (LDL) cholesterol (>160mg/dL), and elevated and high blood pressure (systolic >120 mmHg and diastolic >80 mmHg) are all common in individuals with obesity, which is why obesity is associated with a decline in overall cardiac health (Koenen et al., 2021).

Prior to the second half of the 20th century, prevention and treatment for cardiac diseases were poorly understood and therefore considered to be unavoidable by most Americans. After the premature death of President Franklin D. Roosevelt at age 63 due to "hardening of the arteries," as well as the climbing number of cardiac-related deaths, researchers were incentivized to begin an investigation into cardiovascular health. The Framingham Heart Study is a longitudinal cohort study that began in 1940 and has continued for 75 years. The first cohort of

this study included 5209 individuals, both men and women, over the course of 4 years (1948-1952). This investigation led to the first definition of hypertension (a blood pressure greater than 160/80 mmHg), and the correlation between increased blood pressure and an increased risk for coronary heart disease or stroke (Mahmood et al., 2014). Further, scientists developed medications to treat hypertension and thus reduce the prevalence of heart disease. Future renditions of this study included the same participants at later timepoints in their lives, as well as their spouses and their offspring, to establish genetic ties to cardiac health. These studies also marked a revolutionary stage in modern medicine, where goals switched from treatment to prevention of cardiac disease. Once the correlation between high systolic blood pressure and an increased risk of heart disease was made, researchers began looking at other characteristics and aspects of lifestyle that may lead to poor cardiac health: age, total cholesterol, body mass, abnormalities in the heart's electrical signals, hemoglobin (protein that transports oxygen in the blood) concentration, and the frequency of cigarettes smoked. From here, they assembled the first cohesive list of cardiac risk factors including hypertension, hyperlipidemia, and diabetes mellitus (Mahmood et al., 2014). Each subsequent cohort has led to revolutionary understandings of cardiac disease evaluation, treatment, and prevention, which has provided the foundation for current research in cardiovascular health. This meant analyzing the network of vessels that connect the heart to the rest of the body, as they largely contribute to the pathological state and functionality of the heart itself.

Cardiovascular System & Arterial Function

The cardiovascular system is responsible for distributing oxygen through blood to the organs and tissues and the maintenance of arterial blood pressure. It consists of the heart as a pump and a network of vessels including arteries, arterioles, capillaries, and veins. There are

many cardiovascular parameters we can monitor to assess the function of the cardiovascular system and as it changes with various disease states. The central cardiovascular parameters include heart rate (HR), stroke volume (SV), and cardiac output (Q_c). HR is the number of times the heart contracts per minute, SV is the volume of blood ejected with each contraction of the left ventricle and Q_c, the product of HR and SV, is the total volume of blood pumped from the heart each minute. Q_c represents central cardiovascular parameters whereas systemic vascular resistance represents peripheral cardiovascular parameters. Together, the product of these central and peripheral parameters is arterial blood pressure. Blood pressure is measured as systolic blood pressure (SBP) and diastolic blood pressure (DBP) and reported as SBP/DBP. SBP is the pressure in the arteries when the left ventricle contracts and DBP is the pressure in the arteries during left ventricle relaxation. While both SBP and DBP are important in monitoring cardiac health, studies show a greater risk of heart disease associated with an elevated SBP (Brunt & Minson, 2021; Mahmood et al., 2014; O'Rourke & Kelly, 1993). The American Heart Association classifies blood pressure less than 120/80 mmHg as normal, although it is important to note that too low of blood pressure (< 90/60 mmHg) carries risk beyond the scope of this current project. Standard blood pressure cuffs allow us to make predictions and assessments about cardiac health but where they lack is in their ability to evaluate central blood pressure and stiffening of arteries at the level of the heart. It is important to measure and track these other parameters in people who are at risk for developing cardiovascular conditions, such as individuals with obesity. This is because evaluating arterial health can independently predict cardiovascular risk.

From the aorta, the vascular tree is comprised of arteries, arterioles, capillaries, and veins. The three layers of a vessel are the tunica intima (innermost), tunica media (middle), and tunica adventitia (outermost). The layer most responsible for changing the diameter of the vessel is the tunica media because it houses a layer of smooth muscle. This layer of vascular smooth muscle is the most prominent in arterioles and therefore arterioles play a critical role in the regulation of arterial blood pressure. Vascular smooth muscle is innervated by the sympathetic nervous system and controls the amount of contraction of the vascular smooth muscle. An increase in sympathetic input contracts the vascular smooth muscle, leading to vasoconstriction and a reduction in the vessel's diameter. Conversely, a reduction in sympathetic input relaxes the vascular smooth muscle and increases the diameter. The change in diameter has the greatest effect to the calculation of resistance, as part of the equation for blood pressure. Therefore, acute and chronic changes to sympathetic activity can alter the amount of vasoconstriction of these vessels. Individuals with obesity can have elevated levels of sympathetic activity compared to individuals of normal weight (Smith & Minson, 2012).

The innermost surface of arteries is lined with endothelial cells which play a role in peripheral vascular function. Nitric oxide (NO) is released by endothelial cells and functions to regulate vascular tone and blood flow (Jin & Loscalzo, 2010). NO is a vasodilator, meaning it allows the vascular smooth muscle to relax, effectively expanding the vessel width. This enhances blood flow and plays a role in reducing arterial blood pressure. NO also inhibits vasoconstriction, decreases clotting, inhibits inflammation by blocking immune cells from sticking to the walls of the blood vessel, and inhibits smooth muscle hyperplasia (muscle buildup), all of which decrease arterial resistance (Jin & Loscalzo, 2010). Therefore, a loss in

NO results in peripheral vascular dysfunction. The increase in chronic low-grade inflammation commonly found with obesity can impair NO production and signaling (Higashi et al., 2001).

Another layer of an artery is the extracellular matrix (ECM). The ECM contains collagen, elastin, and specialized proteins that further allow arteries to vasodilate and vasoconstrict in response to the pressure load of the blood flowing through it (Aroor et al., 2018). Changes in the ECM are prompted by an accumulation of collagen and a reduction in elastin. Collagen is responsible for maintaining structure in a vessel while elastin allows for elastic recoil of the vessel. The change in these properties, as with obesity, creates an excessively ridged channel that cannot adequately accommodate high pressure loads without consequences such as high blood pressure (Aroor et al., 2018). The disruption of the relationship between arterial pressure and blood flow is called vascular impedance (G. F. Mitchell, 2021), which is what increases blood velocity through the cardiovascular system and is reflected as a higher pulse and blood pressure (Butlin & Qasem, 2016).

In sum, individuals with obesity are at an elevated risk for cardiovascular disease and this can be preceded by reductions in arterial function. The reduction in arterial function can be in part due to physiological and structural changes that occur with obesity and accumulation of fat within the arteries such as increased pro-inflammatory cytokines, elevated sympathetic activity, a reduction in nitric oxide, and stiffening of the extracellular matrix. Arterial compliance is the ability of arteries to accurately fluctuate in volume in response to changes in pressure within the vessels. Arterial compliance is what is expected from a healthy individual as it is the inverse of arterial stiffness, and a loss of compliance represents an increase in arterial stiffness. Arterial

stiffness is defined as the rigidity of the arterial walls. An increase in arterial stiffness is a risk factor for one of the greatest predictors of cardiovascular disease. While arterial walls naturally stiffen with age, healthy lifestyle habits (i.e. exercise, diet) can be protective whereas conditions such as obesity and insulin resistance accelerate the rate at which this occurs (Koenen et al., 2021). This measure of vascular health is relevant because hypertension can be caused by is arterial stiffness. It is important to note that while arterial stiffness causes an increase in blood pressure, data does not suggest that high blood pressure leads to arterial stiffness (Kaess et al., 2012). Therefore, simply decreasing blood pressure by means of medication will not independently reduce arterial stiffness.

Measurement Of Arterial Stiffness

Pulse wave velocity (PWV), the most widely used non-invasive measure of arterial stiffness, is defined as the speed at which a pulse wave travels from the heart and aorta through the vascular network of the body (Gurovich & Braith, 2011). A higher PWV is indicative of greater arterial stiffness because the pulse is propagated faster down the arterial tree due to a reduction in arterial compliance. A higher PWV constitutes a greater cardiovascular disease risk due to a greater pressure load on the heart (Van Bortel et al., 2012). A heart pumping against high pressure leads to increased cardiac work and fatigue (Butlin & Qasem, 2016). PWV is calculated by dividing the total distance between two arteries by the time (number of cardiac cycles) it took to do so (PWV = Distance/Time) (Van Bortel et al., 2012). A “normal” pulse wave velocity is about 5 m/s and Van Bortel et al. considers a clinically high PWV classification to be any value above 10 m/s. They estimated a 4% increased chance of experiencing a first major cardiovascular event within 8 years of the pulse wave measurement at or above 10 m/s. Over the course of over ten years, the research group found that an increase in carotid-femoral

PWV showed a 6.8% increase in the risk of a negative cardiovascular event such as a myocardial infarction (heart attack), prolonged ischemic episodes (lack of blood flow to the brain), heart failure, or ischemic or hemorrhagic strokes. There is a progressive increase in PWV over one's lifespan, but this increase can be influenced by lifestyle habits. Between adolescence and 70 years of age, PWV generally doubles in magnitude, but today we're seeing these numbers climb to a much greater extent (O'Rourke & Kelly, 1993). The greater prevalence of obesity can be attributed to this trend due to the physiological and structural changes with obesity leading to arterial stiffness.

Pulse waveforms were used in medical practices starting in the second half of the 19th century (Salvi et al., 2015). The first pulse wave recordings were done using a highly accurate, but invasive catheterization procedure. The value that this procedure revealed led to the development of less invasive techniques of gathering the same data. Today, arterial stiffness is quantified by using a technique called applanation tonometry. A tonometer (pressure transducer) records pressure waveform of each pulse originating from the heart. The pressure waveform is simultaneously recorded at two arteries such as the carotid artery in the neck and femoral artery in the thigh. A PWV measured by tonometry has a 90% repeatability coefficient, making it a highly reliable method for use in a research or clinical setting (Davies & Struthers, 2005).

Ideally, a PWV measurement would be obtained at the level of the heart using central blood pressure as this is the pressure profile the heart is exposed most directly to. This is especially true for obese individuals because, as mentioned previously, visceral obesity effects the coronary arteries (arteries of the heart), due to fat accumulation. Unfortunately, it is difficult

to measure blood pressure and pulse waves from the heart without invasive means. Therefore, non-invasive measurements with superficial arteries offers an alternative to the direct and invasive measure that is more accessible. PWV can be measured on many arteries in the body, however the measurements will vary in the same person based on the vessel used (Davies & Struthers, 2005). This is because, as blood moves farther away from the heart and toward the extremities, the vessel loses compliance (stretch), which leads to an increase in pressure. This pressure increase causes a pulse wave to travel at a higher speed, hereby altering the PWV measurement. Therefore, the two distances most commonly used for measuring PWV are the carotid artery of the neck and the femoral artery of the upper hip and thigh (Gurovich & Braith, 2011). These conduit arteries are easily accessible as they lie more superficial and there is less hindrance from nearby bones and muscles. Additionally, these conduit arteries represent the condition of coronary arteries as Mitchell et al. found the strongest relationship between carotid-femoral PWV (G. F. Mitchell et al., 2010). It should be noted that another accurate and minimally-invasive means to measure PWV is through magnetic resonance imaging (MRI), although this method uses large, expensive machinery to do so which may be challenging to access regularly (Butlin & Qasem, 2016). Therefore, using the applanation tonometry technique and the carotid and femoral arteries is considered the gold-standard PWV measurement method, as it is considered the most clinically relevant (Gurovich & Braith, 2011).

In addition to PWV, the shape of the arterial pressure waveform can represent changes in arterial stiffness via pulse wave analysis (PWA). PWA generates a central pulse pressure waveform derived from the pressure wave of a peripheral artery, such as the brachial artery. It is important that the peripheral waveform is corrected to match the central waveform, as systolic

pressure between the aorta and the brachial artery can vary by more than 20 mmHg (Wilkinson et al., 2000). From a peripheral pressure waveform, we can quantify systolic and diastolic blood pressure which can be used to calculate mean arterial and pulse pressures. Mean arterial pressure is calculated as: $diastolic\ pressure + \frac{1}{3}(systolic\ pressure - diastolic\ pressure)$. Pulse pressure is calculated as: $(systolic\ pressure - diastolic\ pressure)$ and is directly related to arterial stiffness and cardiac work. Other important features of the pressure waveform utilized specifically in PWA are the timing and magnitude of the forward and reflected waves. The forward wave occurs due to the contraction of the left ventricle and is the pressure wave moving away from the heart (P1). The reflected wave is due to the transition from low resistance conduit arteries to high-resistance arterioles and is the pressure wave back towards the heart (P2). The difference between these two pressures (P2-P1) is the augmented pressure. Increased stiffness reduces the artery's capacity to accommodate pressure loads, this creates a greater reflected wave, and therefore greater augmented pressure. From this, the augmentation index (AIx) is calculated as: $((augmented\ pressure \div pulse\ pressure)\ X\ 100)$. A more positive AIx indicates a stiffer artery whereas a less positive (or even negative) AIx represents a less stiff artery. It is important to note that heart rate can influence the timing of the reflected wave and therefore AIx. Wilkinson et al. measured AIx between set heart rates of 60 to 110 bpm in individuals with cardiac pacemakers. As heart rate increased, there was a reduction in AIx (Wilkinson et al., 2000). To accommodate for this relationship, AIx can be corrected for and reported at a heart rate of 75 bpm.

In addition to the size of the pressure waves, we can also use the timing of the reflected wave to evaluate levels of arterial stiffness. After the aortic valve closes, it creates a small cleft

in the waveform, known as the dicrotic notch, marking the beginning of diastole. If the reflected wave is found further after the dicrotic notch (later in diastole), this indicates that the blood vessel can more easily adjust to pressure changes and is therefore less stiff. Conversely, a reflected wave located during late systole or early diastole indicates increased stiffness of the arteries (O'Rourke & Kelly, 1993). Due to the stiffening of the arteries associated with excess adiposity, obesity can exacerbate magnitude of the reflected wave, thus increasing AIx. Not only is AIx a measure of arterial stiffness, but it tells us more than a standard blood pressure reading can. A brachial blood pressure only tells us systolic and diastolic blood pressures, without considering the shape of the waveform itself.

Interventions To Target Arterial Stiffness

Individuals with obesity have elevated arterial stiffness in part due to increased adiposity and chronic low-grade inflammation, greater levels of sympathetic activity, and reduced nitric oxide bioavailability (Ely et al., 2018). Therefore, these are potential avenues to target with lifestyle interventions to reduce cardiovascular disease risk in these individuals. One way to prevent and reduce obesity-induced cardiovascular risk is to increase one's total energy expenditure by way of physical activity and structured exercise. Higher cardiorespiratory fitness is considered an important predictor of overall health, independent of weight loss alone (Elagizi et al., 2020). The American College of Sport's Medicine's recommendation to exercise a minimum of 30 minutes per day has been shown to reduce cardiovascular risk factors and diminish unhealthy gains in body weight (Akbartabartoori et al., 2008). Unfortunately, the 2020 National Health Interview Survey from the Center for Disease Control and Prevention (CDC) revealed that only 23.2% of Americans over the age of 18 meet the weekly recommended

physical activity guidelines for aerobic and muscle-strengthening training (*Products - NHIS Early Release Program - Homepage*, 2023). In the context of individuals who are sedentary and are classified as obese, there can be reduced cardiorespiratory capacity and exercise tolerance, increased joint pain, and social barriers such as motivation to regularly exercise at intensities associated with reduced cardiovascular disease risk (Niemiro et al., 2023; Stutts, 2002).

Passive heating, in the form of hot water immersion or sauna bathing, is increasingly being implemented as a potential exercise alternative or additive for targeting cardiovascular outcomes and reducing cardiovascular risk due to similar physiological responses as exercise (Cullen et al., 2020). These include increases in body temperature, cardiovascular demand, and a redistribution of blood flow with increases in shear stress. Additionally, regular exercise can result in a greater anti-inflammatory profile thus mitigating the chronic low-grade pro-inflammation associated with obesity (Gleeson et al., 2011; Petersen & Pedersen, 2005). Therefore, heat therapy may be a more tolerable physiological stressor with the potential for some protective effect for individuals with low exercise adherence.

Aerobic exercise can increase body temperature by 1.0°C in about 30 minutes where passive heating can increase body temperature by 1.0°C in as fast as 10 minutes depending on the modality (Gregson et al., 2002; Saltin & Hermansen, 1966; Tei et al., 1995). The rate of increase in body temperature varies across different exercise and passive heating modalities. An increase of 0.4°C above resting, or 39°C has been commonly suggested for beneficial adaptations (Brunt & Minson, 2021). As body temperature begins to increase, thermoregulation mechanisms occur including the redistribution of blood away from the core and towards the

periphery. It is important to note that during exercise, the working skeletal muscles receive a great deal of the redistributed blood whereas during passive heating there is a redistribution of blood to the skin (Rowell, 1974; Saltin et al., 1998). This redistribution of blood flow increases the demands of the cardiovascular system to maintain an increase cardiac output (Q_c). As mentioned previously, Q_c is the product of heart rate and stroke volume. During exercise, both increases in HR and SV support the increase in Q_c where the increase in Q_c during passive heating is mainly due to increases in heart rate (Brunt & Minson, 2021). The increase in heart rate can be similar between passive heating and low- to moderate-intensity exercise but are dependent on the modality, time, and intensity of both stimuli (Amin et al., 2021; Thomas et al., 2016). The repeated increase in cardiovascular demand strengthens cardiac muscle and allows for improved ability to distribute blood throughout the body.

With the increase and redistribution of peripheral blood flow comes an increase in shear stress. Shear stress is the frictional force imposed on the endothelial lining of the arteries by blood flow. Antegrade shear stress is forward blood flow moving from the heart to the periphery on the inner walls of a blood vessel. This directly stimulates the production and release of NO therefore relaxing the vascular smooth muscle (Carter et al., 2014). This is significant in that it is the main physiological process for endothelial remodeling and improving arterial compliance (Carter et al., 2014). Retrograde shear stress, on the other hand, is the backward blood flow moving toward the heart. While some retrograde flow and shear stress is normal, excess retrograde shear stress has negative implications for vascular function (Thijssen et al., 2009). By increasing retrograde shear stress with the use of cuffs on the forearms, there was a reduction in

brachial artery flow-mediated dilation, indicating a reduction in vascular function (Thijssen et al., 2009).

Exercise and passive heating can also improve the inflammation balance between pro- and anti-inflammatory cytokines to favor a less inflammatory state (Gleeson et al., 2011; Petersen & Pedersen, 2005). Additionally, with physiological stressors such as exercise and heat stress, there is activation of heat shock proteins. Heat shock proteins are specialized cells that help maintain normal cellular function by reducing inflammation and improving cellular signaling, all of which can be impaired in individuals with obesity (Archer et al., 2017). This cascade of events not only protects the body from the current stressor, but it leads to a greater tolerance to heat for subsequent exposures (Périard et al., 2016).

Passive Heating & Arterial Stiffness

While previous evidence shows aerobic exercise to be effective at reducing arterial stiffness in individuals with obesity, the overlap of mechanisms with passive heating may also serve as a potential means to reduce arterial stiffness in this clinical population (Collier et al., 2015; Donley et al., 2014). The magnitude of adaptations developed following heat therapy may be dependent on type of therapy, duration, temperature, and frequency (Périard et al., 2016). The forms of passive heating commonly used include hot water immersion, traditional (Finnish) sauna bathing, far-infrared sauna bathing, and water-perfused suits. Hot water immersion sessions are typically in water temperatures between 38-42°C for 30 to 60 minutes (Brunt & Minson, 2021). Traditional (Finnish) saunas are between 70-100°C with 10-20% relative humidity (Kukkonen-Harjula & Kauppinen, 2006) for 1 to 3 intervals of 5 to 20 minutes.

Between sauna intervals, users may participate in cooling modalities such as cold showers or cold water immersion (Heinonen & Laukkanen, 2018). Far-infrared sauna sessions are between 45-60°C for 15 to 30 minutes, where far infrared panels emit infrared waves as radiant heat (Beever, 2009). Lastly, water perfused suits are typically between 30 to 90 minutes with circulating water temperatures of ~50°C.

Acute Heating & Arterial Stiffness

Acute, or single, heat exposure can reveal mechanistic responses to passive heating where repeated, chronic bouts of a stressor lead to beneficial physiological adaptations. Therefore, it is important to understand what occurs acutely to better understand how repeated bouts can lead to these beneficial adaptations. With an acute bout of heating, studies either report no change or a reduction in pulse wave velocity.

Lee et al. investigated the effects of a single traditional Finnish sauna session (30 minutes at 73°C and 10-20% humidity) on cardiovascular parameters including heart rate, blood pressure, and arterial stiffness via pulse wave velocity (PWV) and augmentation index (AIx). These measures occurred before, immediately after, and 30 minutes after the sauna session. All participants (n=102, ages 32-75 years) had at least one cardiovascular risk factor such as dyslipidemia, hypertension, obesity, diabetes, family history of coronary heart disease, or a history of smoking. Compared to before heating, the single sauna session significantly decreased carotid-femoral PWV (Pre: 9.8 ± 2.5 m/s vs. Post: 8.6 ± 1.6 m/s) and mean arterial pressure (Pre: 99 ± 15 mmHg vs. Post: 94 ± 10 mmHg), but there were no changes to AIx (Pre: 9.8 +/- 16% vs. Post: 4.1 +/- 15.8%). All values returned to baseline following a period of recovery (Lee et al.,

2018). This data suggests that 30 minutes in a Finnish sauna can have an acute impact on arterial stiffness.

Caldwell et al., examined the effects of passive heating with a water perfused suit and exercise in the heat on arterial stiffness. The study included 9 adult participants (n = 3 females) of normal weight (BMI 24.1±2.8 kg/m^2) who underwent 4 trials each in a randomized order: 50 minutes supine (Control), 50 minutes supine with a water perfused suit, 30 minutes of cycling at 50% VO_2 peak in cool conditions (15°C) and 30 minutes of cycling at 50% VO_2 peak in warm conditions (40°C). Arterial stiffness was assessed by measuring PWV using a Doppler ultrasound at baseline and after each trial (immediately after, 15 min, 30 min, 45 min, and 60 min). Central PWV was determined using the carotid and femoral arteries while peripheral PWV was measured using 1) the carotid artery and radial artery in the wrist (upper) and 2) the femoral artery and dorsalis pedis artery in the foot (lower). There was no change in central or upper peripheral PWV between any time points for the control trial or either exercise trial. There was a decrease in upper peripheral PWV immediately after (-106 ± 33 cm/s) and 15 minutes after (-100 ± 29 cm/s) passive heating compared to pre-heating (Caldwell et al., 2017). This data suggests that 50 minutes of passive heat stress using a water-perfused suit can acutely decrease arterial stiffness in the peripheral arteries.

Additionally, acute hot water immersion also has an effect on arterial stiffness. Sugawara and Tomoto examined 10 healthy men before and 10 minutes after a 5-minute immersion in hot water (40-41 °C) to heart level. Arterial stiffness was measured carotid-femoral PWV (central) and femoral-ankle PWV (peripheral) using an applanation tonometry. There was a 7.5% (897 ±

150 vs 830 ± 115 cm/s) decrease in aortic PWV and a 3.1% (897 ± 150 vs 830 +/- 115 cm/s) decrease in peripheral PWV after water immersion (Sugawara & Tomoto, 2020). There was no difference in aortic augmentation index and aortic blood pressure (Sugawara & Tomoto, 2020). These findings suggest that very short-term warm water immersion can also reduce central and peripheral arterial stiffness.

Localized lower limb hot water immersion has also been found to effect vascular function, independent of whole body heat stress. Cheng et al. studied the effect of a 45-minute ankle- and knee-level hot water (45 °C) immersion in 16 young, healthy participants (9 female, 8 male). Arterial stiffness measurements were completed before and done 15-minutes post limb immersion. Arterial stiffness was evaluated using carotid-femoral and femoral-foot PWV with applanation tonometry. There was no difference in carotid-femoral PWV, but there was a decrease in femoral-foot PWV for knee-level submersion (8.4 ± 1.2 vs 7.7 ± 1.1 m/s) (Cheng et al., 2021). Data from this study suggests that acute improvements in vascular function may be subject to the site of heating since most improvements were observed in peripheral tissue rather than centrally. Further, this study shows that a greater portion of the body exposed to heat could lead to more notable benefits.

Together, the above studies suggest that an acute bout of heating with different modalities can transiently reduce arterial stiffness, with a greater effect on peripheral arterial stiffness compared to central. These changes in stiffness are likely due to vascular changes, such as increased compliance, to accommodate thermoregulatory mechanisms for heat loss (increased

peripheral blood flow). However, and as mentioned above, not all studies report a reduction in arterial stiffness on a central or peripheral level with passive heating.

Eight young participants (3 men and 5 women) of normal BMI (< 30 kg/m^2) were passively heated with a water-perfused suit until core body temperature rose 0.5, 1, and 1.5 °C above baseline. The purpose of the study was to determine whether successive increases in core body temperature decreases central (carotid-femoral) and peripheral (carotid-radial) arterial stiffness as measured by PWV with a Doppler ultrasound. There were no changes in central or peripheral PWV. However, there was a decrease in central (r = -0.89) and peripheral (r = -0.93) PWV with increasing body temperature within individual participants where the participants who had the highest normothermic baseline pulse wave velocities saw the greatest reduction following heat exposure (Ganio et al., 2011). This may imply that individuals who have greater arterial stiffness, such as those with obesity, might benefit more from heat stress than individuals with more normal arterial stiffness.

As mentioned above, arterial stiffness increases with normal aging. A study conducted by Schlader et al. examined whether age influences the effects of passive heating on arterial stiffness. They assessed 8 healthy and young (26 ± 5 years) and 8 healthy and old (70 ± 4 years) adults prior to and during mild (0.6 °C) and moderate (1.3 °C) increases core temperature with water-perfused suits for a 90-minute duration (~49 °C). Carotid-femoral PWV with applanation tonometry was used to assess central arterial stiffness. While the older individuals did have a significantly higher baseline PWV than the younger group (8.8 ± 2.3 vs 5.6 ± 0.9 m/s), there was no significant change in PWV for either group following heat exposure (Schlader et al.,

2019). This implies that changes in arterial stiffness following heat stress may not be influenced by age, but rather health status. Therefore, age-related stiffening of the arteries is not easily adaptable, but health-induced arterial stiffness may respond to a heat stimulus.

The acute changes in response to heat exposure are likely not due to changes in the elastin-collagen fibers or remodeling of the arterial wall which may occur with repeated heat therapy. The lack of changes could be due to also be due to differences in methodology (i.e., timing, duration, population, etc.). Additionally, while water-perfused suits provide a well-controlled heating stimulus in a research setting, the applicability of these to a real-world setting are less than modalities such as water immersion and sauna bathing. Finally, there is a lack of data for the acute heating effects of arterial stiffness in individuals with obesity.

Repeated Heat Therapy & Arterial Stiffness

The Kuopio Ischemic Heart Disease Study, a cohort study on 2,300 middle-aged Finnish men, showed a significant decreased risk for developing a cardiovascular disease and all-cause mortality was decreased by 40% with regular sauna use. Men who used the sauna 4-5 times per week had a 50% decreased risk and men who used the sauna 2-3 times per week had a 27% decreased risk when compared to men who used the sauna once per week (Laukkanen et al., 2015). This reveals that there are cardiovascular benefits to repeated heat therapy.

One of the first clinical trials relating the physiological benefits of heat therapy was an 8-week hot water immersion (40.5°C) study involving young, sedentary individuals. After the heat therapy, there were changes to cardiovascular health marked by increases in flow mediated

dilation and reductions in arterial stiffness, resting mean arterial pressure, and carotid artery wall thickness compared to the thermoneutral water immersion group (Brunt et al., 2016). With similar methodology but in a different population, healthy, middle-aged and older (57-79 years old) adults participated in 30 hot water immersion sessions for 60 minutes in each session. The hot water immersion group saw an average reduction in PWV of about 0.7 m/s across the study protocol, while the thermoneutral water immersion group saw no change in PWV (Nguyen et al., 2021). While these studies show promising results of the potential cardiovascular benefit to heat therapy, other forms of heat therapy must be investigated as alternative forms of passive heat therapy.

One specific clinical group of individuals are at elevated risk for obesity and cardiovascular disease is women with polycystic ovary syndrome (PCOS). Therefore, these individuals may benefit from repeated heat therapy to reduce these clinical risks. Ely et al. included 18 young women with obesity (BMI 41.3±4.7 kg/m^2) and diagnosed PCOS and assigned them to either the control group or the heat therapy group. The heat therapy group completed 30 sessions of hot water immersion (40.5 °C) for 60 minutes each across 8 to 10 weeks while the control group did not complete any heating sessions. Participants were assessed for vascular function before and after all heating exposure. Vascular function was quantified by blood pressure, carotid and femoral artery thickness, and flow mediated dilation (FMD). The results of this study indicated a reduction in systolic and diastolic blood pressure, a reduced carotid (Pre: 0.054±0.005 to Post 0.044±0.005 cm) and femoral (Pre: 0.056±0.000 to Post: 0.042±0.005 cm) wall thickness, and an improvement in FMD for those in the heat therapy group (Ely et al., 2019). There were no changes in vascular function for those in the control group. This

study indicates that repeated bouts of heat therapy can improve vascular function without changes in body weight and composition.

In a similar experimental design but with a different heating modality, Debray et al., investigated the effects of repeated sauna bathing in individuals with coronary artery disease (CAD). CAD is characterized by a buildup of plaque within the walls of the arteries that supply the heart. The study included 41 participants with stable CAD who were randomly assigned to a heat therapy (n=21) or control (n=20) protocol. Heat therapy consisted of Finnish sauna sessions (79°C, 13% humidity) for 20-30 minutes each at 4 times a week for 8 weeks for a total of 32 sessions. The control group was instructed to continue activities of daily living for the deration of the study. Arterial stiffness, flow mediated dilation and blood pressure were measured before and after the 8-week protocol. Arterial stiffness was assessed by carotid-femoral PWV using the applanation tonometry method. The study found no significant change in PWV, FMD, systolic, or diastolic blood pressure (Debray et al., 2023). This suggests that repeated Finnish sauna bathing may have no impact on vascular health in adults with CAD.

A specific form of far-infrared sauna bathing utilized a practice called Waon therapy. It consists of sitting in a far-infrared sauna for 15 minutes at 60°C followed by 30 minutes of sitting in a temperature-controlled room wrapped in blankets (Miyata & Tei, 2010a). Most of the investigations with this type of far-infrareds sauna bathing have been in inpatient heart failure and peripheral artery diseases patient groups. In one study, Waon therapy sauna sessions were completed on average at 5 to 7 days a week for 2 to 4 weeks (Miyata et al., 2008; Miyata & Tei, 2010b; Ohori et al., 2012). They saw improvements in flow-mediated dilation, left ventricular function, six-minute walk distance, oxidative stress, and inflammation (Fujita et al., 2011;

Miyata et al., 2008; Miyata & Tei, 2010b; Ohori et al., 2012) While there was no direct measure of arterial stiffness, the results show promise in the effects of repeated far-infrared sauna bathing on cardiovascular function.

Altogether, the purpose of this study was to examine the effect of a 30-session infrared sauna intervention on PWV in individuals with obesity. We hypothesized that individuals with obesity would see a decrease in PWV following sauna therapy. Heat therapy may be a promising option in a clinical or leisurely setting in addition to or as a replacement for typical exercise since not everyone meets the exercise recommendations or can exercise at an intensity to gain cardiovascular benefit. Further, it is important to assess physical fitness in a clinical population because it can be a strong predictor of all-cause mortality than other clinical tests typically performed in a doctor's office (Cullen et al., 2020). Despite encouraging data indicating improvements in many of the factors involved in arterial stiffness and overall cardiac health following heat therapy, further research is warranted into the direct impact of infrared sauna therapy on PWV in individuals with obesity.

Methods

We recruited 5 individuals to participate in this study (4 men, 1 woman, age: 34±10 years, BMI: 35.5±3.8 kg/m^2). All participants were non-smoking, obese (defined as a BMI 30-45 kg/m^2) men and women and were not participating in more than 120 minutes of moderate physical activity a week. After providing verbal and written informed consent, participants completed a physical activity and a health history questionnaire to determine they met the inclusion criteria (i.e., sedentary, obese adults) while ruling out exclusion criteria (i.e., diagnosed

cardiovascular disease with the exception of elevated or stage I hypertension, type II diabetes, or taking medications that affect blood pressure or insulin sensitivity). Participants were randomized to the control group or the heat therapy group. The characteristics of the participants between heat therapy and control groups are shown in Table 1. The heat therapy group completed 30 infrared sauna sessions (45-60 ℃, 3-4 times per week) between 30-45 minutes each over an 8–10-week period. Participants in the control group did not participate in the sauna sessions. All participants were instructed to maintain their normal activities of daily living for the duration of the study.

All participants completed three vascular function visits throughout the duration of the study. The first vascular function visit occurred at week 0 (PRE), and prior to heat exposure for the heat therapy group, to establish a baseline. The second vascular function visit took place at the midpoint of the study, between 4-5 weeks for the control group or after 14-16 infrared sauna sessions for the heat therapy group (MID). The third vascular function visit occurred after 8-10 weeks for the control group or after all 30 infrared sauna sessions were complete for the heat therapy group (POST). The vascular visits were scheduled at least 48 hours after the last sauna session to avoid any acute effects of passive heating on the parameters of interest. Each vascular function visit included a pulse wave analysis (PWA) reading as well as a pulse wave velocity (PWV) measurement, described in detail below.

All study visits took place at the Bowerman Sports Science Center in Hayward Stadium at the University of Oregon. Prior to the vascular function visit, participants were asked to refrain from heavy exercise, medications, and supplements (except for oral contraceptives) for 24 hours, caffeine and alcohol for 12 hours, and food for at least 8 hours prior to each visit. At the

beginning of each vascular visit, participants filled out a health history update questionnaire to confirm adherence to the pre-visit instructions and completed a physical activity questionnaire. Participants provided a urine sample to be tested for hydration via urine specific gravity (Atago Refractometer, Bellevue, WA) and changed into a t-shirt and loose-fitting shorts. Height and weight were measured with a standard scale and stadiometer. The circumference of participants' waist and hips were measured to calculate waist-to-hip ratio as an additional means to quantify body composition in our participants. The participants were instructed to lay in the supine position on a padded table for the remainder of the vascular study visit. The SphygmoCor® XCEL (ATCOR, New South Wales, Australia) was utilized for the assessment of PWA and PWV. One blood pressure cuff was placed on the upper arm and a second blood pressure cuff was placed on the upper thigh. Both blood pressure cuffs were placed on the right side of the body for all visits because previous research indicates as much as a 26.5% difference in blood pressure between arms (Salvi et al., 2015). The assessment of arterial stiffness was one of three vascular measurements assessed during the vascular function visit and was completed second during the visit. Prior to the assessment of arterial stiffness, participants completed 20 minutes of quiet supine rest and an additional 30-40 minutes to obtain the first vascular measurement. Therefore, participants had been supine for at least 50 minutes before assessments of arterial stiffness were made. The PWA included one brachial blood pressure measurement followed by a 10-second brachial blood pressure waveform recording and analysis. This was repeated twice as the initial PWA is only considered a baseline and not used for data interpretation. The second PWA was measured, recorded, and used for analysis. Our measurements (in mm) were made along the using anatomical landmarks. These measurements included the distance between 1) the common carotid artery (CCA) in the neck and the sternal notch at the top of the sternum bone, 2)

the CCA and the most proximal part of the thigh cuff, 3) the sternal notch and the thigh cuff, and 4) between the femoral artery and the thigh cuff. The sternal notch is used in these measurements because it estimates the location of the aorta, which can be found deep to the sternal notch. We used these four locations because data shows a single measurement between the CCA and the femoral artery overestimates the real distance by 25.4% (Van Bortel et al., 2012). For the PWV measurement, a pencil-sized tonometry probe was placed on the right CCA to measure the beat-to-beat pressure waveform of the CCA. Once the pulse signal met the required guidelines standardized within the SphygmoCor®, the CCA pulse signal was recorded while simultaneously inflating the femoral cuff to obtain a beat-to-beat pressure waveform of the femoral artery. We chose to use a femoral blood pressure measurement rather than placing a tonometer over the femoral artery due to its more invasive location on the body. These simultaneous blood pressure waveforms paired with the measurement distances were analyzed within the SphygmoCor® to calculate pulse wave velocity. Once the first PWA and PWV assessments were complete, both processes were repeated, starting with the brachial blood pressure and distance measurements along the body, and ending with the PWV measurement. The average of the two PWA and PWV measurements were used for analysis. If the first two PWV measurements were not within 0.2 m/s of each other, a third PWA and PWV were conducted, and the median value was used for analysis.

For the sauna sessions, participants arrived at the laboratory, provided a urine sample to test hydration status determined via urine specific gravity, and obtained a nude body weight in a private room. If the urine hydration status was above 1.020, the participant was provided up to 5 mL/kg of body mass of water. For sauna visits 1-5 and 30, the participant self-inserted a rectal thermistor ~10 cm past the anal sphincter to measure body temperature and were instrumented

with temperature buttons (iButtons) to calculate mean skin temperature (D. Mitchell & Wyndham, 1969). For all sauna sessions, participants wore a telemetry heart rate monitor (Polar). The participant entered and remained seated in the sauna for 30 to 45 minutes, with all participants completing 45 minutes by the 5th sauna session. During the sauna heart rate, rectal temperature, and sauna temperature were recorded every 5 minutes. Every 10 minutes, participants reported their rate of perceived exertion, ("how hard to you feel your body is working?" with the BORG 6-20 scale), thermal sensation ("how does the temperature of your body feel?"; 1 (cold) to 7 (hot) in 0.5 increments), thermal comfort ("how comfortable does the temperature of your body feel?"; 1 (comfortable) to 4 (very uncomfortable) in 0.5 increments), and sweating sensation ("are you sweating, if so how much?"; 0 (not sweating) to 10 (most sweating ever) in 0.5 increments). The details from the sauna visits are shown in Table 2.

Statistical Analyses

The data was analyzed with a two-way analysis of variance (ANOVA) for group (Control vs. Heat Therapy) and time (Pre, Mid, and Post). In the case of missing values, a mixed effects model was used. Post hoc Holm-Sidak Test were used to account for multiple comparisons in the case of a significant main or interaction effect. All statistical analyses were performed in Prism (GraphPad Prism, version 10.3). Significance was set at $p < 0.05$. Data are presented as mean ± standard deviation.

Results

The anthropometric characteristics of the participants are shown in Table 1. There was a group effect for weight where the Heat group had a lower weight compared to the Control group at Pre, Mid, and Post. There was no effect of time or interaction effect for weight. There were no

main or interaction effects for body mass index, waist circumference, hip circumference, or waist-to-hip ratio.

		Time			P-value		
	Group	**Pre**	**Mid**	**Post**	**Group**	**Time**	**Group x Time**
Weight (kg)	Control	123±1	124±5	126±4	0.0434	0.4263	0.7698
	Heat	105±9†	105±7†	106±7†			
Body mass index (kg/m^2)	Control	38.8±4.4	39±2.6	40±2.9	0.0726	0.4484	0.8075
	Heat	33.8±0.5	34.0±1.2	34.2±1.5			
Waist Circumference (cm)	Control	112±4	112±0	115±1	0.3101	0.3213	0.9664
	Heat	105±5	105±6	108±10			
Hip Circumference (cm)	Control	125±14	134±0	126±7	0.0893	0.9165	0.6845
	Heat	115±2	113±3	116±7			
Waist-to-Hip Ratio	Control	0.90±0.06	0.84±0	0.91±0.04	0.6372	0.7102	0.6479
	Heat	0.91±0.05	0.92±0.09	0.92±0.04			

Table 1. Anthropometric Characteristics

Weight, body mass index (BMI), waist and hip circumferences, and waist to hip ratio for the Control (n=2; 1 man, 1 woman) and Heat (n=3, 3 men) groups across the protocol (Pre, Mid, and Post). Values are reported at mean ± standard deviation. The data were analyzed with a two-way ANOVA or a mixed-effects model if data was missing and post-hoc Holm Sidak Tests for multiple comparisons. *: different from PRE within group ($p < 0.05$); †: different from Control ($p < 0.05$).

The mean values during the first and last sauna session are shown in Table 2 for the participants in the Heat group. All 30 sauna sessions were completed within 9 weeks and participants tolerated the sessions well.

	First Sauna Visit	**Last Sauna Visit**	**All Sauna Visits**
Sauna Time (min)	32±3	45±0	43±4
Sauna Temperature (°C)	54±7	54±5	54±5

Sauna Heart Rate (bpm)	102±8	96±7	102±10
Δ Heart Rate from Pre-Heating (bpm)	11±6	7±3	9±5
Sauna Rectal Temperature (°C)	37.4±0.2	37.1±0.2	37.3±0.2
Δ Rectal Temperature from Pre-Heating (°C)	0±0.1	-0.2±0.1	-0.2±0.1
Mean Skin Temperature (°C)	35.8±0.2	35.7±1.5	36.2±1.4
Δ Mean Skin Temperature from Pre- Heating(°C)	6.6±1.5	7.0±1.5	7.0±1.4
% Δ Body Mass	-0.27±0.22	-0.30±0.03	-0.35±0.14

Table 2. Summary of Sauna Visits

Sauna time (min), temperature (°C) heart rate (bpm), rectal temperature (°C), skin temperature (°C), and % body mass for participants between the first, last, and overall mean of the sauna visits. The average change in heart rate (bpm), rectal temperature (°C), and skin temperature (°C) are calculated from the pre-heating values obtained prior to participants entering the sauna. Values are reported as mean ± standard deviation.

The cardiovascular and hemodynamic values are shown in Figure 1. There was no effect of time (p = 0.9848), group (p = 0.0851), or group x time interaction (p = 0.2795) for heart rate at PRE vs. MID vs. POST for Control (68±3 vs. 64±4 vs. 64±9 bpm) or Heat (69±2 vs. 74±3 vs. 74±6 bpm) (Figure 1A). There was no effect of time (p = 0.4290), group (p = 0.4790), or group x time interaction (p = 0.9289) for systolic blood pressure at PRE vs. MID vs. POST for Control (118±31 vs. 109±6 vs. 110±9 mmHg) or Heat (128±18 vs. 120±14 vs. 124±19 mmHg) (Figure 1B). There was no effect of time (p = 0.4825), group (p = 0.1062), or group x time interaction (p = 0.3234) for diastolic blood pressure at PRE vs. MID vs. POST for Control (64±13 vs. 70±4 vs. 62±4 mmHg) or Heat (89±16 vs. 81±6 vs. 81±9 mmHg) (Figure 1C). There was no effect of time (p = 0.1889), group (p = 0.2317), or group x time interaction (p = 0.2189) for mean arterial blood

pressure at PRE vs. MID vs. POST for Control (81±19 vs.81±4 vs. 77±6 mmHg) or Heat (100±18 vs. 93±8 vs. 93±13 mmHg) (Figure 1D). There was no effect of time (p = 0.1889), group (p = 0.4205), or group x time interaction (p = 0.2189) for pulse pressure at PRE vs. MID vs. POST for Control (54±18 vs. 39±3 vs. 48±6 mmHg) or Heat (39±3 vs. 39±9 vs. 43±11 mmHg) (Figure 1E).

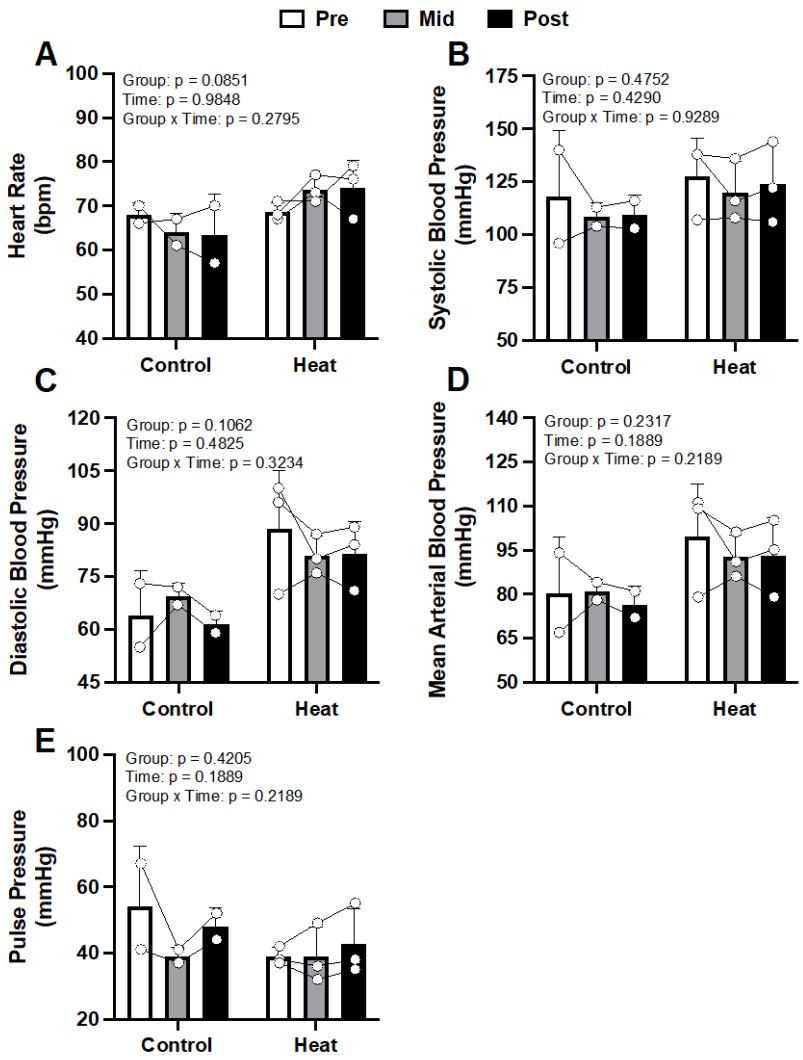

Figure 1. Cardiovascular and Hemodynamics

Heart rate (A), systolic blood pressure (B), diastolic blood pressure (C), mean arterial pressure (D), and pulse pressure (E) across time (Pre, Mid, and Post) between Control (n=2; 1 man, 1 woman) and Heat (n=3, 3 men) groups. Values are reported at mean ± standard deviation with individual values shown in the open circles. The data were analyzed with a two-way ANOVA or a mixed-effects model if data was missing and post-hoc Holm Sidak Tests for multiple comparisons. *: different from PRE within group ($p < 0.05$); †: different from Control ($p < 0.05$).

The arterial stiffness values are shown in Figure 2. There was no effect of time (p = 0.5457), group (p = 0.6348), or group x time interaction (p = 0.9700) for augmentation pressure at PRE vs. MID vs. POST for Control (8±7 vs.5±8 vs. 7±12 mmHg) or Heat (10±6 vs. 8±2 vs.

9±3 mmHg) (Figure 2A). There was no effect of time (p = 0.5026), group (p = 0.6604), or group x time interaction (p = 0.7113) for augmentation index at PRE vs. MID vs. POST for Control (22±21 vs.16±24 vs. 16±29 %) or Heat (25±11 vs. 24±2 vs. 24±7 %) (Figure 2B). There was no effect of time (p = 0.7371), group (p = 0.5568), or group x time interaction (p = 0.3912) for augmentation index @ 75 bpm at PRE vs. MID vs. POST for Control (15±24 vs. 8±30 vs. 8±35 %) or Heat (19±12 vs. 21±2 vs. 22±5 %) (Figure 2C). There was no effect of time (p = 0.4605), group (p = 0.3817), or group x time interaction (p = 0.3412) for pulse wave velocity at PRE vs. MID vs. POST for Control (6.7±0.9 vs. 6.2±0.2 vs. 6.5±0.6 m/s) or Heat (7.6±1.5 vs. 7.7±1.6 vs. 8.0±2.1 m/s) (Figure 2D).

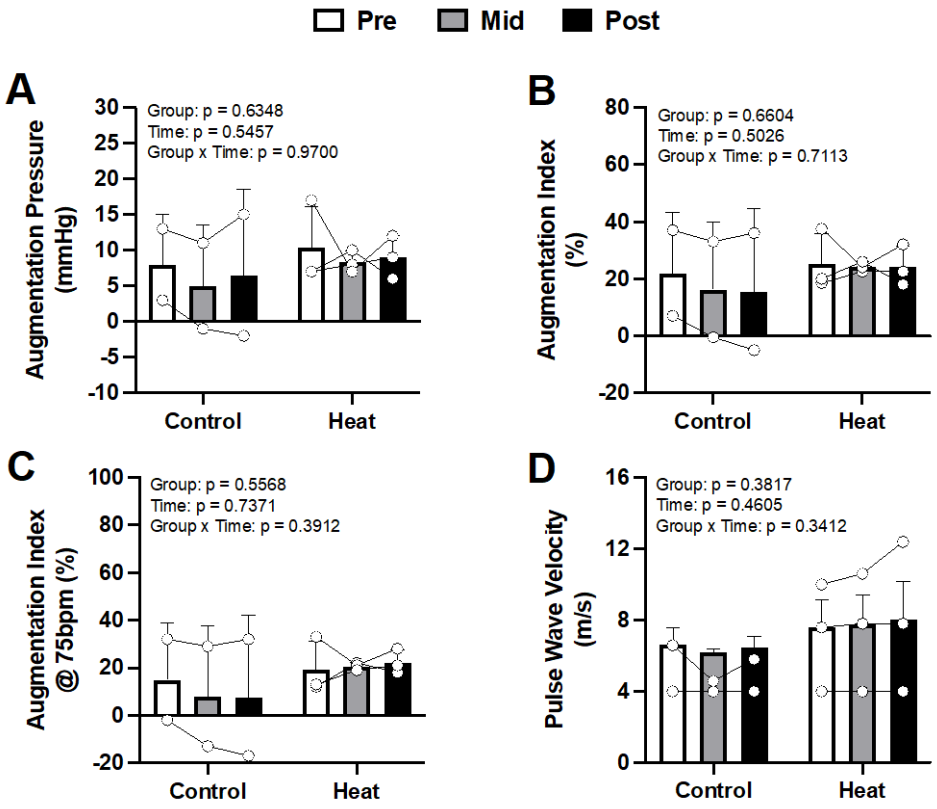

Figure 2. Arterial Stiffness

Pulse wave velocity (A), augmentation pressure (B), augmentation index (C), and augmentation index @75 bpm (D) across time (Pre, Mid, and Post) between Control (n=2; 1 man, 1 woman) and Heat (n=3, 3 men) groups. Values are reported at mean ± standard deviation with individual values shown in the open circles. The data were analyzed with a two-way ANOVA or a mixed-effects model if data was missing and post-hoc Holm Sidak Tests for multiple comparisons. *: different from PRE within group ($p < 0.05$); †: different from Control ($p < 0.05$).

Discussion

Individuals with obesity are at a risk for developing cardiovascular disease which in part can be due to increased arterial stiffness. Heat therapy may be a promising modality to target arterial stiffness and therefore reduce cardiovascular risk within this specific population. Compared to other forms of heat therapy, less is known as to whether repeated far-infrared sauna bathing is effective at targeting arterial stiffness. We tested the hypothesis that repeated far-

infrared sauna bathing will reduce arterial stiffness, measured by PWV, in individuals with obesity. Our main findings are that repeated far infrared sauna bathing did not have an effect on PWV in individuals with obesity. Additionally, there were no differences in secondary outcomes including blood pressure, augmentation pressure, and augmentation index. Therefore, there was no change to arterial stiffness with repeated far-infrared sauna bathing in individuals with obesity. Both acute and repeated heat therapy studies have revealed reductions in PWV (Brunt et al., 2016; Lee et al., 2018; Nguyen et al., 2021; Sugawara & Tomoto, 2020), however not all previous work show a reduction in PWV. The variance within these previous and our findings may be due to differences in methodology between heating stimulus and PWV measurement.

There are multiple forms of passive heating including hot water immersion, Finnish sauna bathing, and far-infrared sauna bathing. The main differences between the modalities are the temperatures and the timeline (continuous vs. interval) within a single session. We chose far-infrared sauna therapy because it may be a more tolerable form of passive heating, evidence supports improvements in cardiac and vascular outcomes in a chronic heart failure patients, and these types of saunas are becoming more accessible to the general public (Miyata et al., 2008; Miyata & Tei, 2010b; Ohori et al., 2012). However, to our knowledge, there are no reports of the effects of repeated far-infrared sauna on arterial stiffness, specifically within individuals with obesity.

The average temperature reached during our sauna sessions was 54 ± 5°C. Hot water immersion sessions typically occur in 38-42°C water (Brunt & Minson, 2021), but there is a reduced capacity to for evaporative heat loss via sweating due to the hydrostatic pressure effects

of water immersion. Finnish sauna bathing typically occurs between 70-100°C at 10-20% humidity (Heinonen & Laukkanen, 2018). Aside from the temperatures of far-infrared saunas being lower than Finnish saunas, the main difference between the two types of saunas is the presence of far-infrared waves. The far-infrared waves emitted from panels within the sauna penetrate the peripheral tissues about 3 to 4 cm (Mero et al., 2015). This may imply a more direct heating stimulus and the exposure to the far-infrared waves may be more important than the temperature of the sauna itself. To our knowledge, there has not been a direct comparison between these two different types of saunas to confirm this. While we followed the established temperatures for far-infrared bathing sessions (40 to 60°C) (Beever, 2009), it could be that a larger thermal load is needed to target arterial stiffness in individuals with obesity. Debray et. al saw no change in arterial stiffness in adults with coronary artery disease following 8 weeks (32 sessions) of Finnish sauna bathing at 79°C and 13% relative humidity (Debray et al., 2023). Therefore, even with higher temperatures, 8 weeks of repeated sauna bathing with higher temperatures may not be enough to effect arterial stiffness in populations with elevated cardiovascular disease risk. As far-infrared temperatures are lower, this could imply a more prolonged use of far-infrared saunas (> 8 to 10 weeks) is required to have changes to arterial stiffness in individuals with obesity.

Previous reports with repeated far-infrared sauna bathing utilized a practice called Waon therapy. This form of far-infrared sauna bathing includes sitting in a custom far-infrared sauna for 15 minutes at 60°C followed by 30 minutes of sitting in a temperature-controlled room wrapped in blankets (Miyata & Tei, 2010a). The participants in this study were an inpatient heart failure patient group and they completed sauna sessions between 5 to 7 days a week for 2 to 4

weeks (Miyata et al., 2008; Miyata & Tei, 2010b; Ohori et al., 2012). Our protocol differed in that we completed sauna sessions 3 to 4 days a week for 9 weeks and our participants had almost three times the exposure to far-infrared waves. We believe that the 3 to 4 sessions a week utilized in our protocol may be more realistic for the general public as time is the biggest barrier to participating in exercise (Felicia Cavallini et al., 2020). While taking time to sauna bathe versus participate in exercise does not differ in reducing the barrier of time, far-infrared sauna bathing may be more tolerated and appealing to a population with lower cardiovascular tolerances. Therefore, adherence may be greater with sauna bathing but a direct comparison for adherence between passive heating and exercise has not been made. Additionally, it could be that shorter, more frequent exposures to far-infrared waves are required to instill beneficial adaptations, as shown with the inpatient Waon therapy studies. Further, the clinical population participants could have had greater dysfunction than our participants and therefore had a greater window of opportunity to see beneficial changes. For example, Ganio et al. reported no change to arterial stiffness with acute heating at the group level. However, those with the highest normothermic baseline pulse wave velocity had the greatest reduction during the acute heating (Ganio et al., 2011). Therefore, individuals with higher pulse wave velocity due to obesity maybe more likely to have a reduction with heat therapy.

The conditions of the sauna are relevant to address as the rise in body temperature is one of the similar physiological changes between exercise and passive heat therapy that may induce beneficial adaptations, such as reducing arterial stiffness. The increase in body temperature with passive heating may reduce arterial stiffness by mechanisms including but not limited to increased shear stress and nitric oxide bioavailability, decreasing sympathetic activity, and

lessening the presence of pro-inflammatory cytokines and immune cells. Previous research indicates that these adaptations occur after a 0.4°C increase in core body temperature or once core body temperature reaches and is maintained at 39°C (Brunt & Minson, 2021). We did not see a change in rectal temperature in our participants across the sauna sessions which was somewhat surprising based on previous findings. Previous studies with far-infrared sauna bathing report increases in pulmonary arterial blood temperature of 1.0-1.2°C during the sessions (Miyata et al., 2008; Miyata & Tei, 2010b; Ohori et al., 2012; Tei et al., 1995), but they did not directly measure arterial stiffness. Therefore, it is unknown if arterial stiffness was reduced with the use of far-infrared sauna in their population and protocol. This research group reported changes in other variables, such as nitric oxide signaling, which is one mechanism to target arterial stiffness due to obesity. Repeated increases in body temperature to about 38.3-38.5°C with hot water immersion resulted in reductions of both central and peripheral pulse wave velocity (Brunt et al., 2016; Ely et al., 2019). Therefore, the lack of change in rectal temperature in our participants may explain the lack of change to arterial stiffness.

Although rectal temperature did not change, we report mild increases in heart rate, skin temperature, and sweating. Together, these imply there was still a mild thermal load with the far-infrared sauna sessions. There was an average change in heart rate between the start and end of a sauna sessions of 9 ± 5 bpm and the average heart rate at the end of all sauna sessions was 102 ± 10 bpm. These heart rates are between heart rates reported with Finnish sauna bathing sessions (81-96 bpm) and hot water immersion (106-108 bpm) (Brunt et al., 2016; Debray et al., 2023; Lee et al., 2018). The American College of Sports Medicine recommends at least 150 minutes of moderate intensity (40-59% age-predicted maximum heart rate) or 60 minutes of vigorous

intensity (60-85% age-predicted maximum heart rate) exercise a week (Liguori & Medicine (ACSM), 2020) to benefit cardiovascular health. Regular exercise has been associated with reductions in arterial stiffness (Liu et al., 2023). While our changes in heart rate are much less than the recommended exercise intensities, it is important to note that some increase in cardiovascular work is better than none, especially in a sedentary population with low baseline cardiorespiratory fitness. Passive heating may serve as a liaison to develop the tolerance and routine to meet the exercise frequency, intensity, and durations as there have been similar improvements in cardiorespiratory fitness levels between heat therapy moderate exercise (Bailey et al., 2016). There was an average change in skin temperature between the start and end of sauna sessions of 7.0 ± 1.4°C and the average skin temperature at the end of the first five and last sauna sessions was 36.2 ± 1.4°C. The increase in skin temperature was less compared to the skin temperatures reported by Debray et al with Finnish sauna bathing. Further, there was an average 0.35% reduction in body mass and a calculated sweat rate of 0.5 L/h, indicating our participants were sweating. Both of these were calculated from changes in nude body weight corrected for fluid intake or urine output, and sweat rate accounted for the sauna session time. Our participants also reported increases in perceptions of thermal sensation, thermal discomfort, and sweating during the sauna sessions. While perceptual scales are only subjective measures versus objective measures, they begin to develop a tolerance for being "uncomfortable." Gradually, this tolerance may lead to improved capability of withstanding a greater physiological stressor, such passive heating and/or exercise, which could increase participation and adherence.

We utilized the gold-standard of carotid-femoral artery pulse wave velocity. This represents a measure of central arterial stiffness, which is an independent determinant of

cardiovascular risk, and therefore relevant for assessing cardiovascular risk in individuals with obesity (Ben-Shlomo et al., 2014). We did not see a reduction in pulse wave velocity (7.6 ± 1.5 to 8.0 ± 2.1 m/s) in our participants with repeated far-infrared sauna bathing or compared to the time control group (6.7 ± 0.9 vs 6.5 ± 0.6 m/s). To our knowledge, there are no reports of acute or repeated far-infrared sauna bathing on central pulse wave velocity. Our results are similar to the work of Ely et. al and Debray et. al who also did not report a change in central pulse wave velocity with repeated hot water immersion and Finnish sauna bathing (Debray et al., 2023; Ely et al., 2019). Brunt et. al did report a reduction in central pulse wave velocity in sedentary adults after 8 weeks of hot water immersion (60 min in 40.5°C water), but as stated above, they saw much larger increases in body temperature than our participants (38.4°C)(Brunt et al., 2016). Arterial stiffness can also be quantified within peripheral arteries. While there are considerations when using peripheral arteries to quantify stiffness due to structural changes, these may be more effected by thermoregulatory mechanisms with passive heating due to increases in peripheral blood flow. For example, Ely et al. did not find a change in central stiffness but did report a reduction in brachial ankle pulse wave velocity (Ely et al., 2019).

Lastly, arterial stiffness increases progresses overtime with increasing age (G. F. Mitchell, 2021). This progression can be slowed by lifestyle interventions (i.e., exercise) but also progressed faster due to factors such as obesity. Just as the development of arterial stiffness takes time, it could also take time to improve. While physiological changes can occur (i.e., nitric oxide bioavailability), obesity-induced structural changes within the extracellular matrix and vascular smooth muscle also play a role in arterial stiffness (Sehgel et al., 2015; Lang, 2011). Therefore, it could be that a more prolonged use of far-infrared sauna bathing may be necessary to target these

structural changes leading to arterial stiffness in individuals with obesity. To our knowledge, there are no studies investigating prolonged use of far-infrared sauna bathing similar to the prospective work by Laukkanen et al. for the association with all-cause mortality and cardiovascular risk with Finnish sauna bathing (Laukkanen et al., 2015).

Conclusion

In summary, the far-infrared sauna sessions were a mild thermal stimulus compared to previous reports of Finnish sauna bathing and hot water immersion. As the adaptations associated with heat therapy are mainly driven by changes in body temperature, this could be one explanation as to why we did not see a change in arterial stiffness in individuals with obesity. Therefore, with minimal changes in body temperature, we predict there may have been minimal stimuli to stimulate responses including shear stress, nitric oxide bioavailability, heat shock proteins, reductions in pro-inflammatory cytokines – all of which may play a role in potentially mitigating obesity-induced arterial stiffness. These continued investigations of heat therapy, such as the current protocol, are helpful in determining if there is an "optimal" recommendation for frequency, intensity, duration, and modality. The overarching goal to increase accessibility and adherence to alternatives and/or additives to exercise to target cardiovascular health, especially in populations at elevated risk.

Considerations

In addition to the conclusions above, there are a few considerations within our protocol. This project is part of a larger clinical trial with additional variables of vascular function (flow-mediated dilation), blood biomarkers (inflammatory cytokines), and metabolic signaling (insulin

responses). As the project is ongoing, we do not have all outcome variables analyzed to draw further conclusions about these early findings. Further, we do not have direct measures of parameters such as resting sympathetic activity, which has been shown to be reduced with heat therapy. We recognize the very small sample size within the current report and are continuing participant recruitment. While we analyze the grouped data, it is important to note the individual variability within the responses, which is why we chose to show the individual values in our figures. There may be meaningful changes for certain individuals. All participants were asked to maintain activities of daily living; however, fluctuations and stresses are sometimes outside of our control as researchers such as additional stressors including occupation, finance, and academics. Further, participants were not blinded to their study protocol, which may have led to internal bias or subconscious changes in lifestyle.

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