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EFFECT OF BODY MASS INDEX ON POST-EXERCISE HEMODYNAMIC RESPONSES

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THESIS

A thesis submitted in partial fulfillment of the
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By

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ABSTRACT OF THESIS

EFFECT OF BODY MASS INDEX ON POST-EXERCISE HEMODYNAMIC RESPONSES

To assess the relationships of body mass index (BMI) on arterial stiffness at rest and post-maximal treadmill graded exercise testing (GXT).

Forty-four apparently healthy, young adult males (22.1 ± 0.48 years) were recruited and divided into either a healthy weight (H, ≤24.9 kg/m^2), overweight (OV, 24.9-29.9 kg/m^2) or obese (OB, ≥29.9 kg/m^2) group based on BMI. All subjects underwent arterial stiffness (carotid-femoral pulse wave velocity, cfPWV), blood pressure (BP), pulse pressure (PP), mean arterial pressure (MAP) and body composition (bioelectrical impedance analysis, BIA) measurements at rest. Following the GXT, measures of arterial stiffness (cfPWV) and BP were acquired.

Resting measures of cfPWV, BMI, systolic BP, diastolic BP, MAP, and PP were significantly ($p < 0.05$) greater in OV and OB compared with H. Compared with OV, OB had a greater BMI. Relative peak oxygen consumption (VO_{2peak}) was greater in H compared with OV and OB ($p<0.05$). Systolic BP was positively associated, whereas VO_{2peak} was inversely related to cfPWV ($p<0.05$). No significant inter-group interactions were observed with cfPWV after the GXT. However, interactions were observed for SBP, DBP and PP ($p<0.05$).

In young men with varying BMI, SBP and VO_{2peak} were associated with resting cfPWV. However, similar cardiovascular responses were observed between groups after a maximal GXT.

KEYWORDS: Arterial stiffness, carotid-femoral pulse wave velocity, maximal graded exercise test, systolic blood pressure, VO_2.

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CHAPTER ONE: REVIEW OF THE LITERATURE

Introduction

Cardiovascular diseases (CVD) are the leading cause of death in the United States (Hoyert et al. 2012, CDC 2013) with arterial stiffness being an independent predictor of major CVD related events (Doonan et al. 2011, Safar et al. 2013, Weisbrod et al. 2013). The impairment of central arterial function is one of the earliest manifestations of vascular deterioration in humans (Shirwany et al. 2010, Cavalcante et al. 2011, Redheuil et al. 2011, Corden et al. 2013). It has been well established that the aging arteries undergo structural change over time due to constant "wear and tear" (Sutton-Tyrrell et al. 2005, O'Rourke et al. 2007**,** Weisbrod et al. 2013). However, other factors can lead to premature deterioration of arteries and will be addressed in subsequent sections of this review.

Obesity is a risk factor resulting in greater cardiovascular disease development that is associated with arterial stiffness (Sutton-Tyrrell et al. 2005). Chronic processes, such as greater collagen deposition and elastin deterioration, accompany obesity and are key mechanisms in the stiffening of arteries (Airaksinen et al. 1993, Shim et al. 2011). While studies have shown obesity increases the stiffness of the aorta and it's branches, there are gaps in the understanding of the mechanisms behind this occurrence and the consequences.

The purpose of this literature review is to: 1) review basic physiology of the vascular system, 2) further explore causalities and mechanisms of arterial stiffness,

3) consequences of this biological event, and 4) address the gaps in the research.

Arteries

The cardiovascular system is a complex system that not only contains one of the most vital organs of the body, the heart, but also encompasses a vast network that is the vascular system. The vascular system is composed of arteries, veins, and capillaries that circulate blood throughout the body to deliver oxygen to working organs and muscles. Arteries are responsible for two major functions: 1) To act as a conduit delivering oxygen rich blood from the left ventricle of the heart to the working systems in need of that oxygen, and 2) to cushion the heart's generated pulsations so the capillary blood flow is continuous (Nichols et al. 2005, Safar et al. 2006, O'Rourke et al. 2006). When both of the functions of the arterial system work efficiently, pressure waves travel away from the heart (Nichols et al. 2005, O'Rourke et al. 2006), and the reflected waves travel back to the heart and arrive during diastole to enhance coronary blood flow (O'Rourke et al. 1967, Nichols et al. 2005, O'Rourke et al. 2006).

Disease processes lead to dysfunction and adverse cardiovascular events. There are approximately 30 million repetitive pulsations per year that pump through the arterial system. This repetition causes not only fatigue, but also damage to the arteries themselves, resulting in greater stiffness. The fracture to the lamella causes the arteries to stiffen, reflections to return earlier to the heart, which consequently raises aortic systolic pressure and decreases aortic diastolic pressure

(O'Rourke et al. 2006). The decrease in aortic diastolic pressure leads to a decrease in coronary blood flow, causing a decrease in oxygen supply that can result in ischemia, and possibly cell death.

Arterial Stiffness

Arterial stiffness is an important and independent predictor of cardiovascular risk (Diez 2007). Many factors are involved in the structural change to the vascular system that causes arterial stiffness, including cellular and non-cellular changes. Cellular changes include smooth muscle cell hypertrophy and/or hyperplasia, while non-cellular changes include increased collagen deposition, reduction in the elastin/collagen ratio, and alterations in the organization of collagen and elastin fibers (Et-Taouil et al. 2003, Diez 2007). Whether the change in structure is cellular or non-cellular, these changes do not occur uniformly, rather they are distributed throughout the vascular tree (Galis et al. 2002, Diez 2007). Changes that lead to arterial stiffness mostly occur in the central arteries such as the aorta, while the peripheral arteries, such as the brachial and radial, experience these changes more sparingly (Gillessen 1995, Diez 2007).

Smooth muscle cells and extracellular matrix proteins are found more abundantly in resistance arteries versus large arteries, 70% versus 50% respectively, thus it is thought that cellular changes that lead to arterial stiffness are more abundant in resistance arteries (Et-Taouil et al. 2003, Diez 2007). Arterial stiffness occurring in larger arteries is more likely due to non-cellular changes (Et-

Taouil et al. 2003, Diez 2007). No matter the cause of stiffness, structural changes are visible as increasing intima-medial thickness of the vascular wall by two-three times, and is usually observed between the ages of 20-90 years (O'Leary et al. 1999, Diez 2007). Studies that histologically examine the structural changes of arterial stiffening have shown increased amounts of collagen, broken and frayed elastin molecules, abnormal endothelial cells, and infiltration of smooth muscle cells (Lakatta 2003**,** Diez 2007).

Role of Elastin and Collagen in Arterial Stiffness

Studies have shown that when isolating elastin and collagen in tissues, collagen makes the major contribution to the stiffening of arterial walls (Burton 1954. Dobrin et al. 1984, Diez 2007). It has further been shown that when in the presence of elastase, a protein that breaks down elastin, the geometry of an artery is altered. In contrast, when an artery is in the presence of collagenase, a protein that breaks down collagen, there are changes in the mechanical properties without significant changes to the geometry. When collagen is broken down, the production of collagen increases which then increases arterial stiffness. The loss of elastin influences the diameter and volume of the arterial wall, while also increasing stiffness (Dobrin et al. 1984, Diez 2007).

Changes in the content of extracellular matrix proteins leads to an inflammatory response that reduces quantities of elastin and an increase in collagen. The increase in production of collagen is caused by breaks in the integrity

of collagen's cross-linked matrix that usually provides strength to the vessel wall. The breaks in the matrix cause a physiological response that results in an increased collagen content to increase integrity. However, the collagen is distributed in a more disorganized fashion, causing arterial stiffness. The disruption of elastin molecules' cross-linked matrix contributes to the weakening of the elastin network, which causes mineralization by calcium and phosphorus. This dysregulation contributes greatly to arterial stiffness (Cattell et al. 1996, Diez 2007).

Collagen

Arterial stiffness has been classically recognized to be a result of the structural components within the walls of arteries (Glagov 1972, Chothia 1997, Labat 1998, Diez 2007). Collagen is a structural protein found in the extracellular matrix that is characterized in the triple helix formation formed by three polypeptide chains (Van der Rest et al. 1993, Diez 2007). Most collagens found in the human arterial system are synthesized by fibroblasts (Diez 2007). Normally, only small amounts of collagen fibers are broken down, but with vascular disease(s), breakdown occurs much more rapidly (Diez 2007). Collagenolytic enzymes, or enzymes that break down collagen, typically have a steady balance with their inhibitors, and maintain regular activation (Bode et al. 2003, Visse et al. 2003, Diez 2007). While homeostasis is maintained in healthy vascular cells, the well controlled balance between the active proteinases and inhibitors with disease are disturbed, causing collagen fibers to breakdown much more rapidly increasing collagen

production (Diez 2007).

This disturbance in homeostasis can be detrimental to the vascular system, and the biomechanical properties of the vessels are largely dependent on the quantities of fibrillar collagens and elastin (Robins et al. 1995, Diez 2007). Collagen is a structural protein that runs longitudinally and spirally in the vascular wall to both allow and resist expansion of the vessel (Wolinsky et al. 1967, Diez 2007). There are numerous types of collagen in arteries. Type I fibers are of larger diameter and provide strength to the tissue, whereas type III fibers are of smaller diameter, and are associated with increased flexibility of the vessel (Barnes et al. 1999, Diez 2007). Collagen is not only thought to provide strength and flexibility to the vascular system, but can contribute in the regulation of vascular tone, which refers to the contractile activity of the vessel relative to the maximally dilated state (Davis et al. 2000, Diez 2007). The disturbance in vascular homeostasis in terms of collagen when vascular disease is present will disrupt vascular structure and tone (Diez 2007).

Elastin

While collagen is an important protein for both the structure and function of the vascular system, elastin is the most abundant protein that is subject to negative effects of increased pulse pressure (Rosenbloom et al. 1993, Debelle et al. 1993, Diez 2007). Elastin is an insoluble protein that represents approximately 90% of elastic fibers, however, elastin is also detectible in resistance vessels (Sherratt et al. 2001,

Diez 2007). The cross-linking process that forms its structure enables the function of elastin. This process is essential in the function of large arteries as elastin distends during systole and recoils during diastole (Sherratt et al. 2001, Diez 2007).

The structure of arterial walls is disrupted with vascular diseases due to changes in collagen and elastin homeostasis. A complex process of interactions between stable and dynamic factors that determine the structural and functional changes of the vessel wall leads to the development of arterial stiffness (Diez 2007). Factors that contribute to these changes include hemodynamic forces (Et-Taouil et al. 2003, Diez 2007), genetic factors (Laurent et al. 2005) and various extrinsic factors including hormones, salt, lipids and glucose regulation (Zieman et al.2005).

Measures of Arterial Stiffness

It has been established that arterial stiffness has a major role in the prediction and occurrence of cardiovascular events (Sutton-Tyrrell et al. 2005, Mitchell et al. 2010). Clinicians are beginning to integrate measurements of arterial stiffness into assessment of patients (Laurent et al. 2006). Currently, the "gold standard" of measuring arterial stiffness is aortic pulse wave velocity (cfPWV) (Laurent et al. 2006, Doonan et al. 2011).

Pulse Wave Velocity (PWV)

PWV is an indirect measurement of arterial stiffness that can be determined using a number of different devices (Laurent et al. 2006). When measuring PWV,

the aorta is the major vessel of interest for two reasons: 1) the thoracic aorta makes the largest contribution to the arterial buffering function, which enables the smooth and consistent wave of blood throughout the arterial tree (Nichols et al. 2005, Laurent et al. 2006), and 2) the aPWV is an independent predictor of cardiovascular disease in many populations (Sutton-Tyrrell et al. 2005, Laurent et al. 2006, Mitchell et al. 2010).

PWV is a method of measuring arterial stiffness that has been generally accepted as simple, non-invasive, and reproducible. The "gold standard" PWV method to assess aortic stiffness is the carotid-femoral PWV measurement (cfPWV) (Laurent et al. 2006, O'Rourke et al. 2007, Doonan et al. 2011). This is a measure that reflects the aPWV, because it is measured along the aortic and aortic-iliac pathways. The cfPWV measurement has been used in numerous studies that have demonstrated its value in predicting cardiovascular events (Sutton-Tyrell et al. 2005, Laurent et al. 2006, Mitchell et al. 2010).

PWV is determined by measuring the waveforms at the foot of the carotid and femoral waves. The cfPWV measurement sites are the right common carotid artery and the right femoral artery. PWV is measured by dividing distance in meters by the time delay, or transit time (Laurent et al. 2006). Transit time is defined as the time of travel of the foot of the wave over a known distance. The foot-to-foot method is the most commonly used for estimating transit time. It is at the end of diastole that the steep rise in the pressure waveform begins (Laurent et al. 2006). The distance in the equation used to determine PWV is the distance between the carotid

and femoral measurement sites. These two sites are used because they are in closer proximity to the aorta that provides more accurate measures of the aPWV (Van Bortel et al. 2002, Laurent et al. 2006, Mitchell et al. 2008).

Measurements taken at peripheral sites, such as the brachial artery, are not used as often as the cfPWV. Along the arterial tree, elastic properties change. As the arteries move distally, the arterial properties become stiffer due to the elastic property changes and reflection sites are closer together the more peripheral the arteries due to increased branching and musculature (Laurent et al. 2006, O'Rourke et al. 2006). Reflection sites are areas in the arteries that have plaque build up, or other forms of damage that allow pressure waves to rebound off the arterial wall and continue its travel back to the heart (O'Rourke et al. 2006).

To put the changes along the arterial tree into perspective, the central PWV (aorta) in young, healthy adults is typically 4-5 meters per second, while in the abdominal aorta PWV increases to 5-6 m/s, and in the femoral artery, it is increased to 8-9 m/s (Nichols et al. 2005, Laurent et al. 2006). These numbers indirectly represent arterial stiffness. The faster the velocity of the pulse wave, the stiffer the arteries.

In healthy arteries, when the vessels demonstrate healthy elastic properties, PWV is low and the reflective wave returns back to the aorta during diastole. When the arteries have stiffened, PWV rises, and the reflective wave returns back to the aortic root earlier. This adds to the forward pressure of the wave moving away from the heart and increases the systolic pressure (Laurent et al. 2006, O'Rourke et al.

2006).

Measurement of arterial stiffness can be taken using a number of different devices. Using the SphygmoCor system (AtCor, Itasca, IL), pressure waves are recorded sequentially from two sites. Transit times are recorded using an electrocardiograph (EKG). The proximal carotid and distal femoral pulse waves are measured using a single high-fidelity applanation tonometer pressure sensor. The transit time is calculated in relation to the R-wave from the EKG recording by taking the time between the EKG and proximal pulse at the carotid artery, and subtracting from the time between the EKG and the distal pulse at the femoral artery to obtain the pulse transit time. The reference point used is the initial part of the pressure waveform. The measurements are taken between the two sites a short time apart so there is little to no variation in heart rate. A small change in heart rate (<5bpm) will have little to no effect on measured pulse transit time (Laurent et al. 2006).

Central PP, SBP, AIx, and Arterial Stiffness

Reflection sites are closer together in peripheral arteries due to more musculature and a smaller diameter, which increases PWV. Reflection sites are located closer together in peripheral arteries versus central, because they are more abundant. In contrast, central arteries have reflection sites that are located further apart and typically have more elastic properties, resulting in a slower PWV. SBP and PP that are measured at the brachial artery should not be confused with central SBP and PP, as it will be different at the carotid site. The pressure wave changes shape as

it travels down the aorta to the periphery while SBP and PP rise with distance from the heart and DBP and mean arterial pressure (MAP) fall very slightly. PP nearly doubles in the periphery, and is a result of stiffer arteries (Safar et al. 2013).

The augmentation index (AIx) is defined as a measure that determines wave reflections. Specifically, AIx reflects a change in reflection sites as a percentage of the second systolic peak relative to the first systolic peak generated by the pulse waveform. A change in reflection sites is present with arterial stiffening, and results in an earlier return of the pulse wave and amplification of pressure. AIx's main determinants are not only a higher PWV, but also diastolic blood pressure and height, which are related to reflection sites, age, obesity and aortic PWV. It is expressed as a percentage of the pulse pressure (Mackenzie et al. 2002, Laurent et al. 2006), and the lower the central AIx, the greater the amplification pulse wave (Safar et al. 2013). The amplification of the wave keeps the central systolic blood pressure and PP low, which provides protection for the heart against afterload, or the stress developed in the walls of the left ventricle during systole (Laurent et al. 2006, Safar et al. 2013).

With age, amplification is greatly reduced, and a reduction in amplification is associated with a significant increase in cardiovascular risk (Benetos et al. 2010, Safar et al. 2013). The AIx increases progressively with age, until approximately age 60 where it typically plateaus, but can be compared against normal data at different ages. Since AIx is influenced by heart rate, it is generally normalized by correcting for a heart rate of 75 beats per minute (bpm), and is noted as AIx@75 (O'Rourke et

al. 2007).

SBP, PP, and the AIx not only increase with age, but also with hypertension, hyperlipidemia, and diabetes mellitus, and all increases are reflective of an increase in arterial stiffness (Laurent et al. 2006). A change in reflection sites due to a variety of phenomenon, such as plaque build up and calcification due to poor diet and/or lack of exercise, also influences a faster return of the wave to the aortic root, increasing pulse pressure. This increase in central pulse pressure results in an increase in pulsatile hemodynamic stress in microcirculation to the heart and brain, because these vital organs are exposed to central arteries' higher pulse pressure versus lower pressure typical of the peripheral arteries such as the brachial (Mitchell 2008). This end-organ damage provides an additional rational for the central arteries being of major concern in both research and clinical settings.

It is important to note that hypertension, hyperlipidemia, and diabetes mellitus can be results of obesity. The change occurs because SBP, PP, and AIx are dependent on the speed of wave travel, the amplitude of the reflective wave, reflection sites, and all are changed as a result of arterial stiffness (Laurent et al. 2006).

Blood Pressure

Since blood pressure is an influencing factor on the pulse wave velocity, it is important to discuss the trends of blood pressure during and after exercise. During exercise, typical trends of blood pressure are for SBP to increase from baseline with

intensity, and DBP to either remain similar to resting blood pressure or even drop an insignificant amount. Aerobic exercise, acute or chronic, has been shown to lower or maintain blood pressure acutely in normotensive subjects. In hypertensive subjects, an even more significant decrease in blood pressure has been reduced up to 12 mmHg (Cardoso et al.2009). It has been suggested the mechanism that causes this phenomenon is that arteries remain dilated for some time following the completion of an exercise bout, but the heart is no longer beating as many times per minute, because the oxygen demand to muscles that were in use during exercise is no longer elevated (Cardoso et al. 2009).

Blood pressure has not been studied extensively in normotensive patients over time. In hypertensive patients, however, studies have shown similar results to acute exercise. The intensity of exercise and duration of a program determines the effect on hypertensive patients' blood pressure overtime. Studies have shown adherence to an exercise program chronically decreases both systolic and diastolic blood pressure (Cardoso et al. 2009), which will in turn help to lessen arterial stiffness.

With a decrease in blood pressure after exercise, it would be expected that arterial stiffness would decrease after exercise. It is known that excess weight in overweight and obese populations effects blood pressure due to excess lipids circulated in the blood, creating more plaque deposits which narrows the arteries. However, a rising question is how excess weight effects PWV.

Elevated blood pressure is often present in overweight and obese

individuals, even in younger populations (Fahs et al. 2009). Investigations have shown that when comparing healthy weight, overweight, and obese populations' SBP without exercise intervention, the overweight and obese populations have greater SBP when compared to the lean group, and obese populations have significant differences in arterial stiffness when compared to both overweight and lean groups. This can even be said in younger populations when there is no current cardiovascular disease present. When excess weight is carried by younger populations, increases in both blood pressure and arterial stiffness are observed (Fahs et al. 2009).

Weight Classification and Arterial Stiffness

For decades, it has been known that weight status affects the health of an individual. Even short-term weight gain can alter arterial stiffness due to changes in insulin insensitivity, activation of the sympathetic nervous system, and inflection of smooth muscle tone (Orr et al. 2008, Corden et al. 2013). Obesity also has a major impact on the aorta and it's arterial branches directly. In fact, while it has previously been mentioned that arterial stiffness occurs with age (Sutton-Tyrrell et al 2005, Weisbrod et al. 2013) and changes in collagen and elastin (Diez 2007), it is most frequently found in obese individuals (Baynard et al. 2009). While these factors are correlated with obesity defined by BMI, it is uncertain how adiposity modifies arterial function (Corden et al. 2013).

Recent studies have suggested that obese subjects with concentric left

ventricular remodeling, or hypertrophy, and diastolic dysfunction, not all have hypertension. Hypertension may not be necessary for left ventricular hypertrophy to occur in obese individuals (Peterson et al. 2004, Wong et al. 2004, Shim et al 2011). Arterial stiffness is observed in individuals with impaired glucose tolerance, type II diabetes, and/or metabolic syndrome, although the mechanisms are unknown (Baynard et al. 2009).

It has been shown that elevated glucose concentrations following an oral glucose tolerance test have strongly associated increases in glucose with arterial stiffness in both normal and impaired glucose tolerance (Ohshita et al. 2004, Huang et al. 2007, Baynard et al. 2009). This suggests that while those with glucose intolerance have an increase in arterial stiffness, normal glucose tolerance individuals can also experience increases in arterial stiffness with an acute bout of hyperglycemia (Baynard et al. 2009).

Investigations have shown an approximately 7% increase in central arterial stiffness after an administration of a high-fat, high-carbohydrate, high-calorie meal in obese individuals, aged 39-60 years, with and without metabolic syndrome (Baynard et al. 2009). Researchers suggest that this outcome could be the result of the age of the participants, as other studies have shown no change in endothelial function in response to a glucose load in young, healthy weight volunteers (Siafarikas et al. 2004, Major-Pedersen et al. 2008, Baynard et al. 2009).

Obesity, over the past few decades, has become an epidemic not only in the United States, but worldwide (Shim et al. 2011). As mentioned, obesity is well

known to be an independent predictor of cardiovascular morbidity and mortality (Manson et al. 1995, Calle et al. 1999, Shim et al. 2011). However, there is another weight class to consider in-between healthy weight and obese. This classification is that of "overweight". Overweight is not to be disregarded, as it is also associated with diminished cardiovascular fitness levels and an increase risk of cardiovascular diseases, including heart failure (Kenchaiah et al. 2002, Shim et al. 2011).

Similar to obese individuals, those who are overweight suffer from conditions including hypertension, dyslipidemia, and diabetes mellitus. Recent studies have also reported that an increased risk of left ventricular diastolic dysfunction is not only found in obese individuals as thought previously, but is also found in overweight individuals (Russo et al. 2011, Shim et al. 2011). Moreover, evidence suggests higher levels of adipose tissue and a higher BMI (body mass index) have adverse effects on the vascular system, because it increases arterial stiffness (Danias et al. 2003, Wildman et al. 2003, Shim et al. 2011).

In overweight individuals, studies have shown that a slight diet-induced weight gain increases large artery stiffness in healthy young adult men (Orr et al. 2008, Fahs et al. 2009, Shim et al. 2011). Research indicated that while the mechanism for the change in arterial stiffness in overweight subjects is currently unknown, a few possible mechanisms have been discussed. These mechanisms include endothelial dysfunction causing a reduction in vasodilation capacity during exercise, possible influence of adiposity on reflecting sites, and exercise-induced neurohormonal activity (Shim et al. 2011).

While overweight and obese adults have been shown to increase arterial stiffness, most of these studies look at adults whom are middle-aged. Zebekakis et al. (2005) observed the association between obesity and arterial stiffness across a wide range of ages in women. The findings show that obesity is associated with arterial stiffness across all age ranges (Zebekakis et al. 2005). These findings suggest that no matter the age of the subject, arterial stiffness will be increased in the obese versus healthy weight individuals.

Recent studies have further assessed this issue using a subject pool of males and females ages 18-72 (Zebekakis et al. 2010, Corden et al. 2013). BMI and body fat percentage analyzed using a bioelectrical impedance device have been recorded to determine subjects' weight status, and body fat has a direct relation with PWV due to an increase in blood lipids that lead to greater plaque build-up, thus more reflection sites (Zebekakis et al. 2010, Corden et al. 2013). One explanation to an increase in arterial stiffness with an increase in body fat is that a cumulative lifetime exposure to excess body fat may influence the increase in arterial stiffness (Singh et al. 2008, Corden et al. 2013). This suggests that aging may have the primary influence on arterial stiffening, but an increased body weight can cause premature stiffening.

Over the years, many studies have used exercise to observe changes in arterial stiffness in addition to diet changes. It is not only important to understand the effects diet has on premature arterial stiffness, but also how exercise influences arterial stiffness.

Exercise Intervention

Over the past several decades, countless studies have explored the effects of exercise on individuals with diseases ranging from arthritis, to cancer, to cardiovascular diseases. More recently, the focus has been narrowed as more specific causes for these diseases have been identified. Studies have used populations varying in age, gender, weight class, and disease status.

Investigations analyzing arterial function in healthy young men following exercise have revealed that acute bouts of intense exercise effects many aspects of arterial function (Rakobowchuk et al. 2009, Ranadive et al. 2012, Collier et al. 2010). BP and PP have a positive correlation with exercise: the more intense the bout of exercise, the greater the response in BP and PP. After intense bouts of Wingate exercise testing, studies have shown BP returns to resting values after approximately 15 minutes. PWV increases immediately following exercise in healthy young men in a similar pattern, but returns to resting values approximately 20 minutes post-exercise (Rakobowchuk et al. 2009). After the return to baseline, BP, PP and PWV continue to decrease approximately 8% below baseline up to 60 minutes post-exercise (Rakobowchuk et al. 2009, Collier et al. 2010). However, exercise in the upper versus lower extremities produce varying effects on the arterial system. Upper limb exercise produces a more systemic effect on PWV, lowering PWV at various measured sites whereas lower limb exercise decreases aPWV as it produces greater effects in arteries in the lower limbs, such as femoral artery. This suggests that upper limb exercises may have a greater effect on aortic

BP, PP, and PWV (Ranadive et al. 2013). While understanding how healthy arteries respond to exercise is necessary, there are many comorbidities that alter how well arteries function, and thus, response to exercise varies.

Smoking cigarettes is a comorbidity that causes damage to the arterial tree resulting in an increase in BP, PP, and PWV. Research focusing on otherwise healthy young males has demonstrated that non-smokers are able to reach higher levels of exercise during maximal exercise tests when compared to smokers. Smoking increases not only resting PWV, but also immediately following exercise. Post-exercise, it takes smokers longer to return to baseline PWV. This information implies smoking can diminish the vascular response (Doonan et al. 2011).

Another comorbidity that produces negative effects on arterial function is obesity. Explorations into effects of exercise on arterial stiffness in obese populations have shown significant differences in BP, PP, and PWV before and after exercise (Baynard et al. 2009, Shim et al. 2011). An excess amount of body weight to classify an individual as "overweight" is enough to produce differences in BP, PP, and PWV. At baseline, BP, PP, and PWV are higher in overweight populations than health weight. Similar to smokers, older overweight women and obese individuals generate higher BP, PP, and PWV post-bicycle exercise, and take a longer amount of time to return to baseline (Shim et al. 2011). Currently, there are no studies that have examined the effects of exercise in obese populations; however, improvements in PWV have been seen in this population chronically (Yokoyama et al. 2004, Casey et al. 2008, Baynard et al. 2009, Shim et al. 2011). Small reductions in PWV after

weight loss in overweight or obese middle-aged adults have been shown, but whether the effect is similar in younger adults remains unknown (Corden et al. 2013).

Although arterial stiffness has shown to increase in obese individuals over an extended period of time, it has not been studied whether or not there is an immediate response in the arteries, and how the arteries respond over an extended period of time. There are few data available on the effects of elevated body fat on early vascular disease in healthy subjects (Corden et al. 2013).

Conclusions

Arterial stiffness is recognized as an independent predictor of cardiovascular events. Arterial stiffness is a phenomenon that occurs inevitably with aging, but is caused from other comorbidities such as poor diet, lack of exercise, being overweight/obese, and diabetes. Cardiovascular diseases have been a major focus in research for decades; more recently arterial stiffness has become a major focus of study both in research and clinical settings.

Research has concentrated on arterial stiffness in populations varying in age, gender, race, and disease state. Some studies have focused solely on arterial stiffness measures including PWV, while others have also studied elements that effect arterial stiffness including HR, PP, and BP. As stated previously, with a decrease in blood pressure after exercise, it would be expected that arterial stiffness would decrease after exercise, and AIx decreased since blood pressure directly effects

these measurement. Studies have been preformed to examine the effects of exercise on AIx and PWV, but few have looked at the effects beyond the first couple minutes following exercise. Even fewer studies have examined the effects of exercise on arterial stiffness based on weight status. Finally, to our knowledge, none have been completed that compare arterial responses based on weight classification following a maximum exercise test to examine the trends for 60 minutes in young males.

Taking this information into consideration, while also considering the limitations of studies done previously on the topic of arterial stiffness, future research is needed. Studies in this literature review assessed the effects of exercise on subjects who were either overweight or obese (Baynard et al. 2009, Shim et al. 2011), while another focused on the differences in arterial stiffness between BMI classifications without the effects of exercise (Fahs et al. 2009). Since obesity has been an increasingly major problem in the United States, and is linked to the development of type II diabetes mellitus, hyperlipidema, CVDs, and various other major health issues, there is more research that needs to be done focusing on this population in terms of arterial stiffness.

CHAPTER TWO: INTRODUCTION TO THE PROBLEM

Cardiovascular diseases (CVD) are the leading cause of death in the United States (Hoyert et al. 2012, CDC 2013) with arterial stiffness being an independent predictor of major CVD related events (Doonan et al. 2011, Safar et al. 2013, Weisbrod et al. 2013). In fact, the impairment of central arterial function is one of the earliest manifestations of vascular dysfunction (Shirwany et al. 2010, Cavalcante et al. 2011, Reheuil et al. 2011, Corden et al. 2013).

The cardiovascular system is a complex system that not only contains one of the vital organs of the body, but also encompasses a vast network that is the vascular system. The vascular system is composed of vessels that circulate throughout the body to deliver much needed oxygen to working organs and muscles. The arterial system is very effective, and when both of the functions of the arterial system work efficiently, pressure waves travel away from the heart (Nichols et al. 2005, O'Rourke et al. 2006), and the reflected waves travel back to the heart and arrive during diastole to enhance coronary blood flow (O'Rourke et al. 1967, Nichols et al. 2005, O'Rourke et al. 2006). The combined conduit and cushion functions of the vascular system develop wave reflection to enhance coronary blood flow, making the cardiovascular system structured for optimal efficiency (O'Rourke et al. 1967, Nichols et al. 2005, O'Rourke et al. 2006).

Arterial stiffness is a phenomenon that occurs naturally with age, as it has been well established that aging arteries undergo structural change over time due to

constant “wear and tear” independently of cardiovascular disease (Sutton-Tyrrell et al. 2005, O’Rourke et al. 2007**,** Weisbrod et al. 2013). Overtime, the arterial system experiences dysfunction and disease. There are approximately 30 million repetitive pulsations per year that pump through the arterial system. This repetition causes not only fatigue, but also fracture to the elastin of arteries. The fracture causes the arteries to stiffen, reflections to return earlier to the heart, which consequently raises aortic systolic pressure and decreases aortic diastolic pressure (O’Rourke et al. 2006).

While the aorta and major branches inevitably stiffen with age (Sutton-Tyrrell et al 2005, Weisbrod et al. 2013), obesity is a major primary risk factor that contributes to arterial stiffness (Sutton-Tyrrell et al. 2005) even in adolescence (Urbina et al. 2010, Weisbrod et al. 2013). Chronic processes, such as greater collagen deposition, accompany obesity and are key mechanisms in the stiffening of arteries (Airaksinen et al. 1993, Shim et al. 2011). As with age, arterial stiffness also occurs with obesity independent of atherosclerosis (Sutton-Tyrell et al. 2001, O’Rourke et al. 2007, Weisbrod et al. 2013). While obesity has shown to increase the stiffness of the aorta and it’s branches, research is lacking in clinically relevant populations.

Research has focused on arterial stiffness in populations varying in age, gender, race, and disease state. These studies have taken various measures of arterial stiffness at the radial artery to analyze the pressure waveform, and carotid-femoral pulse wave velocity (cfPWV) to determine central arterial stiffness. The

"gold standard" PWV method is the carotid-femoral PWV measurement (cfPWV) (Laurent et al. 2006, O'Rourke et al. 2007, Doonan et al. 2011).

The cfPWV measurement directly reflects the aortic PWV, because it is measured along the aortic and aortic-iliac pathways. The left ventricle encounters the blood from these vessels fist, so it makes these arteries responsible for most of the physiological effects that lead to arterial stiffness (Laurent et al. 2006). In addition, other vital organs, such as the kidneys and brain, are affected by an increase in central pulse pressure as it results in an increase in pulsatile hemodynamic stress (Mitchell 2008).

Studies have looked at the effects of exercise on arterial stiffness based on weight status showing that immediately following exercise, a greater BMI results in a higher cfPWV (Rakobowchuk et al. 2009, Ranadive et al. 2012, Collier et al. 2010). However, to our knowledge, none have been completed comparing arterial response following a maximum exercise test in a population with differing BMIs, and follow the trends for 60 minutes in young males. In addition, obesity is an increasingly major problem in the United States, and being linked to the development of type II diabetes mellitus, hyperlipidema, CVDs, and various other major health problems. There is more research that needs to be done focusing on this population in terms of arterial stiffness for these reasons.

The purpose of this study was to determine whether differences in weight according to body mass index (BMI: Healthy weight, overweight, obese) influences arterial stiffness prior to and in response to a maximal exercise treadmill test in

apparently healthy young adult males. It was hypothesized that higher BMI would result in increased resting measures of cfPWV, SBP, DBP, mean arterial pressure (MAP), and PP, and be associated with a lower relative maximal oxygen capacity (VO_{2max}). It was also hypothesized that immediately following maximal exercise, higher BMI would result in a greater increase in cfPWV, BP, MAP, and PP when compared to subjects with a lower BMI, and it would take a greater amount of time for subjects with higher BMI to return to resting values.

CHAPTER THREE: METHODOLOGY

Participants

Forty-four male subjects between the ages of 18-35 years were voluntarily recruited by flyer. Subjects were divided into groups based on body mass index (BMI) as healthy weight (BMI ≤24.9 kg/m^2), overweight (BMI 25.0-29.9 kg/m^2), and obese (BMI ≥29.9 kg/m^2). Informed consent was obtained from each subject, and a physical activity readiness questionnaire (PAR-Q) and the American College of Sports Medicine (ACSM) Health/Fitness Questionnaire were completed by each subject. Subjects were excluded if two or more cardiac risk factors were present. Smokers, or subjects who have quit smoking within <6 months were also excluded from the study. Additional exclusion criteria included presence of high blood pressure, diabetes, heart complications including heart murmurs or known coronary artery disease, HIV or AIDS, or if the subject had any orthopedic limitations that prevented strenuous exercise. Subjects were excluded if their weight was over 113.4 kilograms (kg) due to weight limits on scale used for weight measurement. This study was approved by the Institutional Review Board.

Study Design

Subjects completed all testing in a single session in the Exercise Physiology Laboratory located at the University of Kentucky. After informed consent was given, and health questionnaires completed, baseline measurements were obtained; height

within nearest 0.1 centimeter (cm) and weight within 0.1 kilogram (kg) were measured using a wall-mounted Seca GmbH & co. KG stadiometer (Hamburg, Germany) and an American Digital Scale, Teraoka Weight-System PTE.LTB, model DI-10 (Singapore), respectively. BMI was calculated by dividing weight in kilograms by height in meters squared. Waist and hip circumferences were measured in centimeters using a Creation Health Products measuring tape (Orlando, Florida). In accordance to the ACSM guidelines, three nonconsecutive waist and hip circumferences were obtained within 0.1cm and the mean measurement used for subsequent analyses (ACSM, 2014). Waist to hip ratio (W:H) recorded using the formula waist (cm)/hip (cm). W:H was classified by the following criteria: low cardiac risk= <.83, moderate risk= .83-.88, high risk= .89-.94, and very high risk= > or = .95 (ACSM, 2014).

Subjects were then asked to rest for ~10 minutes in the supine position in a temperature-controlled room. After 10 minutes, resting heart rate and blood pressure were taken manually using a Polar a1 heart rate monitor (Polar Electro, Kempele, Findlan), Welch Allyn sphygmomanometer (Skaneateles Falls, NY) and a Littmann Stethoscope (3M, Cynthiana, KY). The heart rate monitor was placed on each subject prior to lying in the supine position, and blood pressure was taken at the brachial artery on the left side of the body.

A Bodystat QuadScan 4000 (Bodystat, British Isles) bioelectrical impedance device was then used to measure percent body fat, and was calibrated before each subject. Four electrodes were placed on each subject: 2 at the right hand (at the

wrist joint and across the metacarpals), and 2 at the right foot (at the ankle joint and across the metatarsals). A resting 12-lead EKG was acquired in the supine position using a Nihon Kohden ECG-1550A (Irvine, California). Each resting EKG was reviewed by the Primary Investigator to ensure no abnormalities were present. Individuals with abnormal EKGs were excluded from the study.

Resting PWV was measured by cfPWV using a SphygmoCor high-fidelity applanation tonometer pressure sensor (AtCor, Itasca, IL). cfPWV measurements were taken at the carotid and femoral arteries on the right side of the body. Pressure waves were recorded sequentially from the two sites, and transit times were recorded using the SphygmoCor's EKG . The transit time was calculated in relation to the R-wave from the EKG recording by taking the time between the EKG and proximal pulse at the carotid artery, and subtracting from the time between the EKG and the distal pulse at the femoral artery to obtain the pulse transit time. The reference point used was the initial part of the pressure waveform. The measurements were taken between the two sites a short time apart so there is minimal variation in heart rate (<5bpm).

After all resting measurements were acquired, a modified Bruce protocol was used for maximal treadmill exercise testing. Treadmill speed and grade were increased every two-minutes. Speed increased by 0.4 miles per hour, and grade increased by 2% until a 10% incline was achieved, after which only speed increased (Table 3.1).

Table 3.1 Modified Bruce Protocol

Stage	Time	Workload	
		MPH	Grade (%)
1	0-2	3.2	0
2	2-4	3.6	2.0
3	4-6	4.0	4.0
4	6-8	4.4	6.0
5	8-10	4.8	8.0
6	10-12	5.2	10.0
7	12-14	5.6	10.0
8	14-16	6.0	10.0
9	16-18	6.4	10.0
10	18-20	6.8	10.0

Oxygen consumption was measured simultaneously throughout exercise using a Parvomedics Trueone 2400 metabolic cart (Parvo, Sandy, UT). The metabolic cart was calibrated before each maximal graded exercise test (GXT) using a compression gas tank and three-liter calibration syringe. Volitional exhaustion was the end-test criteria. Achievement of VO_{2peak} was determined if the subject met 2 of the following criteria: respiratory exchange ration (RER) of ≥ 1.15, no increase in heart rate despite an increase in intensity, age predicted heart rate max (220-age) achieved, or a rate of perceived exertion (RPE) using the Borg Scale of greater than or equal to 17. Heart rate, blood pressure, RPEs, and EKG were monitored and recorded at the end of each stage throughout the duration of the exercise test.

Immediately following exercise, the subject returned to supine position. PWV and BP were recorded at 2 minutes, 5, 10, 20, 30, 45, and 60 minutes post exercise. BP measurements were taken of the left side of the subject, and cfPWV measurements were taken on the right side of the body.

Statistical Analysis

All baseline data are presented as mean ± standard error, and statistical analyses were completed using JMP 10 (SAS Institute, Cary, North Carolina). One-way analysis of variance (ANOVA) tests were used to test differences in baseline subject characteristics. Multivariate regression analyses were used to examine the relations between significant differences in baseline characteristics with arterial stiffness (cfPWV). A two-way repeated measures ANOVA was used to evaluate changes in cfPWV, SBP, DBP, MAP, and PP for post-maximal test data. Tukey posthoc analyses were used where appropriate. Level of significance was set at $p < 0.05$ for all statistical analyses.

CHAPTER FOUR: RESULTS

Baseline

All baseline data for healthy (H), overweight (OV), and obese (OB) groups are presented in Table 4.1. Compared with N, OV and OB had a greater BMI, body fat percent (BF%), systolic blood pressure (SBP), waist circumference (WC), hip circumference (HC), and cfPWV; whereas, maximal volume of oxygen consumed (VO_2) during exercise was lower, ($p < 0.05$; Table 4.1). Compared OB with OV had greater BMI, WC, and HC ($p<0.05$, all; Table 4.1).

Table 4.1 Baseline Subject Characteristics.

Characteristic	Healthy (n=17)	Overweight (n=17)	Obese (n=10)
Age (years)	21.53 ± 0.73	22.71 ± 0.77	22.1 ± 1.13
BMI (kg/m^2)	22.68 ± 0.39	26.81 ± 0.34*	31.99 ± 0.57**
BF%	10.71 ± 0.76	16.45 ± 0.89*	19.80 ± 1.60*
SBP (mmHg)	114.00 ± 1.46	122.82 ± 1.86*	121.20 ± 1.64*
DBP (mmHg)	69.53 ± 1.85	71.65 ± 1.72	69.40 ± 1.58
PP (mmHg)	44.47 ± 4.28	51.18 ± 4.50	51.80 ± 6.56
MAP (mmHg)	84.35 ± 1.51	88.71 ± 1.37	86.67 ± 1.00
WC (cm)	77.62 ± 1.27	87.06 ±0.97*	95.96 ± 2.07**
HC (cm)	94.57 ± 0.92	102.47 ± 0.90*	111.94 ± 0.93**
W:H	0.82 ± 0.01	0.85 ± 0.01	0.86 ± 0.02
VO_{2peak} (ml/kg/min)	57.55 ± 1.00	49.36 ± 1.25*	48.14 ± 1.39*
cfPWV (m/s)	4.81 ± 0.13	5.81 ± 0.12*	5.50 ± 0.30*

*p <0.05 vs. Healthy weight. **p<0.05 vs. Healthy weight and Overweight. Body mass index (BMI), body fat percentage (BF%), systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP), mean arterial pressure (MAP), resting heart rate (RHR), waist circumference (WC), aortic pulse wave velocity (cfPWV), and maximum volume of oxygen consumed during exercise (VO_{2peak}).

Multivariate regression analyses were used to further assess the baseline differences associated among subjects in BMI, BF%, SBP, WC, and VO_{2peak} and their

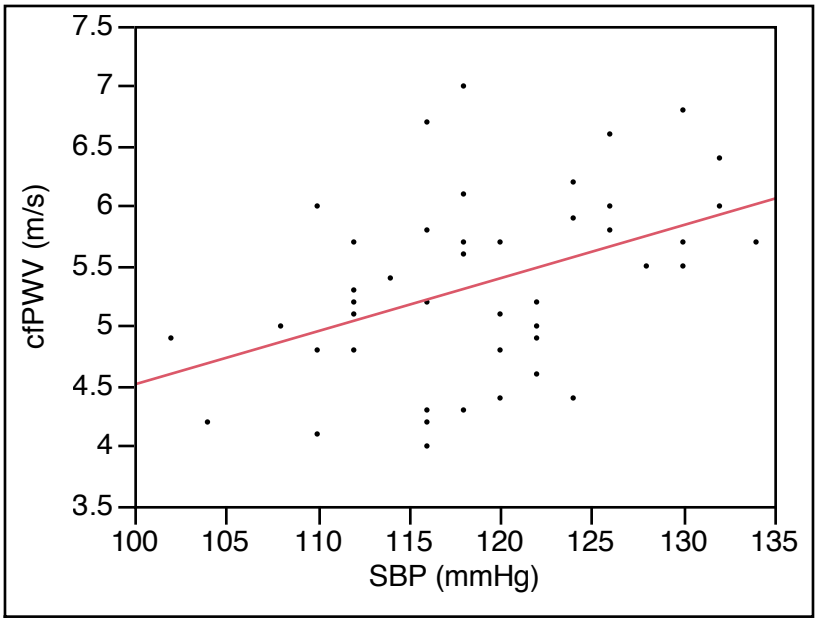
relation to arterial stiffness. From the multivariate regressions, bivariate regressions were used to demonstrate the strength relationship between variables that showed a correlation as a result of the multivariate regression analyses. A positive correlation for SBP (r= 0.44; Figure 4.1) and an inverse correlation with VO_2 (r= 0.50; Figure 4.2) with arterial stiffness were observed ($p < 0.05$, both; Table 4.2).

Table 4.2. Systolic Blood Pressure (SBP) and Peak Oxygen Consumption vs. carotid-femoral Pulse Wave Velocity (cfPWV).

Characteristics	R^2 value	p-value
SBP	0.19	0.0335*
VO2	0.25	0.0115*

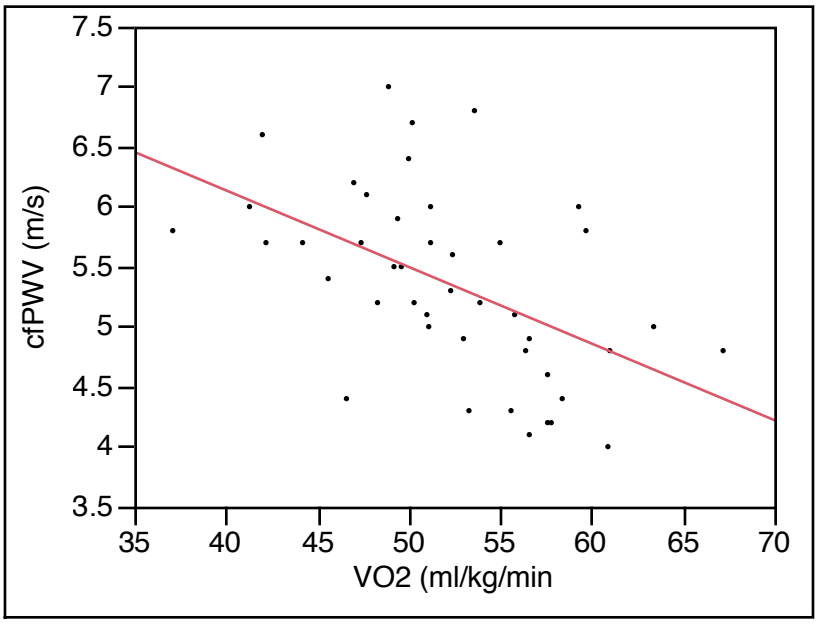
*p <0.05 vs. cfPWV.

Figure 4.1. Systolic Blood Pressure (SBP) vs. carotid-femoral Pulse Wave Velocity (cfPWV) (n=44).



r=0.44, r^2= 0.19. *p <0.05.

Figure 4.2. Peak Volume of Oxygen Consumption (VO_2) vs. carotid-Femoral Pulse Wave Velocity (cfPWV) (n=44).



r=0.50, r^2= 0.25. *p <0.05.

Post-Maximal Graded Exercise Test

Main effects of BMI and time were observed for cfPWV and MAP during the post-maximal graded exercise test (post-maximal GXT) period (p <0.05; Table 4.3), whereas significant interactions were noted for SBP, DBP, and PP (p <0.05; Table 4.3). SBP was greater in OV vs. H at 10, 20, 30, 45, and 60 minutes, and OB was greater vs. H at 2, 5, and 10 minutes post test (p <0.05; Figure 4.3). DBP was greater in OV compared with H at 30 minutes, and OV vs. OB at 2, 5, and 10 minutes; whereas OB was lower vs. H at 2 and 5 minutes (p <0.05; Figure 4.4). Pulse pressure (PP) was greater in OV vs. H at 5 minutes, OB vs. H at 2 and 5 minutes, and OV vs. OB at 2, 5, and 10 minutes (p <0.05; Figures 4.5). Figures 4.6 & 4.7 represent

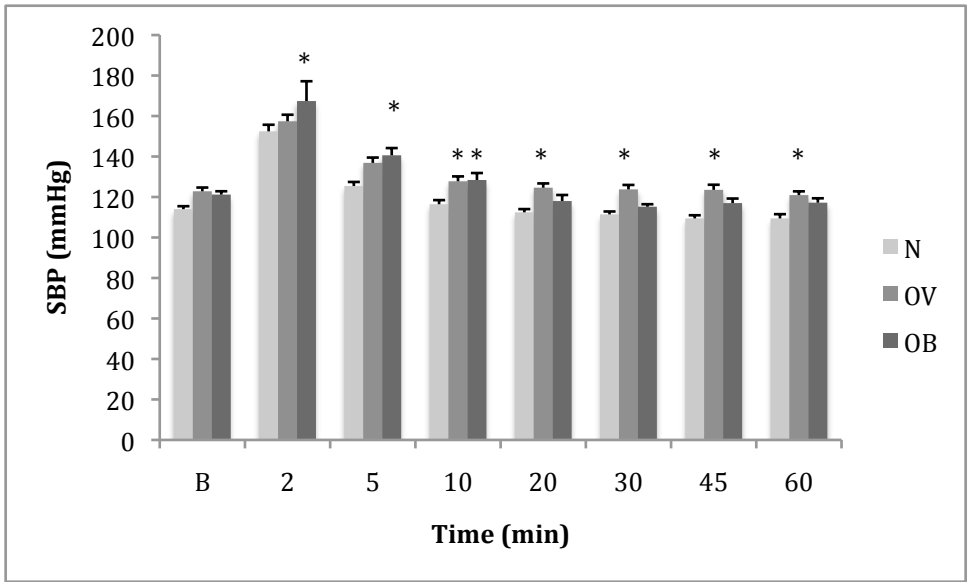
mean arterial pressure (MAP) and cfPWV post-maximal GXT. No interactions were found, but there were main effects of time and BMI ($p < 0.05$; Figures 4.6 & 4.7).

Table 4.3. Statistical Analysis for Post-Maximal Graded Exercise Test Hemodynamic Values by Body Mass Index (BMI) and Time.

Characteristic	BMI	Time	Interaction
SBP (mmHg)	0.0012*	<0.0001*	0.0201*
DBP (mmHg)	0.0378*	<0.0001*	0.0002*
PP (mmHg)	0.0142*	<0.0001*	<0.0001*
MAP (mmHg)	0.0043*	<0.0001*	0.0528
cfPWV (m/s)	0.0037*	0.0010*	0.1948

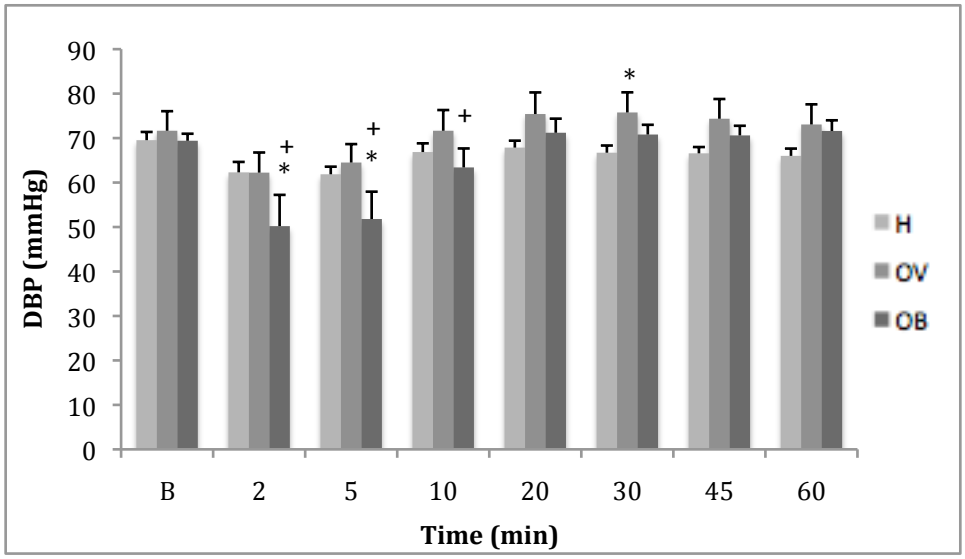
*p <0.05. Systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP), mean arterial pressure (MAP), carotid-femoral pulse wave velocity (cfPWV).

Figure 4.3. Post-Exercise Systolic Blood Pressure (SBP) Responses by Body Mass Index in 44 Male Subjects.



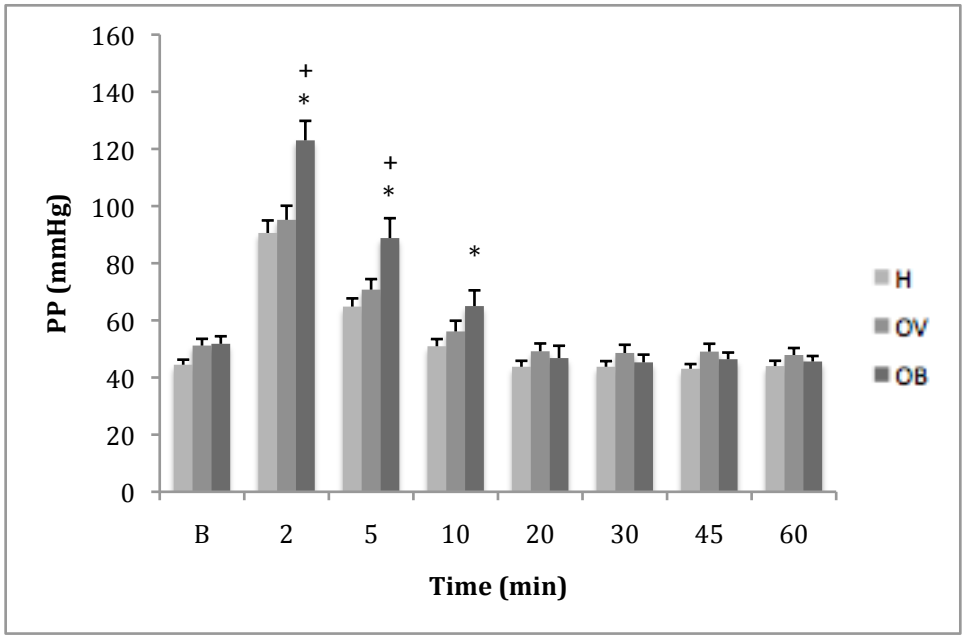
*p <0.05 N vs. OV or OB. Healthy (H), Overweight (OV), Obese (OB). Baseline (B).

Figure 4.4. Post-Exercise Diastolic Blood Pressure (DPB) Responses by BodyMass Index in 44 Male Subjects.



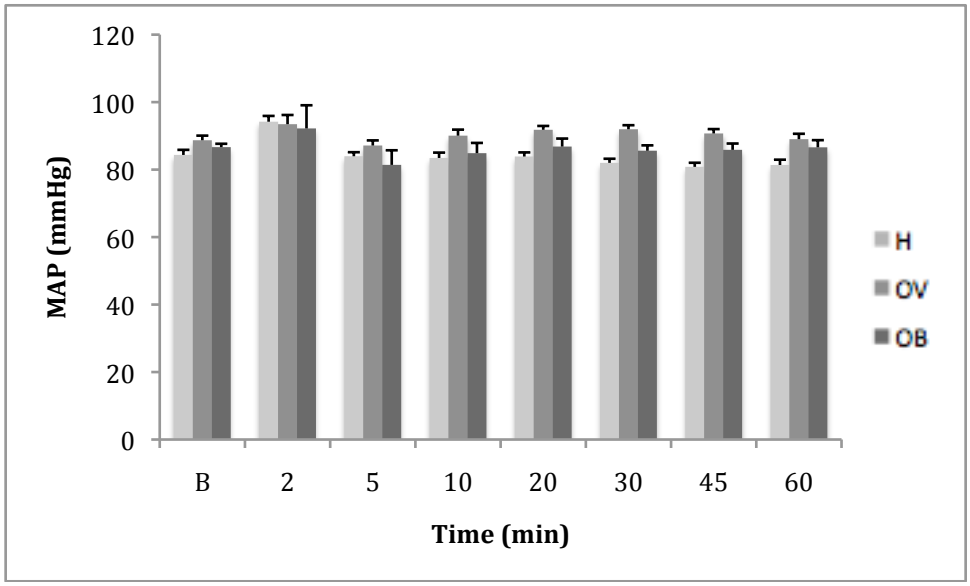
*p <0.05 N vs. OV or OB, +p < 0.05 OV vs. OB. Healthy (H), Overweight (OV), Obese (OB). Baseline (B).

Figure 4.5. Post-Exercise Pulse Pressure (PP) Responses by Body Mass Index in 44 Male Subjects.



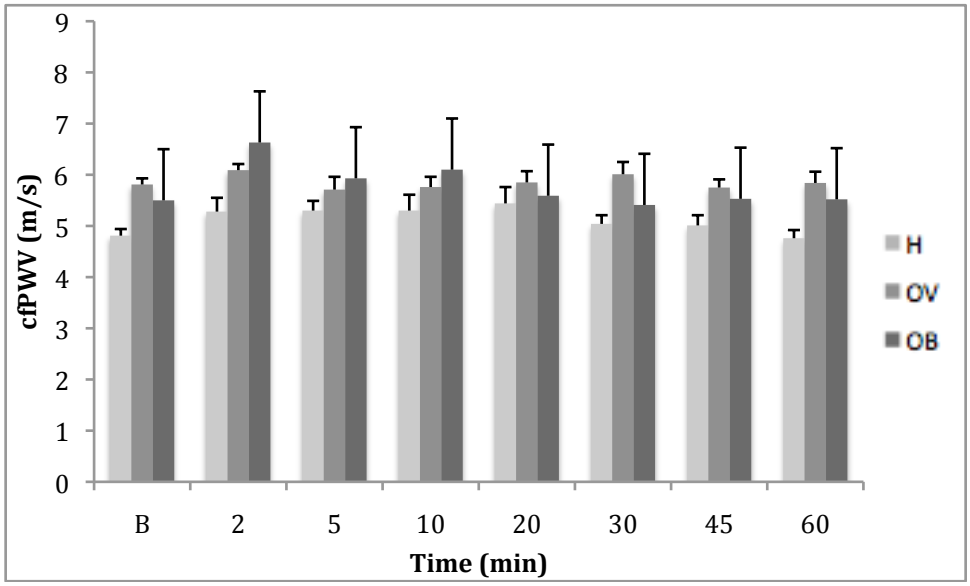
*p <0.05 N vs. OV or OB, +p < 0.05 OV vs. OB. Healthy (H), Overweight (OV), Obese (OB). Baseline (B).

Figure 4.6. Post-Exercise Mean Arterial Pressure (MAP) Responses by Body Mass Index (BMI) in 44 Male Subjects.



p <0.05, main effect of time and BMI all. Healthy (H), Overweight (OV), Obese (OB). Baseline (B).

Figure 4.7. Post-Exercise carotid-femoral Pulse Wave Velocity (cfPWV) Responses by Body Mass Index (BMI) in 44 Male Subjects.



p <0.05, main effect of time and BMI, all. Healthy (H), Overweight (OV), Obese (OB). Baseline (B).

CHAPTER FIVE: DISCUSSION

Major Findings

The major findings of this study were primarily post-maximal GXT, cfPWV was significantly different for BMI and time, however, no interaction was observed indicating all groups had a similar hemodynamic response to a max GXT. Secondary findings that demonstrate cfPWV is significantly related to SBP and VO_{2peak}: SBP was directly correlated with cfPWV, and $VO_{2\ peak}$ was inversely correlated with cfPWV in apparently healthy young men with varying adiposities. In addition, increases in BMI influences SBP, DBP, MAP, PP, and cfPWV directly, and VO_{2peak} inversely.

Systolic blood pressure and VO_{2peak} are the two variables that would best predict a higher cfPWV. There is a significant direct relation between SBP and cfPWV indicating a rise in SBP will increase cfPWV and stiffen arteries. This finding is similar to reports in mice (Weisbrod et al. 2013), and Caucasian and African-American men and women across the lifespan (Vaitkevicius et al. 1993, Franco et al. 2005, Laurent et al. 2006, Mitchell 2008, Fahs et al. 2009, Mitchell et al. 2010, Yan et al. 2014). Increased SBP is associated with greater arterial stiffening as assessed by cfPWV and is, in part, explained because cfPWV is a predictor of cardiovascular events (Doonan et al. 2011, Safar et al. 2013, Weisbrod et al. 2013). An increase in cfPWV, regardless of the cause, can result in an increase in SBP leading to hypertension, and an increase in SBP can lead to an increase in cfPWV (Doonan et al. 2011, Safar et al. 2013, Weisbrod et al. 2013).

We observed an inverse association between VO_{2peak} and cfPWV. These data indicate that a greater relative VO_{2peak} is associated with a lower cfPWV and arterial stiffness. This finding is supported by previous studies in healthy Caucasian and African-American men and women and in individuals with Type 2 Diabetes Mellitus who also demonstrate a higher VO_{2peak} capacity and a lower cfPWV (Seals et al. 2008, Loimaala et al. 2009, Yan et al. 2014). When there is an increase in relative VO_{2peak}, the cardiovascular system becomes more efficient. The heart's stroke volume increases, thus more blood is delivered with one cardiac cycle. This lowers heart rate and stress from the forward wave, decreasing cfPWV. Importantly, VO_{2peak} is also considered a predictor of cardiovascular events in younger and older adults, with and without disease, which may influence arterial stiffness and CVD risk (Vaitkevicius et al. 1993, Francis et al. 1999, Manson et al. 1999, Sutton-Tyrrell et al. 2005, Seyoum et al. 2006, Seals et al. 2008).

In contest, other studies have found differing results. However, instead of comparing cfPWV to VO_{2peak} at baseline based on BMI, these studies focused on the change in $VO_{2\ peak}$ vs. cfPWV after breif aerobic exercise training programs lasting 10 days to several weeks. VO_{2peak} measured before and after a short exercise program results in increases in VO_{2peak} with little to no change in cfPWV (Baynard et al. 2009, Asamoah et al. 2012, Kitzman et al. 2013). This could be explained, in part, due to the length of the exercise training programs. Chronic aerobic training programs have resulted in changes in VO_{2peak}, and cfPWV. Studies have shown habitual exercise can lower cfPWV in men and women across adulthood along with other

cardiovascular measures such as BP and PP (Vaitkevicius et al. 1993, Tanaka et al. 2000, Moreau et al. 2003, Kawano et al. 2006, Seals et al. 2008). It is suggested that the aerobic training will increase VO_{2peak}, followed by decreases in SBP, PP, and cfPWV in healthy adult men and women, as well as special populations such as those with Down Syndrome (Cardoso et al.2009. Hu et al. 2013, Safar et al. 2013, Weisbrod et al. 2013). In relation, with the present data and supporting previous data, fitness as measured by VO_{2peak} may be more influential on cfPWV than present body fat at a younger age, such as the subject population in this study (22.1 ± 0.48 years) (Corden et al. 2013).

Baseline Findings

BMI, BF%, SBP, WC, HC, $VO_{2peak,}$ and cfPWV were significantly different when comparing H vs. OV and OB at baseline. The only significant differences between OV and OB groups were BMI, WC, and HC. These changes can be explained due to the differences in BMI, as shown previously (Airaksinen et al. 1993, Franco et al. 2005, Sutton-Tyrrell et al. 2005, Orr et al. 2008, Fahs et al. 2009, Zebekakis et al. 2010, Shim et al. 2011, Corden et al. 2013, Kappus et al. 2014). Studies have shown that the higher the percentage of adipose tissue present, the higher the BP, WC, HC, and cfPWV (Franco et al. 2005, Fahs et al. 2009, Shim et al. 2011, Kappas et al. 2013). The lack in differences between OV and OB in SBP, BF%, and cfPWV could be explained due to no differences in VO_{2peak} as explained previously (Seals et al. 2008, Loimaala et al. 2009, Yan et al. 2014). VO_{2peak} has been identified as a predictor of

cardiovascular events as supported by previous studies observing young and old, men and women, with and without disease (Vaitkevicius et al. 1993, Francis et al. 1999, Manson et al. 1999, Sutton-Tyrrell et al. 2005, Seyoum et al. 2006). There is an inverse association between VO_{2peak} and cfPWV and SBP, as well as percent body fat in adult men and women of Caucasian and African-American ethnicities (Vaitkevicius et al. 1993, Franco et al. 2005, Laurent et al. 2006, Mitchell 2008, Fahs et al. 2009, Mitchell et al. 2010, Yan et al. 2014). Should there have been differences in VO_{2peak}, differences may have been seen in cfPWV, and SBP.

Although BMI, BF%, and WC were significant between H vs. OV and OB, these variables were not significant in terms of cfPWV. These results differ from previous publications in that the literature provides evidence that BMI and BF% are significant predictors of cfPWV, because an increase in excess weight has previously shown to increase cfPWV (Orr et al. 2008, Fahs et al. 2009, Zebekakis et al. 2010, Shim et al. 2011, Corden et al. 2013, Kappus et al. 2014). This could be explained due to the subjects that participated in the study. The population was physically active as shown by an above average relative VO_{2peak} for all groups.

Post-Maximal Graded Exercise Test Findings

The post-maximal GXT data indicate there is no differential response in cfPWV between the healthy weight, overweight and obese groups. However, cfPWV had a main effect of time and BMI, all BMI groups averaged, and time points averaged, meaning that overall, H, OV, and OB groups had significantly different

cfPWVs. A lack in interaction could be explained due to the average age of the study participants (22.1 ± 0.48 years). It has recently been suggested by an investigation that studied adult women ages 18-72 years that arterial stiffness is largely unaffected by percent body fat until middle age (Corden et al. 2013). A potential explanation to this phenomenon is that adipose tissue may not have an immediate effect on the vascular system, but it is an adverse event that occurs over time (Corden et al. 2013).

Post-maximal GXT, notable interactions were observed for SBP, DBP, and PP at various time points between groups. Differences in time and BMI were present in MAP, similar to that of cfPWV, with no interactions.

Changes in MAP can be explained due to the differences in SBP and DBP between groups. Initially, there were no differences in MAP, which can be explained by the initial responses in SBP and DBP. SBP increased from baseline, and DBP decreased from baseline. There have been few studies that have looked into the response of DBP, specifically. Following exercise, it is normal for diastolic blood pressure to decrease, however, there is little evidence to suggest DBP decreases more significantly in obese adults versus overweight and/or healthy weight groups (Brett et al. 2000, Cardoso et al. 2009, Rakobowchuk et al. 2009, Kappus et al. 2014). Since MAP is the average arterial pressure during a cardiac cycle, it explains how the average would not be different over the first time points. Beginning at the 10-minute time point, both SBP and DBP begin to return to baseline. Due to the significant differences found at baseline between SBP and DBP, it can explain the

differences in MAP. However, what is not explained by this logic is that there are no differences between H and OV nor H and OB. Looking at the data post-exercise SBP and DBP remain lower in OB vs. OV from 10 minutes to 60 minutes, resulting in a lower MAP. As cfPWV, this could also be a result of cardiovascular fitness. While, on average, the OB group had a lower VO_{2peak}, but the difference was insignificant.

Systolic blood pressure and PP are positively correlated with exercise intensity (Rakobowchuk et al. 2009). This explains the initial response to exercise. Increases in SBP are evident in all groups and eventually return to baseline by approximately 20 minutes post-maximal GXT, as supported by previous studies (Rakobowchuk et al. 2009, Collier et al. 2010). Post-exercise hypotension was shown in these studies as BP and PP continue to decrease approximately 8% below baseline up to 60 minutes post-exercise, which relate to the present study (Rakobowchuk et al. 2009, Collier et al. 2010). For SBP, H was significantly lower vs. OB at 2, 5, and 10 minutes, while H was significantly lower vs. OV at 10, 20, 45, and 60 minutes post-maximal GXT.

DBP was significantly higher at 2 and 5 minutes for N vs. OB, 2, 5, and 10 minutes for OV vs. OB, and finally, significantly lower at 30 minutes for H vs. OV. Normal blood pressure response to exercise is not just for SBP to increase, but DBP to decrease initially (Cardoso et al.2009), and is the trend that was observed in this study. Subjects followed a similar trend to SBP in this category in that the obese group did not have as great of a response as the overweight group. This could be due to the large variability within the obese group.

PP is the difference between SBP and DBP, which can explain why there were significant differences only in the first 10 minutes post-maximal GXT. Differences were seen in H vs. OB at 2 and 10 minutes, H vs. OV at 5 minutes, and OV vs. OB at 2 and 5 minutes. This can be explained from the SBP and DBP responses. Initially, significant changes were observed in these measurements until approximately 20 minutes post-maximal GXT, where these values returned to baseline. For these measurements, SBP, DBP, and PP, did have a significant reaction overtime denoting each BMI group responded differently overtime. These responses could be explained again because of VO_{2peak} and cardiovascular fitness of the groups, as previous literature has described (Cardoso et al. 2009, Fahs et al. 2009, Shim et al. 2011). In addition, the data was not analyzed by ethnicity. A recent study has shown differences in cfPWV and other cardiovascular measurements based on ethnicity, which could help explain differences post-maximal GXT (Yan et al. 2014).

Supporting the hypothesis, higher BMI is associated with greater resting cfPWV, SBP, DBP, MAP, and PP, and a lower VO_{2max}. It was hypothesized that the greater the BMI, the greater the response to exercise in cfPWV, SBP, DBP, PP, and MAP. These measurements initially responded as hypothesized in that the higher the BMI, the greater the response to the exercise for SBP, DBP, PP, and cfPWV. The OB group experienced the greatest responses to the max GXT in SBP, DBP, PP, and cfPWV followed by OV, and finally H. However, the time for the cardiovascular hemodynamics to return to resting values was not different between groups.

CHAPTER SIX: CONCLUSIONS

In conclusion, the major findings of this study demonstrate SBP has a significant direct correlation on cfPWV, and VO_{2peak} has a significant inverse correlation on cfPWV. This indicates that the greater SBP, the greater arterial stiffness, and higher VO_{2peak}, the lesser the arterial stiffness. At baseline, the higher the BMI, the higher SBP, DBP, MAP, PP, and cfPWV, and the greater the BMI, the lower the $VO_{2peak.}$ Post-maximal GXT, while significant differences were observed between BMI and time, no interaction between groups overtime was found in cfPWV. This indicates that while there were significant differences between groups in relation to cfPWV, all groups had a similar hemodynamic response to a max GXT.

This study had a number of limitations that could have influenced the results. First, the subjects were recruited by flyer, and volunteers participated who met inclusion criteria making it a convenience sample. The subjects were above average when compared to normative values in terms of cardiovascular fitness based off of VO_{2peak}, which could have influenced the outcomes. In addition, this study was approved to include subjects with only one cardiovascular risk factor. This could explain responses in blood pressure, and thus, cfPWV, because if a subject was obese, he was considered to already possess one cardiovascular risk factor, and could not be used in the study if he had any additional risk factors, including elevated blood pressure. Due to the equipment available, subjects weighing over 113.40kg were excluded because the scale used to weigh each subject had this

weight limit. This could provide another possible explanation for the outcomes. Thus, further research is suggested to observe the changes in arterial function in H, OV, and OB groups following a maximum treadmill exercise test.

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VITA

EDUCATIONAL INSTITUTIONS ATTENDED AND DEGREES AWAREDED

Miami University	Bachelor of Science (2011) Exercise Science and Health Promotion Minor: Sociology

PROFESSIONAL APPOINTMENT

2012-2014	Graduate Teaching Assistant: University of Kentucky, Department of Kinesiology and Health Promotion, Lexington, Kentucky
2013-2014	Personal Trainer and Fitness Instructor: FIT Lexington, Lexington, Kentucky
2013-2014	Trainer: Title Boxing Club, Lexington, Kentucky
2014	Exercise Physiology Intern: University of Kentucky Healthcare, Cardiopulmonary Rehabilitation, Lexington, Kentucky
2013	Physical Therapy Intern: St. Joseph's Hospital, Outpatient Physical Therapy, Lexington, Kentucky
2013	Exercise Physiology Intern: Baptist Health Lexington, Cardiac Rehabilitation, Lexington, Kentucky
2012	Sales Recruiter: Total Quality Logistics, Cincinnati, Ohio
2011-2012	Corporate Recruiter: Reynolds and Reynolds, Dayton, Ohio
2011	After School Activities Leader: Stewart Elementary School, Cincinnati Public Schools, Cincinnati, Ohio
2009	Group Activities Leader: Healthworks!, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

ACADEMIC AWARDS

2012-2014	Teaching Assistantship and full scholarship: University of Kentucky, Department of Kinesiology and Health Promotion, Lexington, Kentucky
2010	Service Leadership Award: Miami University, Oxford, Ohio

TEACHING EXPERIENCE

2012-2014	Graduate Teaching Assistant: University of Kentucky, Department of Kinesiology and Health Promotion, Lexington, Kentucky
2013-2014	Personal Trainer and Fitness Instructor: FIT Lexington, Lexington, Kentucky
2013-2014	Trainer: Title Boxing Club, Lexington, Kentucky
2011	After School Activities Leader: Stewart Elementary School, Cincinnati Public Schools, Cincinnati, Ohio
2009	Group Activities Leader: Healthworks!, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

RESEARCH EXPERIENCE

2013-2014	Graduate Thesis: University of Kentucky, Department of Kinesiology and Health Promotion, Lexington, Kentucky—Acute Exercise and Arterial Function Based on Body Composition (Title; Effect of Body Mass Index on Post-Exercise Hemodynamic Responses)
2012-2013	Laboratory Assistant: University of Kentucky, Department of Kinesiology and Health Promotion, Cardiovascular Physiology Laboratory, Lexington, Kentucky

CERTIFICATIONS

- American Red Cross Adult/Child CPR/AED and First Aid Certification Issued November 2012
- CITI Human Research Certified, University of Kentucky Issued 2013