Cardiff School of Sport

DISSERTATION ASSESSMENT PROFORMA:

Empirical [1]

Student name:	Sian Carrick		
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Dissertation title:	Can vascular structure and function change by altering brachial artery blood flow using an external pressure cuff pulsation technique		
Supervisor:	Professor Rob Shave		

Comments	Section
	Title and Abstract Title to include: A concise indication of the research question/problem. Abstract to include: A concise summary of the empirical study undertaken.
	Introduction and literature review To include: outline of context (theoretical/conceptual/applied) for the question; analysis of findings of previous related research including gaps in the literature and relevant contributions; logical flow to, and clear presentation of the research problem/ question; an indication of any research expectations, (i.e., hypotheses if applicable).
	Methods and Research Design To include: details of the research design and justification for the methods applied; participant details; comprehensive replicable protocol.
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	Discussion and Conclusions [2] To include: collation of information and ideas and evaluation of those ideas relative to the extant literature/concept/theory and research question/problem; adoption of a personal position on the study by linking and combining different elements of the data reported; discussion of the real-life impact of your research findings for coaches and/or practitioners (i.e. practical implications); discussion of the limitations and a critical reflection of the approach/process adopted; and indication of potential improvements and future developments building on the study; and a conclusion which summarises the relationship between the research question and the major findings.
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CARDIFF SCHOOL OF SPORT

DEGREE OF BACHELOR OF SCIENCE (HONOURS)

SPORT AND EXERCISE SCIENCE

CAN VASCULAR STRUCTURE AND FUNCTION CHANGE BY ALTERING BRACHIAL ARTERY BLOOD FLOW USING AN EXTERNAL PRESSURE CUFF PULSATION TECHNIQUE

PHYSIOLOGY AND HEALTH

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CAN VASCULAR STRUCTURE AND FUNCTION CHANGE BY ALTERING BRACHIAL ARTERY BLOOD FLOW USING AN EXTERNAL PRESSURE CUFF PULSATION TECHNIQUE

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I would like to thank the Cardiff Metropolitan Technicians who helped with data collection. This included Jane Black, who collected all FMD data.

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ABSTRACT

Purpose: There are numerous contributors that cause changes to vascular structure and function, most revolve around exercise. A major determinant of vascular change is shear stress, which is influenced by the amount of force placed on the artery. An external cuff pulsation intervention will attempt to regulate blood flow and alter shear stress; this will clarify whether blood flow changes acute vascular structure and function. If proven, additional rehabilitation processes for individuals suffering from angina or vascular damage may be benefited.

Method: Physically active males volunteered as participants. A non-invasive method of Flow-Mediated Dilation was used to assess the vascular adaptations before and after a 5-minute cuff pulsation intervention at 60% of their systolic blood pressure.

Results: A significant difference was found when comparing time to peak arterial dilation (TTPAD) before and after the intervention (86.7 $\pm$ 16.0 sec; 107.95 $\pm$ 36.3 sec, respectfully). There were slight changes found in other variables such as delta diameter, shear rate and arterial diameter, however, no significant difference was identified. Moreover, blood pressure remained relatively constant throughout the whole procedure.

Conclusion: The results show that a cuff pulsation intervention increases TTPAD significantly, but has little acute effect on vascular response in other variables. This may be due to the extent that the cuff stresses the artery. In addition, the availability of Nitric Oxide, the mediator of vascular dilation may also play a role in the vasodilation of an artery, as the stimulus to release Nitric Oxide is too little to make an effect and causes an increase TTPAD. Greater external pressure may therefore result in significantly different acute adaptations.

Key Words: Shear Stress, Flow-mediated Dilation, Nitric Oxide, Acute Vascular response, Cuff Pulsations.

CHAPTER ONE

INTRODUCTION

1.0. INTRODUCTION

The cardiovascular system is an essential component of the human body. It holds two main responsibilities; distribution and exchange. Blood distributes Oxygen (O_2), amino acids, fatty acids and water to the working tissues (Levick et al., 2010:3) this increases in response to exercise, where the demand for O_2 is greater (Evans, 1985). Waste products such as carbon dioxide are removed and exchanged via the circulatory system (Klabunde,. 2005:92). Vascular structure is an important component to an individual's health, and becomes stiff with age as the artery loses its elasticity (Ferrari et al., 2003). Therefore, vascular structure and function is often used as an indicator of peripheral vascular disease, and is identified by the thickness of the intima-media (Cheng et al., 2002). The brachial artery is the main artery located in the upper arm and is made up of connective tissue and smooth muscle (Mcardle et al., 2010:334). Forces generated by exercise are therefore compensated through vascular adaptations (Tschakovsky et al., 2003).

During exercise, it has been established that vascular structure and function change (Tschakovsky et al., 2003). Acute responses found during exercise compensate for the additional demands placed on the artery. Acute adaptations found with exercise will bring about chronic arterial adaptations with an exercise intervention over a period of time. Acute change to the vascular system include the increase in blood pressure (BP) and heart rate (HR), both of which alter the structure of a vessel by stressing the vessel wall (Tschakovsky et al., 2003). The increase in blood flow causes a frictional force on the endothelial cells which results in arterial vasodilation (Pohl et al. 1986). Vasodilation of the artery leads to the synthesis of Nitric Oxide (NO), which increases blood flow turbulence and velocity (Gurovich and Braith., 2012). Exercise causes numerous adaptations to the human body. These adaptations include

hypertrophy of skeletal muscle, and increase in mitochondrial density (Thom, 1997). A variety of training modalities affect the structure of an artery; for example, endurance trained individuals have a greater lumen and smaller arterial wall compared to un-trained individual (Green et al., 2012), a greater lumen diameter allows for a greater blood flow to working muscles. Research has stated that flow-mediated dilation (FMD) response will change after an exercise regime (Pullin et al., 2004). FMD is therefore an indicator to an individual's vascular health, and is described as the vasodilatory response of an artery after increased luminal blood flow following complete blood flow occlusion (Thijssen et al., 2010).

Blood vessels are exposed to hemodynamic forces such as shear stress. This is often initiated from changes in blood flow (Li et al., 2004). Shear stress is the stimulus for arterial dilation and is stimulated by the frictional force placed on the endothelium when blood flow increases during exercise (Rooks et al., 2011). Increased shear force is found during different modes of exercise; for example vasculature of an artery is affected by shear rate which is influenced by rhythmic exercise (Thijssen et al., 2009) and acute exercise causes increases in shear stress (Rooks et al., 2011). Shear stress is often identified by FMD because of the endothelia's reaction to increased blood flow. Manipulating shear stress may therefore cause additional arterial adaptations.

The change in vascular structure and function during exercise is partially caused by the increased demand for energy in the working muscles (Wilmore et al., 2008:111). Blood flow increases in proportion to the level of exercise being performed. Metabolic contributors found during exercise influence the vascular properties of an artery. This suggests that metabolism may have a role in the regulation of acute vascular adaptations due to its role in regulating adenosine and NO (Barclay et al., 2001). It has been suggested that the linear relationship between blood flow and metabolic rate,

contribute to acute vascular adaptations (Barclay et al., 2001). Increasing blood flow may therefore cause an enlarged arterial cross sectional area resulting in acute arterial adaptations following an intervention (Green et al., 2002). In addition, there is a time delay between exercise and vasodilatory response when vadsoactive substances diffuse from skeletal muscle to smooth muscle. This time delay suggests that there are additional factors which cause the sudden dilation of an artery (Clifford, 2007).

Finally, it has been noted that an external pressure as low as 25 mmHg show slight increases in BP, and approximately 20% change in vasodilatation of an artery (Kirby et al., 2007). This suggests that arterial structure and function change without exercise. In a previous study arterial diameter increased in response to an intervention (Rooks et al., 2011), suggesting that a cuff pulsation (CP) may have similar result to exercise as there is still force placed on the artery. An inflation cuff may therefore have the ability to mimic blood flow and isolate the mechanical muscular contraction; this causes an increase in HR, BP and body temperature (Shoemaker et al., 1997). Changes in HR and BP suggest that there are numerous contributors that cause alterations to the structure and function of an artery. However, the extent to which these adaptations occur is unknown. Manipulating shear stress may therefore bring about similar adaptations found with exercise with an external compression sequence. Although long term external compressions failed to significantly improve transport capacity in humans, it is suggested that externally applied pressures are still transmitted to the tissue (Roseguini et al., 2010). These external pressures may influence acute vascular structure and function of an artery after a single external compression sequence.

CHAPTER TWO

LITERATURE REVIEW

2.0. LITERATURE REVIEW

2.1. The Structure and Function of an Artery

The cardiovascular system is responsible for the distribution of many essential nutrients and hormones as well as oxygen (O_2) delivery to working muscles (McArdle, Katch and Katch, 2010:460). The exchange of gasses, fluids and electrolytes around the human body help maintain homeostasis (Klabunde, 2005:95). In addition to exchanging gasses, the heart, a myogenic muscular organ, controls both the distribution of hormones and bodily temperature (Levink, 2010:3). The cardiovascular system consists of continuous pumps, high pressure vessel circuits, exchange vessels and low pressure collection (McArdle, Katch and Katch, 2010:304). The brachial artery is one of the main blood vessels located in the upper arm, before splitting at the cubital fossa found at the elbow. Regular exercise causes numerous adaptations to the human body. In response to exercise, physiological adaptations are found. These are dependent on the exercise intensity, modality, frequency and duration (Green et al., 2010). Exercise adaptations include the increase in mitochondrial density and improved respiratory capacity of muscle fibres (Holloszy and Coyle., 1984).

The structure of an artery (Figure 1) is made up of connective tissue layers and smooth muscle, which has vasodilatory responses (McArdle, Katch and Katch, 2010:304), and mechanical properties of elastin (Alkiviadis and Nikos., 2009). Ultrasound techniques provide non-invasive methods of analysing an artery's structure and function (Magagnin et al., 2007). The artery's structure consists of three connective tissue layers: the intima, a single layer of endothelial cells, which secrete vasoactive chemicals such as nitric oxide (NO); the Media, which is a series of smooth muscle cells, causing increased mechanical strength and contractile power; finally the adventitia, which binds to surrounding tissue (Levick, 2010:10).

According to Levick (2010:12), from these layers the average diameter of an artery is 0.1-1.0 cm, depending on the artery identified and trained status of the individual. At rest, the brachial artery diameter is usually around 4.2 mm, but increases from baseline after 2 minutes of fast exercise (Shoemaker et al., 1997).

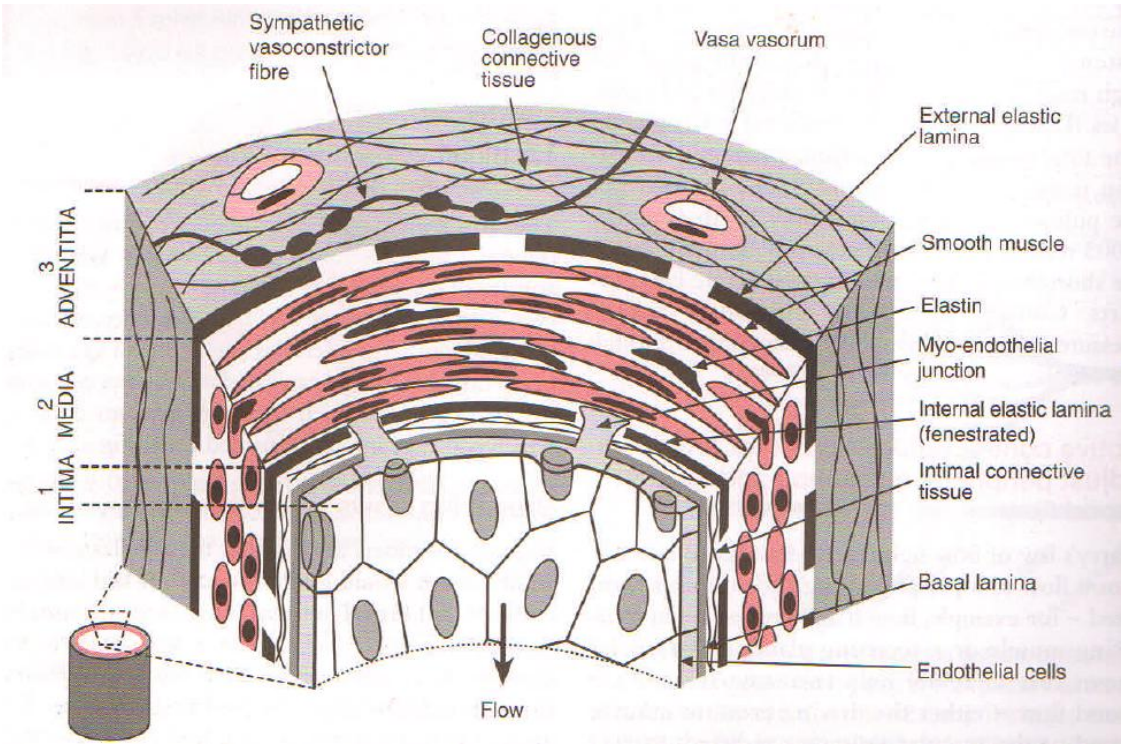

Figure 1. Structure of an artery (Levick, 2010:10)

2.2. The Effect Exercise has on Vascular Structure and Function

Exercise causes a change in blood flow, which alters the structure of a vessel. Hypertension occurs within the vascular system; this involves the thickening of arterial walls, the remodelling of small muscular arteries, and increasing the wall to lumen ratio (Thom, 1997). Blood vessel structure and function influences resting blood flow and blood flow increases in proportion to the level of exercise being performed (Green et al., 2002). This increase may be due to the dilation capacity in arterial cross sectional area (Green et al., 2002), which is influenced by turbulence and blood flow velocity

(Gurovich and Braith 2012). Greater arterial compliance can therefore be seen during high intensity exercise (Fahs et al., 2011). The increased demand for O_2 during exercise places stress on the cardiovascular system, this stimulates the increase in blood flow and the vasodilatory mechanism (Tschakovsky et al., 2003).

An arteries response to exercise is dependent upon the form of exercise, work rate and limb positioning (Kjellmer, 2008). Work rate can be determined by the rate at which a muscle contracts, meaning the degree of dilation is related to the severity of the exercise (Kjellmer, 2008). The faster the rate of contraction the greater the change in local arterial diameter, this suggests that slow contractions fail to influence arterial diameter (Shoemaker et al., 1997).

Trained athletes are often the subjects of arterial remodelling, as they have a greater capacity for blood transportation, compared to the average sedentary individual (Rognmo et al., 2008). Karagounis et al. (2009) supported this, and stated that an untrained group of individuals have a higher mean blood flow velocity and diastolic arterial diameter, than a trained group of judo athletes. Adaptations with regard to endurance training have been well established, and show changes when looking at arterial remodelling. These changes in arterial blood flow are also seen in the femoral artery during lower limb exercises (Dinenno et al. 2001). Although endurance exercises change arterial blood flow, resistance training has less of an effect (Thijssen et al., 2009). When looking at vascular adaptations beneficial results regarding muscular strength and muscle function have been identified (Gordon et al., 2004). Improvement in muscular function indicates that resistance training may have a greater affect on vascular structure and function than what was initially suggested. Resistance trained individuals fail to show differences in flow-mediated dilation (FMD) response, suggesting that arterial structure is not influenced in resistance trained individuals (Rakobowchuk et al., 2005), but may be affected by an acute exercise stimulus.

Although exercise has the ability to alter vascular structure and function, an external stimulus initiated from cuff occlusion may have similar results. Increased blood flow found during exercise can be initiated from an increase in HR (Saltin et al., 1998); however, HR can be influenced from a stimulus independent from exercise. The increase in blood flow allows for greater O_2 transportation. Increased blood flow may therefore be a contributor to the vasodilatory responses found by the vessel (Tschakovsky et al., 2003). During rest, BP can also be increased by an external compression treatment (Thomas et al., 2002), which implies exercise is not the only stimulus that initiates changes in vascular structure and function.

2.3. Blood Pressure changes during Exercise

According to the American College of Sports Medicine's (ACSM) guidelines BP should be 120/80 mmHg (Kaminsky, 2010:35). These values are associated with individuals who are physically active. Exercise is therefore a major factor that influences BP (Guyenet, 2006). For example, exercise induced changes in endothelial function are affected by BP, and are stimulated by dynamic muscular contractions with high contractile activity (Gonzales et al., 2010). The vascular properties found in trained athletes may be the product of chronic vascular adaptations. This suggests that a decrease in BP may result in a change in vascular structure and function; signifying a change in BP during exercise may influence vascular structure (Green et al., 2012). This gives reason to suggest that BP can also change independent of exercise and have a role in regulating vascular structure and function.

2.4.1. Regulation of Vascular Structure and Function

During exercise, the demand for O_2 is greater, which creates an increase in luminal blood flow, changing the structure of the artery (Tschakovsky et al., 2003). These changes cause vasodilatory responses, suggesting that variations in blood flow may influence vascular structure and function (Tschakovsky et al., 2003). The increase in luminal blood flow places greater frictional force on the endothelium layer of an artery (Pohl et al., 1986), this frictional force causes the release of NO derived from adventitial induced NO synthase (Wang et al., 2009).

There are numerous theories that cause the increased production of NO, most revolve around exercise. It has been established that during exercise the release of NO from the endothelium causes the smooth muscle surrounding the vessel to relax, but reduces with high O_2 demand (Wang et al., 2009). Green et al. (2004) however, proposed that NO production may be responsible for the increased demand for O_2. The adventitia is a major producer of vascular reactive O_2 species, and plays a role in regulating hypertension as well as vascular remodelling. The release of sodium nitroprussid affects the adventitia, which mediates the vasodilatory response (Wang et al., 2009). The synthesis of NO is highest in the adventitia, causing the vascular regulatory unit to expand (Barclay et al., 2001), the increased production of NO during exercise causes improved local endothelium-dependent vasodilation in noromotensives (McGowan et al., 2006), and helps regulate BP (Rees, et al. 1989). In addition, the adventitia plays a role in regulating hypertension and vascular remodelling during exercise. Adventitia is the main source of vasoactive hormones and regulates vascular structure and function via autocrine or paracrine signalling mechanisms (Wang et al., 2009). Controversially, the higher demand for O_2 in the working muscles during exercise inactivates NO (Wang et al., 2009), which causes implications to smooth muscle relaxation.

NO inactivation suggests that exercise may have both detrimental and positive effects regarding the release of NO and smooth muscle relaxation.

The debate as to whether NO increases with different modalities of exercise; allowed Maeda et al. (2006) to suggest that resistance training not only increases muscular power by 16%, but also increases the concentration of NO in the plasma. Localised exercise with reference to hand-grip studies fail to influence endothelial function, but demonstrates an increase in peak blood flow; this may be due to the muscle mass recruited and the failure to induce NO (Green et al., 2004). Controversially, metabolic factors that increase in exercising muscles do not affect muscle blood flow, indicating that the vaso-regulatory mechanism found during exercise is due to multiple factors working in conjunction (Tschakovsky and Joyner, 2008). It is suggested that NO is one of these factors and is responsible for the increase in muscle blood flow to an extent (Tschakovsky and Joyner, 2008). The controversial evidence associated with NO availability with increased O_2 demands, this gives reason to suggest that an external CP intervention may further influence the artery to relax, as there is no additional demand for O_2.

2.4.2. Metabolic Contributors affecting the Brachial Artery's Structure and Function

Adaptations are often found in individuals who train regularly; these adaptations can be either acute or chronic. Acute responses are found immediately after an acute intervention, whilst chronic adaptations appear over a prolonged duration. The time taken to return to baseline determines whether these adaptations are acute or chronic. The return to baseline $\geq$60 min after exercise, suggests that the changes are due to chronic effects of day to day resistance training (DeVan et al., 2005), rather than acute changes found during exercise. Acute adaptations found with exercise include changes to

the cardiovascular system; such as the increase in HR and change in BP, these changes alter blood flow and arterial diameter (Tschakovsky et al., 2003) by a function known as shear stress (Carter et al., 2012). This suggests there are many possible metabolic contributors that cause changes in vascular structure and function.

2.4.3. Acute Metabolic Factors during Muscular Contraction that affect Vascular Structure and Function

Metabolism may have a role in regulating the structure and function of a vessel, due to the role of adenosine, NO, arachidonic acid metabolites and endothelial-derived hyperpolarising factors released from the vessels cell wall. In addition, an increase in core temperature found during exercise may regulate vascular structure, as a $\leq$6 ºC increase in temperature changes vascular blood flow (Ooue et al., 2007). Repeated heating therefore causes blood flow levels to increase, leading to greater endothelium-mediated vasodilatory function in humans (Naylor et al., 2011).

The time delay in changing vascular structure during fast contractions, suggests that a vasodilatory signalling mechanism that originates from skeletal muscle contraction, may be responsible for the partial change in vascular structure during exercise (Shoemaker et al., 1997). The time delay for vasoactive substances to diffuse from the skeletal muscle pump to vascular smooth muscle, makes metabolic vasodilatation a bad explanation for the increase in muscle blood flow (Clifford, 2007). It has been stated that during the onset of exercise, there is no neural component initiating the vasodilatory response of an artery, as the vessels remains unaltered for the initial 5 seconds of exercise (Buckwalter and Clifford, 1999). Similar findings were found in rats, where additional vasodilator substances and muscle fibre activity were not the only factors responsible for the change in blood flow (Armstrong et al., 1985). The time taken to

achieve peak arterial diameter (TTPAD) can be determined using FMD and is dependent on the cuff positioning. Brachial artery diameter should be measured continuously between 30 and 70 seconds post deflation to detect maximal dilation values (Arrowood et al., 1998). Berry et al. (2000) observed FMD results under different cuff placements, and concluded that upper arm occlusion was greatest 70-80 seconds after release, were as forearm occlusion was greatest 40-60 seconds (Figure 2). In order to quantify these results the time frame should be the same, suggesting that the accuracy of these results are unsatisfactory.

Distinguishing the period of time that vascular adaptations appear will provide a basis for future training methods. It has previously been established by Kjellmer (2008) that muscular contraction is accompanied by the increase in blood flow, and is determined by the frequency that muscular contractions occur. There is a linear relationship between blood flow and metabolic rate (Barclay et al., 2001), indicating that blood flow is regulated by metabolic contributors. A change in blood flow causes the vascular beds to dilate, increasing muscle blood flow (Barclay et al., 2001). An increase in metabolic rate causes vasodilation in the vascular network. Metabolic contributors are only considered to have an effect on the vasodilatory response to changing blood flow during high metabolic rates, initiated from muscle contractions (Barclay et al., 2001). The replacement of muscular contractions with an external stimulus such as a compression sequence may alter blood flow, and in turn alter vascular structure and function.

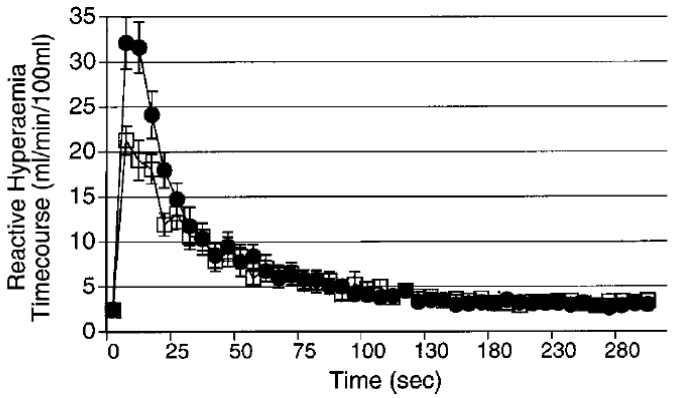

Figure 2. FMD response with increased blood flow, demonstrating the time delay to peak dilation with different cuff placements (Berry et al., 2000)

2.5.1. Flow-mediated Dilation shows changes in Vascular Structure and Function after an acute Intervention

To determine the changes in vascular structure and function FMD is often used. FMD increases in response to an exercise intervention (Rooks et al., 2011), and is described as the vasodilatory response of an artery after an increase in luminal blood flow (Thijssen et al., 2010) (Figure 3). FMD improves progressively, rapidly and reversibly (Pullin et al., 2004) after an acute bout of aerobic exercise (Zhu et al., 2010), which includes the increase in blood velocity and viscosity from baseline (Naka et al., 2003). The percentage change from baseline to maximal vascular dilation after increased blood flow and NO provides an indicator to the acute changes that have occurred in response to exercise (Green et al., 2005). Shear stress influences the endothelial response to NO release and is the mediator for FMD results (Pohl et al., 1985). It has been established that the release of NO is the mechanism behind the change in blood flow during an FMD (Green et al., 2005), which highlights vascular dilation.

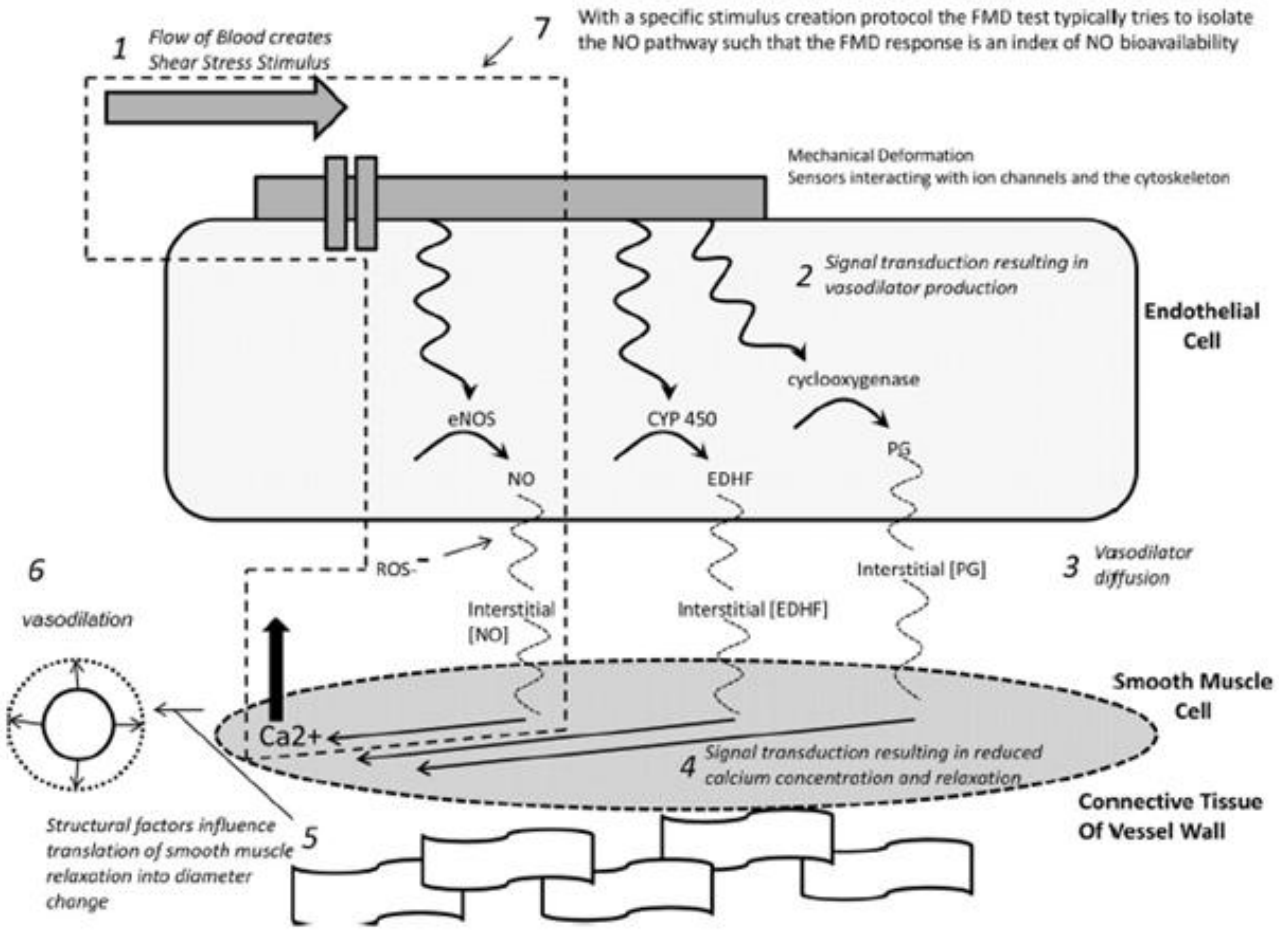

Figure 3. A representation of the main steps involved in an FMD initiating from the shear stress stimulus (step 1) to the vessel diameter change (step 6). Shear stress mechanism activates a signalling mechanism that activates a vasodilatory response, which must diffuse from the endothelial cells to the smooth muscle to trigger a response. (Thijssen et al., 2010)

2.5.2. FMD values change with an Exercise Intervention.

Results clarified by Rooks et al. (2011) suggested that before the intervention arterial diameter decreased in response to the cuff occlusion (3.39 – 3.36 mm), however after the exercise intervention arterial diameter increased (3.47 - 3.5 mm). Similarly arterial velocity and blood flow before cuff occlusion decreased from baseline (21.42 – 10.07 cm/s: 118.04 – 56.85 $ml.min^{1}$), but increased after the exercise intervention (17.78 – 32.54 cm/s: 101.58 – 190.62 $ml.min^{1}$).

The increase in blood flow found during muscular contraction such as hand-grip (Shoemaker et al., 1997) cause an increase in blood flow velocity (Barclay et al., 2001). Whilst blood flow helps maintain PB in exercising muscles (Saltin et al., 1998), the change in blood flow is related to the change in arterial BP (Savin et al. 1997). Due to the changes in arterial diameter found with exercise, it is thought that a CP intervention may bring about similar results.

2.6. Shear Stress is a major contributor that changes Vascular Structure and Function in the Brachial Artery

Shear rate is the force placed on the artery over time, and has implications to the vasodilatory response during different modes of exercise (Carter et al., 2012). Shear stress increases in response to shear rate and fluid viscosity (Levick, 2010:119). Therefore, vascular shear stress is maintained by a autoregulatory mechanism, which causes acute constriction or dilation in the artery, leading to chronic changes in the calibre of an artery (Kamiya et al., 1980). Different shear forces are found in a range of exercises; for example, rhythmic exercises result in increased shear rate patterns (Thijssen et al., 2009). As previously mentioned, FMD results increase after exercise; the increase in shear stress, stresses' the endothelium which improves FMD response (Rooks et al., 2011). The dilation of an artery during exercise facilitates flow conductance and decreases shear stress placed on the endothelium (Shoemaker et al., 1997) resulting in acute changes in arterial structure.

When assessing shear rate, previous studies have suggested that blood flow initiates complex signals that originate from shear forces, which causes an increase in vasodilatory response and production of NO in the endothelium layer of an artery (Jenkins et al., 2012). In addition work by Gnasso et al. (2000) stated that wall shear stress is significantly associated with FMD, and provides the mediator to regulate vessel diameter in response to metabolic factors

associated with exercise. Shear stress however, cannot be the only stimulus that causes changes in arterial diameter after cuff occlusion. It was therefore proposed by Folkow (1978) that changes in arterial structure and function produce a vasomotor response, which causes a variety of vasoactive agents to work in conjunction to enlarge wall to lumen ratio. Blood velocity, for example, causes the vessel diameter to increase by a mechanism independent of shear rate (Shoemaker et al., 1997).

As shear stress is one of the main factors that influences vascular properties during exercise, manipulating shear stress without exercise may bring about similar adaptations with an external compression sequence. Shear forces decrease under different external compressions, a decrease in shear stress is found with greater external pressure until an optimum point (150 mmHg) similar to that found during moderate hand-grip exercise (Roseguini et al., 2010). Although long term external compressions failed to significantly improve transport capacity in humans, it is suggested that externally applied pressures are still transmitted to the tissue (Roseguini et al., 2010). Despite the increase in shear rate during an external compression sequence, Roseguini et al. (2011) concluded that shear is neither advantageous nor detrimental to artery endothelial function, therefore has little role in regulating arterial structure.

2.7.1- Can Blood Flow alter Vascular Structure and Function without Exercise?

The increases in blood flow found during exercise cause the endothelium to react, this affects oxidative metabolism, causing O_2 transport to change (Hughson et al., 1996). The extent to which the artery reacts is dependent on two factors; magnitude of stress and the strength of the material (Fry, 1968). The remodelling of an artery from increased blood flow is related to the structural properties of elastin found in the artery, which is affected by shear stress (Alkiviadis and Nikos., 2009). Therefore, the extent to which blood flow stresses the endothelium determines whether blood flow can alter vascular properties.

There has been much research placed on changes found in vascular structure and function during exercise, but little research conducted to mimic these changes to clarify the cause of vascular adaptations. Research has proven that during exercise vascular structure, HR and BP change (Tschakovsky et al., 2003). However, with an external compression sequence HR, PB and vascular properties also change (Roseguini et al., 2010). The change in BP found with an external compression sequence is similar to that found with mild exercise (Thomas et al., 2002). In addition, it is suggested that a resistive vibration exercise is able to decrease baseline diameters in bed ridden individuals; and the use of resistive exercise alone is insufficient to counteract the vascular adaptations found during bed rest (Van Duijnhoven et al., 2010). Roseguini et al. (2010) looked at changes in intramuscular pressure during exercise, and concluded that only a high pressure inflation above diastolic volume (150 mmHg) have the ability to increase blood flow patterns over a prolonged time. These readings are similar to those found during mild exercise, and suggest vascular changes may be seen with an external compression sequence under high pressures.

A form of external compression treatment identified to improve the quality of life in angina patients is known as Enhanced External Counter Pulsation Therapy (EECP). Three pneumatic cuffs undergo a series of inflation and deflation sequences which aid the return of blood to the central circulation (Erdling et al., 2008). EECP has the ability to improve endothelial function and vascular remodelling in humans (Sinvhal et al., 2003: Braith et al., 2010). It is suggested that EECP improves resting brachial artery diameter (Braith et al., 2010), suggesting that vascular structure and function can change without exercise, and have the potential to provide physical therapy to bed ridden individuals. This implies that an external compression sequence may influence shear stress and alter vascular properties after an acute bout of external compressions.

2.7.2. Vasodilatory response of the Brachial Artery after an Acute External Intervention

The vasodilatory response to an exercise stimulus shows an increase in arterial diameter (Green et al., 2012). At the onset of exercise, muscle blood flow increases and plays a role in the vasodilatation of an artery (Kirby et al., 2007). Van Duinhoven et al. (2010) researched changes in arterial diameter and blood flow; he noted that changes in baseline arterial diameter in individuals who were involved in resistive vibration exercises changed. From this it is suggested that exercise is not needed to alter vascular properties.

There are numerous metabolic contributors causing changes to the vascular structure and function, and a number of mechanisms that affect the changes in vascular structure. These include the systemic sympathetic nervous system, changes in arterial pressure (Tschakovsky et al., 2003), temperature (Ooue et al., 2007), the hormonal response (Clifford, 2007) and blood flow. Distinguishing whether each of these effect changes in vascular structure

independently or work in conjunction with each other will clarify the cause of change to vascular structure and function.

2.8. Conclusion of Research

Exercise causes acute changes in vascular structure and function, and is identified by an FMD. Exercise causes the release of NO from the endothelial cells, which allows the smooth muscle to relax and an increases shear stress. However, the time delay for hormonal release during exercise causes the vessel to dilate after the initial stimulus, suggesting that there are additional factors that cause arterial dilation at the onset of exercise (Clifford, 2007). Research, however has failed to clarify the cause of these changes and have suggested that the metabolic contributors such as increased temperature, hormonal balance and frictional force caused by blood flow effects acute vascular properties. Therefore, this study will isolate muscle contraction whilst externally changing blood flow with a CP technique. The use of an acute external CP intervention will provide clarification as to whether acute vascular structure and function changes are due to the metabolic contributors found with exercise or the change in shear force found with blood flow.

From the literature it is hypothesised that:

1. The percentage change in delta diameter with a change in arterial diameter following a cuff occlusion will increase.
2. Arterial diameter will increase after the cuff occlusion but have minimal changes after the intervention.
3. Shear stress would increase slightly after the cuff occlusion and intervention.

CHAPTER THREE

METHOD

3.0. METHOD

3.1. Participants

To peruse this study ethical approval was granted from Cardiff Metropolitan University. For this study, nine male Cardiff Metropolitan University sports students were informed of the study (appendix 1) and volunteered as participants (appendix 2) (age 20.3 ± 0.8 yr; mass 79.8 ± 8.3 kg; height 177 ± 6.0 cm; BMI 25 ± 2.2). Females were excluded from the study due to hormonal imbalances in the menstrual cycle. Participants abstained from caffeine and vigorous activity on testing days (appendix 4), this accounts for any underlying fatigue or chronic adaptations that may influence results. Participants were free from cardiovascular disease, upper limb injuries, medication, normotensive (>140/90 mmHg) and no-smokers. Participants exercised up to the recommended ACSM guidelines of completing 30 minutes of moderate activity at least five times a week, or 20 minutes of vigorous activity three times a week (Kluwer, ACSM, 2010:46). The chosen participants completed a Physical Activity Readiness Questionnaire (PARQ) to assess their current level of fitness before testing. Prior to testing, each participant was instructed to keep a 24hr training log and food diary. The time of day that each participant was assessed was kept the same, as endothelium-dependant FMD levels vary through the day (Jones et al., 2009).

3.2.1. Procedure

For this study participants attended two sessions (Figure 4), the first of which was a familiarisation session and the second a cuff pulsation (CP) intervention combined with two FMD procedures. To account for physiological changes, HR, BP and weight were taken during the intervention (appendix 3). In addition to baseline anthropometric measurements, FMD values were also accounted for.

FMD was recorded by measuring the change in shear rate and arterial diameter from baseline to maximal vascular dilation and time to peak arterial dilation (TTPAD) after cuff occlusion. To finalise the procedure numerous pilot studies were carried out, this helped distinguish the intervention.

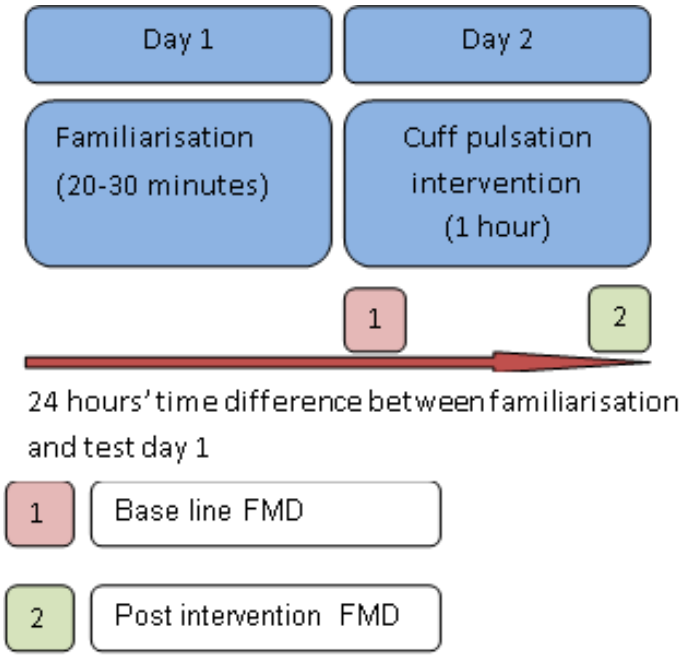

Figure 4. Time scale for experimental measures

3.2.2. Visit one - Familiarisation (approximately 30 minutes long)

For each participant the familiarisation session was completed prior to the laboratory testing, where the participant became accustomed to the CP intervention. Both height (Holtain Fixed Standiometer, Holtain LTD, Pembs, UK) and weight (SECA-Model 770, Vogel and Halke, Hamburg, Germany) were recorded. The pressure placed on the cuff for the CP intervention was determined from a percentage of their systolic BP (60%) this value was finalised by using pilot studies, and prevented complete blood flow occlusion.

The CP was completed for 2-5 minutes in a supine position; this allowed the participant to become accustomed to the procedure. During the visit, familiarisation of an FMD was also completed where forearm blood flow was occluded for 2 minutes.

3.2.3. Visit two

Visit two included baseline measures and the CP intervention. The participant laid in a supine position with their dominant arm extended to the side for 10 minutes prior to the test. During this period a finger finometer (Finometer PRO, Finapres Measurement Systems, Amhen, Netherlands) was used to measure resting BP, and a 3-lead ECG was used to calculate resting HR (Ultrasound, ViVidq, GE Healthcare, Amersham, UK).

The FMD was calculated during five minutes of forearm occlusion. Continuing from this the CP intervention was put in place, and completed for five minutes with a 45 second rest period in the middle before the second FMD was taken. The FMD was measured 3-5 cm proximal to the anticubital fossa, with a segment view of approximately 1.5 cm. HR and BP were recorded throughout the whole procedure.

3.3.1. FMD Measurement

FMD is the percentage change from baseline to maximal vascular dilation over a single cardiac cycle. FMD was measured by the percentage change in shear stress, arterial diameter, maximal dilation values and TTPAD. The cuff was placed distal to the imaged artery, this maximises the dependence of the vasodilatory response on the endothelium (Thijssen et al., 2010). The FMD procedure was based on Thijssen et al’s (2010) guidelines.

3.3.2. Participant Preparation

To ensure that the participants were suitable for the procedure, medical history was considered. Each participant rested in the supine position for 10 minutes before the first assessment with their right arm extended. The inflation cuff was placed distal to the artery (just below the elbow), and inflated to 220 mmHg for 5 minutes.

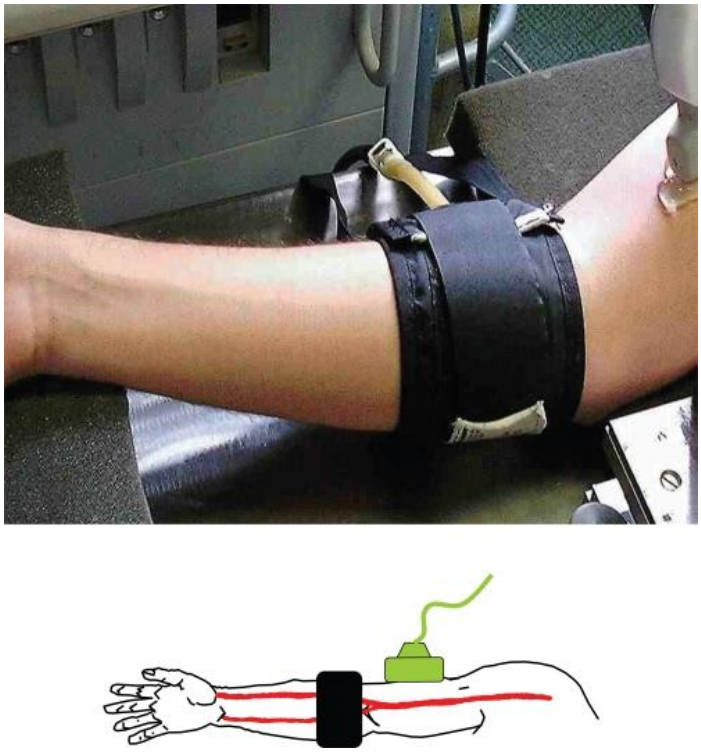

Figure 5. Pressure cuff and imaging probe placement on the forearm.

3.3.3. Protocol

After the participant had rested for 10 minutes, and baseline measures were taken for 1 minute, the cuff was inflated for 5 minutes (first measurement). Post deflation measurements were taken 30 seconds before deflation. Finally, at the onset of deflation, measurements were collected for a further 3 minutes to account for blood flows responses.

3.3.4. Technique

Recording measurements of arterial diameter and shear stress were made throughout the procedure and TTPAD was captured post cuff occlusion. Measurements were calculated using duplex ultrasound (Vivid 7 Dimension, GE Medical Systems). A hand held imaging probe was used to track brachial artery movement, this accounted for any minor contraction whilst collecting the image.

3.4. Measuring Blood Pressure

The BP was recorded throughout the procedure using a finger finometer (Finometer PRO, Finapres Measurement Systems, Amhem, The Netherlands) on the left arm.

3.5. Measuring Heart Rate

HR was measured using a three lead ECG (Ultrasound, Vi Vidq, Amersham, UK) and was recorded throughout the whole procedure.

3.6. Cuff Pulsation Intervention

Acute extravascular pressure was achieved by placing an occlusion cuff (Hokanson, D.E Hokanson Inc, Bellevue, WA, USA) just distal to the elbow (Figure 5). This allowed room for the ultra sound images to be collected on the brachial artery. The cuff was inflated to 60% of their resting systolic BP. Although there is greater arterial dilation in the artery when the blood is occluded from the upper arm, a similar blood flow is found during forearm occlusion (Agewall et al., 2000). Based on Shoemaker et al's. (1996) work the inflation-deflation ratio of the cuff was 1:1. The time interval between each inflation is represented in figure 6.

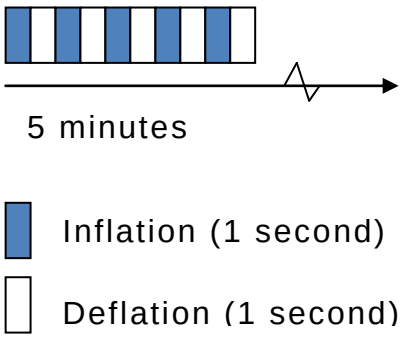

Figure 6. Inflation/deflation sequence applied using the pressure cuff

3.7.1. Data Analysis

Doppler ultrasound at an angle of 60° was used to maximise the sample collection. To capture peak diameter and calculate shear stress continuous edge detection and wall tracking was used. Peak diameter was analysed using automated mathematical algorithms. FMD is presented as the percentage change from baseline to maximal dilatory values. The duration taken to reach maximal dilatory values assessed TTPAD. The brachial artery diameter was measured both before and after arterial occlusion; this was determined using a custom-designed edge detection and wall-tracking software. Shear stress (pa) was calculated externally using the results from arterial diameter (cm) and mean blood flow velocity (cm/s).

3.7.2. Statistical Analysis

FMD variables (delta percentage, shear rate, arterial diameter and TTPAD), BP and HR were compared using a paired t-test on the the SPSS software (IBM, Statistics 19, New York, United states). Statistical analysis of both arterial diameter and shear stress were assessed at baseline and response before and after the intervention. In addition after the occlusion, TTPAD (TTPAD) and delta diameter change was assessed.

CHAPTER FOUR

RESULTS

4.0. RESULTS

4.1. The Purpose of the Study

The purpose of this study was to determine if an acute bout of external cuff pulsations (CP) has the ability to alter the vasculature of the brachial artery. The results will focus on the percentage change in FMD, arterial diameter, shear stress and time to peak arterial dilation (TTPAD) in response to the CP intervention. Shear stress is the main determinant that alters vascular dilation (Kamiya et al., 1980), suggesting that if shear stress changes additional variables may follow.

4.2. Experimental Results

4.2.1. Blood Pressure and Heart Rate response at each stage of the Intervention starting from the Baseline value, FMD, the intervention and the response FMD

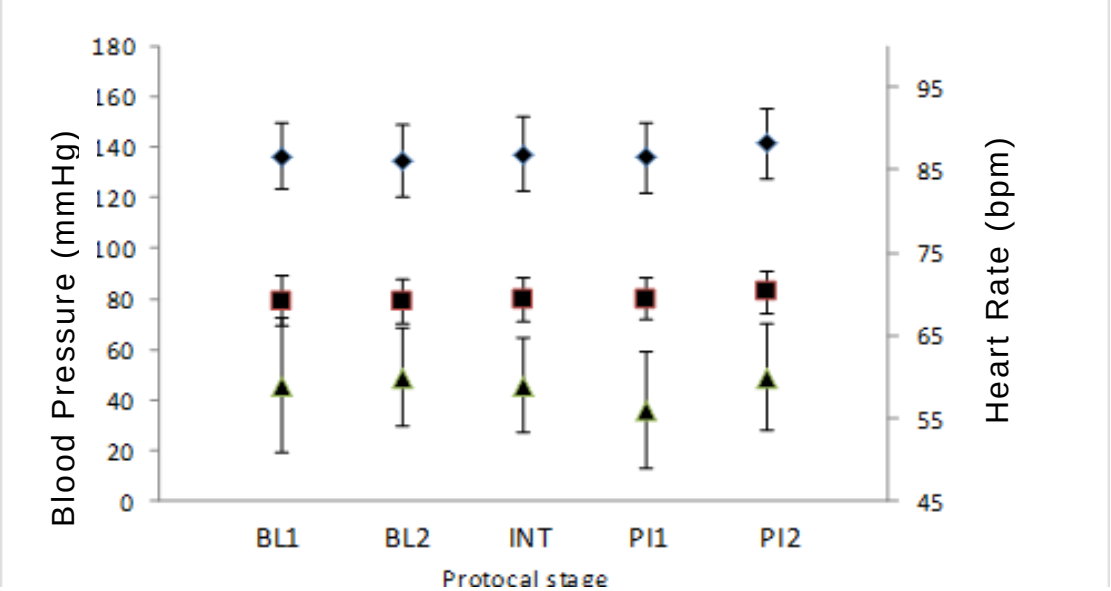

Figure 7. Mean (±SD) blood pressure and heart rate at each stage; pre intervention baseline value (BL1); pre intervention response (BL2); intervention (INT); post intervention baseline values (PI1); post intervention response (PI1).

▲ Heart Rate
■ Diastolic Blood Pressure
♦ Systolic Blood Pressure

Both systolic and diastolic BP remain relatively constant throughout the procedure (Figure 7). HR however, decreases slightly after the intervention from 59 bpm to 56 bpm, but then returns to 59 bpm following the intervention.

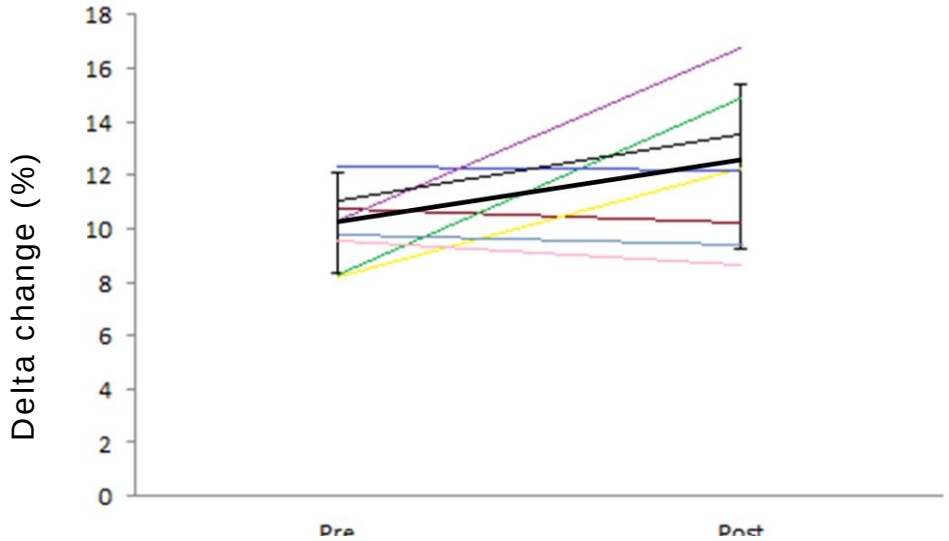

Figure 8. Delta diameter (%) change for each individual before (Pre) and after (Post) the intervention. Bold line represents mean value.

4.2.2. Delta Diameter (%) FMD response before and after the Intervention

It is clear that delta diameter increases by 20.27% after cuff occlusion in response to the intervention (Figure 8). There is a large range of values when comparing pre intervention flow-mediated dilation (FMD) and post intervention FMD, for example participant 5 showed the greatest increase, from 10.36% to 17.81%; whilst participant 8 decreased from 9.23% to 7.88%, this suggests results should be approached with caution.

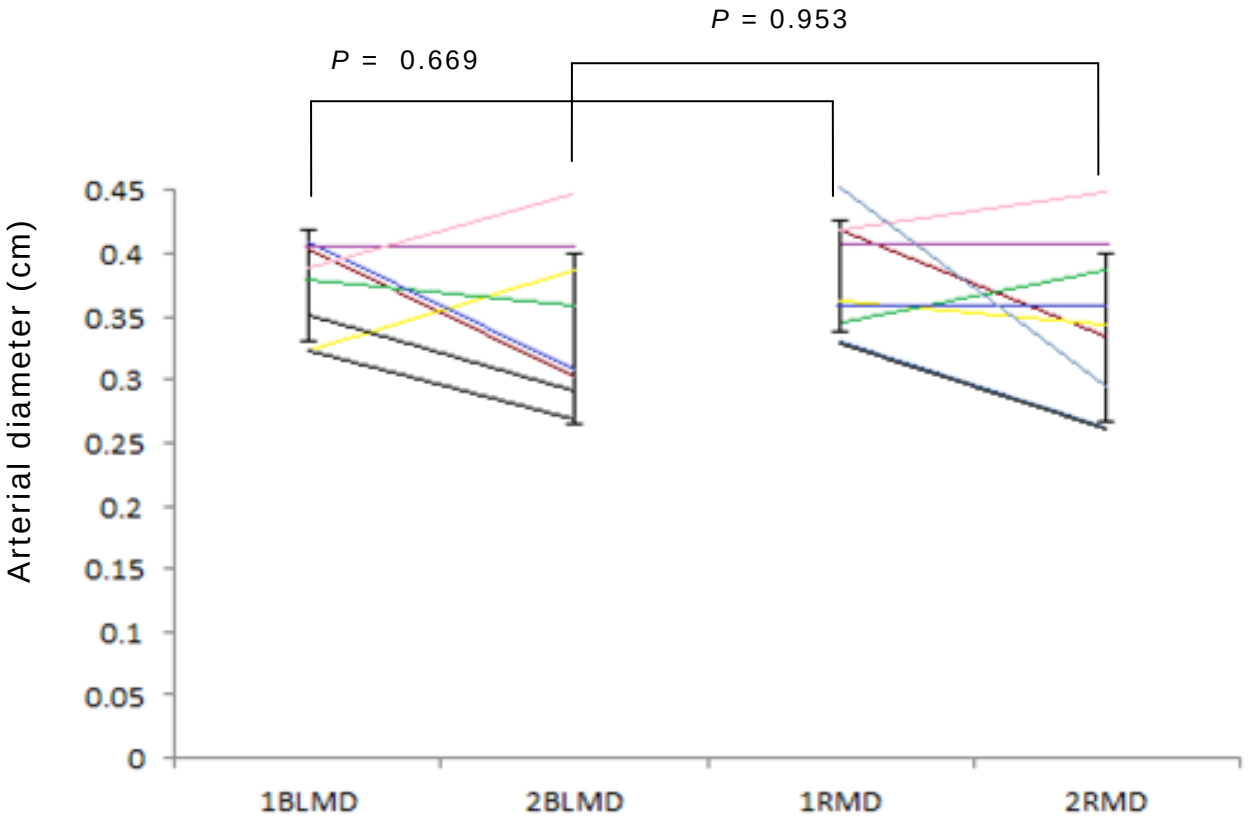

Figure 9. Arterial diameter (cm) change for each participant at baseline arterial diameter pre intervention (1BLMD), compared to baseline arterial diameter after the intervention (2BLMD); arterial diameter response pre intervention (2RMD) and response arterial diameter post intervention (1RMD).

4.2.3. The comparison between Baseline Arterial Diameter and Response Arterial Diameter before and after the Cuff Pulsation intervention in the Brachial Artery

Arterial diameter decreased as a mean result when comparing values before and after the intervention (0.38 cm to 0.33 cm respectfully). Comparing the mean arterial diameter before and after the cuff occlusion showed no change before or after the intervention (pre intervention 0.38 $\pm$ 0.04, 0.38 $\pm$ 0.04 cm: post intervention, 0.33 $\pm$ 0.07, 0.33 $\pm$ 0.07 cm). Individual responses vary, for example participant 1 decreased after the intervention from 0.41 cm to 0.30 cm at baseline, however there was an increase in participant 2 from 0.32 cm to 0.39 cm.

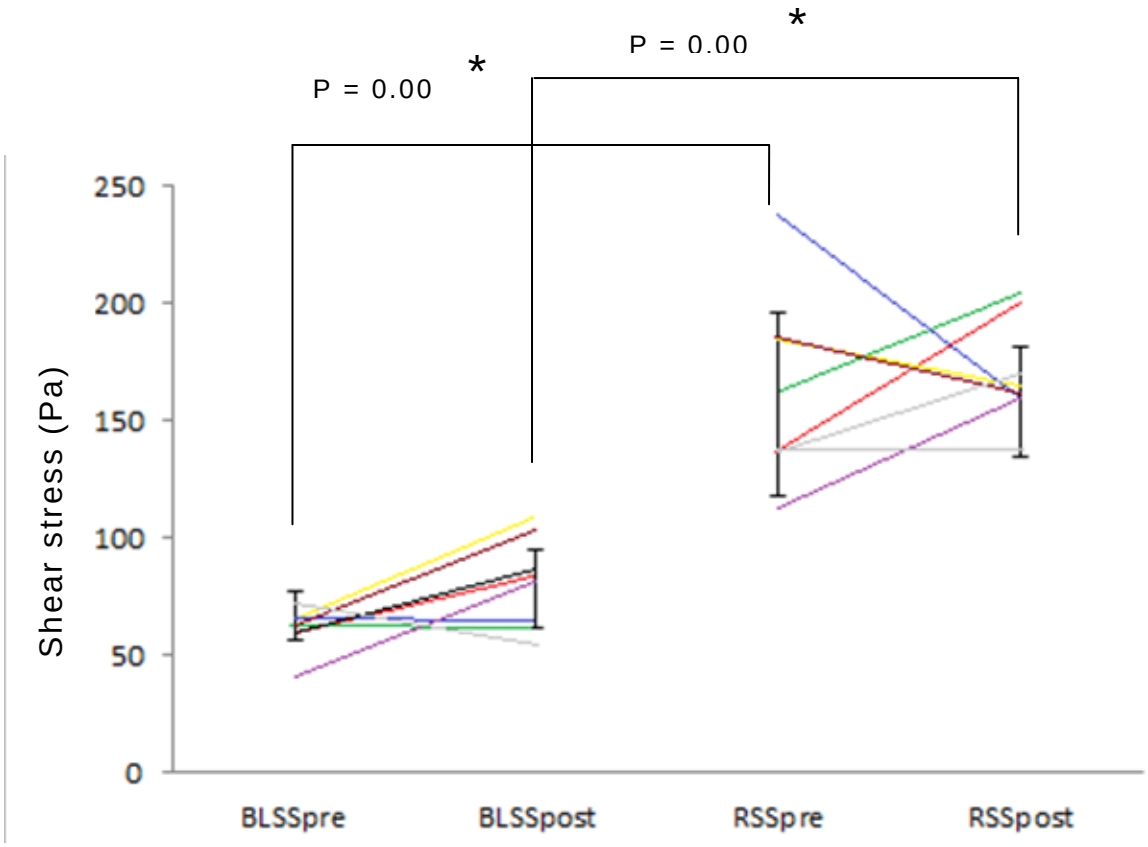

Figure 10. Individual responses of baseline shear stress for the area under the curve before arterial occlusion (BLSSpre) compared to baseline shear stress after the cuff pulsation intervention (BLSSpost); the response shear stress found after cuff occlusion before the intervention (RSSpre) is compared against the response shear stress after the intervention (RSSpost).

*= Significant difference from pre intervention $P < 0.05$

4.2.4. The comparison between Baseline Shear Stress and Response Shear Stress before and after Arterial Occlusion in the Brachial Artery

From the results it is clear that shear stress increases in response to the FMD following cuff occlusion (Figure 10). Before the intervention there was a significant 145.89% increase from baseline to response shear stress, and a significant increase of 97.55% after the intervention. Results however, vary for each participant. The majority of participants increase in both baseline and response shear rate following the intervention, however there are some abnormal results that decrease following the intervention, for example participant 4 decreases from 74.87 pa to 67.10 pa.

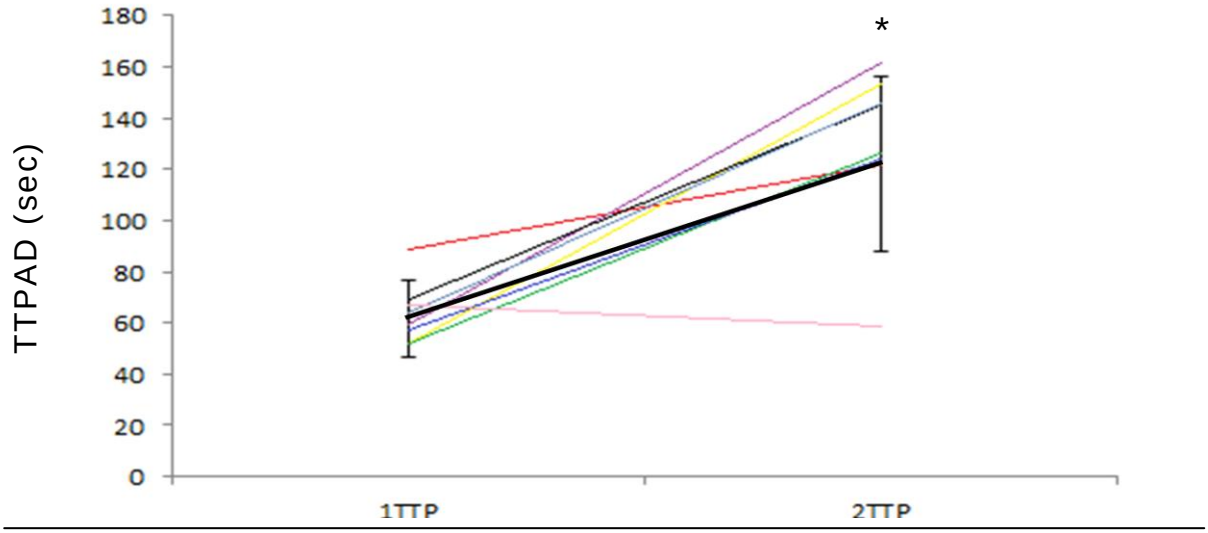

Figure 11. Pre intervention TTPAD after the cuff occlusion (1TTP) and post intervention TTPAD after cuff occlusion (2TTP), bold line represents groups mean value.

*= Significant difference from pre intervention $P < 0.05$

4.2.5. Time to Peak Arterial Dilation after cuff occlusion

TTPAD was assessed before and after the intervention in response to the cuff occlusion (figure 11); it is clear that TTPAD in all but one participant increased. The mean increase following the cuff occlusion was 24.54%

Table 1. The percentage difference for each participant when comparing FMD values before and after the intervention for each participant.

	Percentage change from pre to post intervention (%)							
Participant	1	2	3	4	5	6	7	8
Arterial baseline diameter before cuff occlusion (cm)	-26.54	22.08	-2.89	-34.31	0	-21	-8.24	15.17
Arterial diameter after cuff occlusion (cm)	-27.21	2.9	10.79	-1.91	0.24	-24.92	-36.2	10.89
Shear stress place on the artery before cuff occlusion (Pa)	51.93	34.14	-1.25	-10.39	44.09	30.78	-45.46	-31.27
Shear stress placed on the artery after arterial occlusion (Pa)	32.86	-10.7	25.39	-39.45	25.05	-5.69	14.37	0.5
TTPAD after cuff occlusion (sec)	20.58	253.36	158.7	108.25	176.29	84.33	112.34	-26.37
Delta Percentage change after the cuff occlusion (%)	-9.45	66.60	-44.05	-3.02	-41.83	7.51	-6.19	-14.60

Highlighted individuals represent a decrease after the intervention

4.2.6. Percentage change for each individual following the Cuff Pulsation Intervention

Individual responses vary when comparing the percentage change following the intervention. TTPAD increases in all but one participant this is a relatively consistent difference, shear stress and arterial diameter however, show inconsistency within results as some individuals increase in response to the CP intervention whilst others decreased.

CHAPTER FIVE

DISCUSSION

5.0. DISCUSSION

5.1.1. Experimental Findings

The purpose of this study was to assess the brachial artery response to a cuff pulsation (CP) intervention. Arterial vasculature was assessed before and after an acute bout of CP. A CP intervention will remove the metabolic contributors associated with exercise and allow blood flow to manipulate vascular structure and function.

As some participants failed to meet the required criteria, results should be approached with caution. The increased shear stress during exercise (Laughlin et al., 2008) and the relationship between blood flow and metabolic rate (Barclay et al., 2001), supported the hypothesis that blood flow has the ability to regulate vascular structure and function. Results show that there are minimal changes in arterial diameter, shear stress before and after the intervention. In addition, the change in arterial diameter after the flow-mediated dilation (FMD) resulted in a change in delta diameter, however there was a significant difference found when assessing time to peak arterial dilation (TTPAD) after the CP intervention. These minimal changes suggest that blood flow causes slight changes to vascular structure and function, but influences TTPAD significantly.

5.1.2. Heart Rate and Blood Pressure Results

It is thought that BP may change with an external compression sequence as Thomas et al. (2002) reported similar findings when comparing BP to mild exercise. This was not seen in the present study, as the pressure on the cuff was not as great. BP remained relatively constant with mean systolic BP fluctuating between 138–140 mmHg and diastolic BP fluctuating between 79–80 mmHg (Figure 7). From the ACSM guidelines it is clear that diastolic BP is at a healthy level,

however, systolic BP is higher than the recommended value of 120 mmHg, which raises concern regarding the validity of the results and the health of the participants. HR remains constant in the first stage of the procedure, but decreases during the second baseline measure (Figure 7) this is consistent with Tschakovsky et al. (2003) who reported steady HR. The decrease in HR may be due to the participant's relaxed status, which suggests that the original resting value may not be a true representative of their resting HR; with this in mind, it may be beneficial to increase the time that the participant rested prior to the intervention.

5.1.3. Delta diameter change after Cuff Occlusion in the Brachial Artery

Increases in delta diameter after cuff occlusion is consistent with Black et al. (2002) where arterial diameter increased after arterial occlusion (Figure 12). It is clear that after the intervention delta diameter increases by 20.27% (Figure 8) which is consistent with the first hypothesis.

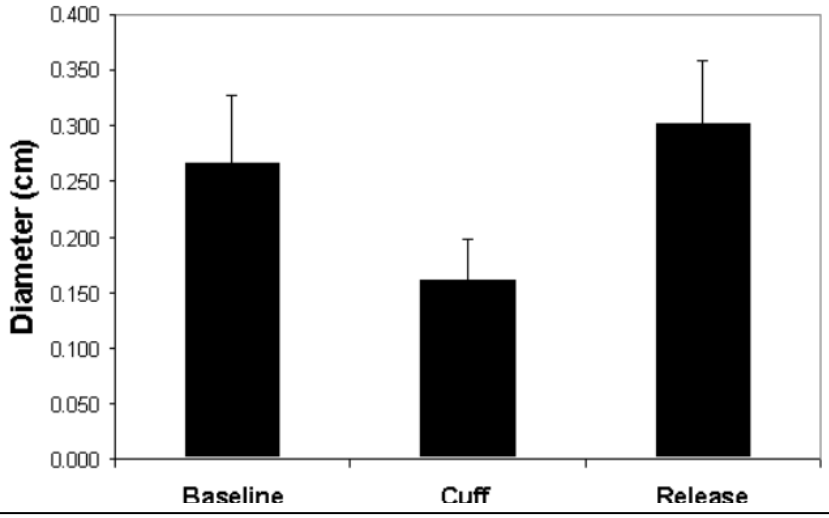

Figure 12. Arterial diameter at rest, during cuff occlusion and after cuff occlusion (Black et al., 2002)

Following the cuff occlusion arterial diameter increased in each individual, however results are inconsistent following an exercise intervention. The percentage increase after cuff occlusion when considered as a mean value was greater, this shows some consistency with Johnson et al. (2012) whose results remained constant. However, when results are individualised, there are inconsistencies that do not correspond with Johnson et al. (2012) for example after the intervention participant 5 increased from 10.36% to 17.81% where as participant 8 decreased from 9.23% to 7.88% this suggests that results should be approached with caution. The differences in results may be due to individual characteristics, and the extent that each participant reacted to the intervention.

5.1.4. Changes in Mean Arterial Diameter before and after an Intervention

From the present study it was observed that arterial diameter does not change following cuff occlusion before or after the intervention (pre intervention baseline, 0.38 $\pm$ 0.04 cm; pre intervention response, 0.38 $\pm$ 0.04 cm; post intervention baseline, 0.33 $\pm$ 0.07 cm; post intervention response, 0.33 $\pm$ 0.07 cm) (Figure 9). Although there was a slight decrease in results after the intervention, arterial diameter does not change in response to the cuff occlusion, this is inconsistent with the second hypothesis. It is possible that there is no significant difference in results when comparing pre and post intervention values, because there is little change in shear stress (Figure 8), which is the mediator of arterial dilation (Pyke and Tschakovsky, 2005).

The individual results (table 1) indicate that there is a wide range of values for each variable; variation in results may be an indicator of the heterogeneous qualities that individuals possess. Arterial diameter increases in response to the cuff occlusion after the intervention for half of the participants, however the remainder showed a reduced

response (table 1). Arterial diameter response to the cuff occlusion after the intervention showed a 36.2% decrease in participant 7, were as participant 8 showed a 10.89% increase. These results do not correspond with that of Rooks et al. (2011), who looked at an exercise intervention and reported an increase in arterial diameter following an exercise intervention (pre intervention, 3.39 mm – 3.36 mm: post intervention 3.47 mm – 3.50 mm).

The minimal changes in arterial diameter may also be influenced by the systemic differences in arterial size before and after arterial occlusion, as baseline artery size was different for each participant (N= 0.375 $\pm$ 0.04 cm) and functional change may not be a true representative of FMD response (Thyssen et al., 2008; Pyke and Tschakovsky 2007). Work by Pyke and Tschakovsky (2007) confirmed that only 64% of FMD response is explained by arterial size. In addition, smaller arteries have greater elastic properties, which may influence their ability to relax under high pressures and reduce the amount of shear force resulting in greater arterial dilation. Baseline arterial diameter may therefore influence the extent that the artery dilates after arterial occlusion. In addition arterial dilation may not be a major contributor to vascular FMD response and is not influenced by blood flow. Finally, increasing shear stress may result in greater arterial dilation after arterial occlusion, and a greater pressure on the cuff may influence the artery's ability to dilate.

5.1.5. Mean change in Shear Stress in the Brachial Artery after the Intervention

The extent to which the artery reacts to a stimulus is dependent on two factors; magnitude of stress and the strength of the material (Fry, 1968). The current findings show that there was a significant difference when comparing baseline shear stress against response shear stress before and after the intervention which is consistent with the third hypothesis. However, no significant difference was identified in shear stress when comparing baseline values and response values (pre intervention baseline, 65.76 Pa, post intervention baseline, 82.53 Pa; pre intervention response, 161.7 + 41.9 Pa; post Intervention response, 163.0 Pa) (Figure 10). These findings are consistent with Dinenno et al. (2001) who reported an increase in tangential shear stress in the femoral artery after an exercise intervention from 8.8 + 0.5 to 11.5 + 0.7 dyn cm^{-2}.

Although NO has been identified as a major contributor to arterial dilation, FMD response has greater sensitivity to shear stress. This suggests that shear stress should be the major contributor influencing arterial dilation following arterial occlusion (Pyke and Tschakovsky, 2005). Although there is less stress placed on the artery with an external compression sequence, it was expected that there would be a slight change in force acting on the artery (Roseguini et al., 2010). Previously it was established that rhythmic exercises increased shear rate patterns (Thijssen et al., 2009). The CP intervention attempted to mimic these changes, but showed no differences. This indicates that changes in blood flow fail to influence shear stress.

The removal of exercise reduces the amount of shear force placed on the endothelium, which in turn reduces the vascular response. Despite this, TTPAD significantly increased after the intervention (pre intervention, 86.7 $\pm$ 16.0 sec; post exercise 107.96 $\pm$ 36.3 sec) without

a major change in shear stress, this implies shear stress may not play a role in regulating the TTPAD. Increasing the change in blood flow by raising the pressure on the cuff during the intervention may result in a greater shear stress which will improve acute vascular response, but may not influence TTPAD.

5.1.6. Time to Peak Arterial Dilation in the Brachial Artery after the Intervention

Interestingly the TTPAD significantly increased in response to the CP intervention (Figure 11) (pre intervention, 86.68 $\pm$ 16.02 sec; post intervention 107.95 $\pm$ 36.31 sec) this is similar to a previous study where exercise conjoined with cuff occlusion showed a similar trend (pre intervention, 34.5 $\pm$ 1.25; post intervention, 40.5 $\pm$ 3.19 at 60 mmHg) (Johnson et al., 2012). The increase may be due to the force of contraction, as dilatory capacity is dependent on the strength of contraction (Barclay et al., 2001), therefore, greater external stimulus may result in greater arterial dilation. From the results, the extent to which shear stress influences TTPAD is minimal; this implies that TTPAD is not influenced by shear forces initiated from an external compression sequence.

Furthermore, the increase in TTPAD may be due to a slower NO stimulus. Increasing the stimulus may decrease the TTPAD as there is greater force to initiate NO release. Due to limited shear stress, NO may not be stimulated to create the vasodilatory response, which leads to increased TTPAD. The increase may also be due to the availability of NO, as the release of NO from the endothelium through the cell wall is both time and situation dependent (Barclay et al., 2001). Although O_2 is known to inactivate NO (Wang et al., 2009) and should result in a decreased TTPAD as more NO is available, there is an increase in TTPAD, suggesting that O_2 does not inhibit NO availability.

Work by Shoemaker et al. (1997), concluded that the time course for maximal dilation is linked to the speed that metabolic contractions occur. Consequently the TTPAD might be influenced by the time interval that each contraction takes occurs during the intervention, as fast contractions show additional increases in arterial diameter (Shoemaker et al., 1997). Increasing the ratio that the cuff contractions occur may stimulate the additional vasodilatory responses and lead to a quicker TTPAD. Although there are numerous suggestions to explain why TTPAD increases and arterial diameter remains constant, it would be beneficial to clarify why these differences occur.

From this study it is clear that manipulating blood flow with an external CP intervention fails to influence shear force and arterial diameter but significantly influences TTPAD. It is possible to increase shear force on the artery by manipulating the pressure on the cuff during the intervention, however caution must be taken when increasing shear forces, as overstretching of the arterial wall may disrupt cell-to-cell connection (Farb et al., 1990).

5.2- Practical Implications

A significant increase in TTPAD following the CP intervention implies that blood flow affects the vascular response of an artery. Shear force, however is not the cause of TTPAD as shear stress had minimal changes when placed with the CP intervention.

Combining past research, and the results found from the present study it is concluded that blood flow affects TTPAD but has minimal effect on additional variables that influence vascular structure and function such as shear stress and arterial diameter. From these results an external CP treatment may be used as a form of treatment for those suffering from vascular illnesses such as angina. With the understanding that vascular structure and function change with blood

flow alone; an external compression sequence may benefit as a form of rehabilitation, similar to that found with EECP (Sinvhal et al., 2003). A CP treatment may be beneficial as the initial form of rehabilitation for individuals who are unable to exercise, which may result in quicker recovery and improve the quality of life for an individual. In addition, the use of CP as a form of treatment for paraplegic individuals, may aid blood flow in specified limbs and prevent further vascular damage. Although, the pressure placed on the cuff is specific for each individual, the percentage of systolic BP applied to the cuff may need to be adapted as only slight changes in FMD were found in most variables after the intervention.

5.3. The Main Limitations and Strengths of the Current Study

5.3.1. Limitations

There are numerous limitations revolving around vascular research. A particular issue with the current study revolves around technician error, number of participants and the trained status of the individuals.

The current study used a hand held imaging probe, which tracks brachial artery movement, it accounts for minor muscular contractions whilst images are collected. Previous studies have used a clamp which compensates for technician fatigue but fails to account for minor muscle contractions, which can have detrimental effects on results. Taking into consideration both the advantages and disadvantages of each method of data collection, the hand held imaging probe was used. Due to the errors that the hand held imaging probe initiated, poor images were collected, which resulted in the removal of one participant from the study, reducing the accuracy of the data set.

For a variety of reasons such as time availability and participant training there was a limited number of participants. This raised concerns when abnormalities were found in results, as it may have influenced the significant differences when comparing the vascular response. Additionally, the past physical activity of the participants may have a role in regulating the vascular structure of the artery (Rognmo et al., 2008). Participants were asked to exercise up to the recommended ACSM guidelines, this proved difficult, as some individuals exercised in the days leading up to the procedure. Physical activity prior to testing may influence vascular response and result in chronic vascular adaptations from day to day resistance training (DeVan et al., 2005). In addition, the trained status of each participant was assessed on their right arm. This raises concerns regarding limb dominance, as differences are seen when comparing dominant and non-dominant limbs when looking at dilatory capacity (Kagaya et al., 2010).

5.3.2. Strengths

Major strengths of this study included the ability to manipulate blood flow using an external stimulus. An external intervention removed metabolic contributors that are associated with exercise such as increasing core temperature and muscular contraction initiated from twitch contractions. The use of an external stimulus therefore, allowed blood flow alone to be the major contributor that causes vascular adaptations. Although the hand held imaging probe raised concerns regarding the quality of the images, it allowed a non-invasive method of measuring an artery's response to an FMD following a CP intervention. Further strengths include the use of Thijssen et al's. (2010) FMD procedure. This allowed vascular structure and function to be assessed externally and compared against other studies.

5.4. Future Directions

Although the present study demonstrated that an external CP has the ability to significantly increase TTPAD, the limitations need to be addressed. Considering the limitations identified, future research may find it useful to account for these restrictions.

A major aspect to this study revolves around the intervention and the pressure placed on the cuff. Research into the acute adaptations under different cuff pressures will provide greater knowledge to the type of force that is applied to the artery; and in turn the amount shear stress influences the artery's dilatory capacity. Shear stress is a contributor to changes in vascular dilation during exercise, comparing exercise and external CP may provide a greater knowledge to the amount shear stress influences vascular dilation as blood flow patterns differ. Additionally, it would be beneficial to compare a variety of exercises and CP interventions against each other to compare blood flow patterns. The comparison of both endurance and resistance exercise against a CP intervention, will give an insight to the similarities and differences that these interventions have against each other, as it has previously been suggested that rhythmic exercises increase shear rate (Thijssen et al., 2009). In the current study physically active participants volunteered, however a trained group of individuals may have different responses when faced with an intervention. The relationship between different trained statuses and sports will allow a greater understanding to the type of stimulus that causes these adaptations.

Further studies may find it beneficial to compare both acute and chronic arterial adaptations in a variety of trained statuses; this will give a more concise view on the vascular adaptations under different interventions, and trained statuses. Distinguishing whether a series of acute CP interventions result in chronic changes in vascular structure

and function will provide greater knowledge to the type of adaptations that occur and the time it takes for them to appear. The extent that chronic adaptations appear may result in a beneficial rehabilitation process for individuals suffering from vascular illnesses such as atherosclerosis.

Finally, conflicting results regarding the increased O_2 demand during exercise may inactivate NO, implies that exercise may have detrimental effects on smooth muscle relaxation (Wang et al., 2009). Monitoring O_2 saturation during an exercise intervention and a CP intervention, will clarify whether an increase in O_2 demand effects smooth muscle relaxation.

CHAPTER SIX

CONCLUSION

6.0. Conclusion

The aim of the study was to assess the acute changes in vascular structure and function with blood flow following a single CP intervention. It was hypothesised that there would be an increase found in shear stress, arterial diameter and TTPAD after the CP intervention. Increases were not expected to be as great as those found by exercise, as the force on the artery is not as extensive. A significant increase ($P > 0.05$) was found in TTPAD following the intervention, whilst delta diameter increased slightly after cuff occlusion, arterial diameter and shear stress had minimal changes. These results give reason to suggest that blood flow alone has the ability to cause acute changes to TTPAD but not maximal diameter and shear stress, however results should be approached with caution due to heterogeneous qualities of each participant.

Shear stress was expected to have a greater response after the intervention than was highlighted from this study as there is still force placed on the artery. Increasing the pressure on the cuff during the intervention may result in improved shear force, impact on maximal dilation and further influence TTPAD. Both systolic and diastolic BP remained constant throughout the procedure, this was expected, as no physical activity was completed by the participant. HR, however, remained constant in the initial stages of the procedure but decreased at the second baseline measure, this result may be due to the relaxed status of the participant.

Several limitations were identified in the current study and future research is advised to account for these limitations, this will allow for a greater understanding of both chronic and acute changes to vascular structure and function, with an external compression sequence. Additional knowledge may also help create a new form of rehabilitation

and aid the quality of life for individuals suffering from vascular illnesses such as angina.

CHAPTER SEVEN

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APPENDICES

APPENDIX 1

Cardiff School of Sport Ethics Committee

Research Participant Information Sheet

Project title: Can vascular structure and function change by altering brachial artery blood flow using an external pressure cuff pulsation technique

The purpose of this document to provide you with information about the research project and to assist you in making an informed decision to see if you would like to be included in the project.

1) Background and aim of the research

One of the most important systems in the human body is the cardiovascular system; it holds great responsibility when coordinating functions such as transport and protection. The circulatory system is a component of the cardiovascular system and plays a role in the transportation of many essential nutrients, gasses and blood cells around the human body, giving it the intention to maintain homeostasis.

The increased demand for energy during exercise alters vascular structure and function. The changes in vascular structure and function during exercise results in increased luminal blood flow and vasodilatatory responses in the artery. However, the cause of these changes are unclear. Therefore, the purpose of this study is to clarify what causes the change in vascular properties, whether it is changes in blood flow, or the metabolic contributors such as thermoregulation and hormone distribution found during exercise.

2) My role as the researcher

The project involves myself, Sian Carrick, Liam Jones, Jane Black, and Prof Rob Shave. Our roles as researchers are to collect data regarding arterial adaptation before and after a external cuff intervention.

Measurements will be collected with using FMD. FMD will be collected in the forearm, it measures the percentage change in vascular structure and blood flow after a 5 minutes of arterial occlusion. Blood flow velocity and arterial diameters will be measured once the cuff is released, causing large blood flow return in the forearm. In addition to the FMD, Blood pressure and Heart rate will be recorded throughout the procedure with the use of a blood pressure cuff and ECG.

3) Your role as a participant

Your role is to attend three laboratory sessions over a one-week period. These sessions will last approximately 1hr.

Visit 1:

Familiarisation

The familiarisation session will take approximately 0.5 hr it will be conducted prior to the laboratory testing. Throughout this period familiarisation of the cuff pulsations will take place. Your HR, PB, Height (cm) and weight (kg) will be recorded during this stage. The pressure placed on the cuff will be a percentage of your systolic BP.

During this visit a familiarisation of an FMD will be completed, your forearm blood flow will be occluded for 2 minutes this will allow you familiarise yourself with the techniques used.

Test day 2: Cuff pulsation intervention

The first FMD will be completed followed by a 5 minute intervention and a additional FMD. FMD involves a 1-minute baseline measure followed by 5 minutes of blood flow occlusion and a 3-minute response

Inflation pattern

Acute extravascular pressure is achieved by a blood pressure cuff connected to an inflation system, this will be inflated to a % of your systolic BP. The pressure cuff will be placed just below the elbow,allowing room for the ultra sound images to be collected on the brachial artery. You will be in a supine position with your dominant arm extended whilst the external cuff will inflate and deflate to a 1:1 ratio.

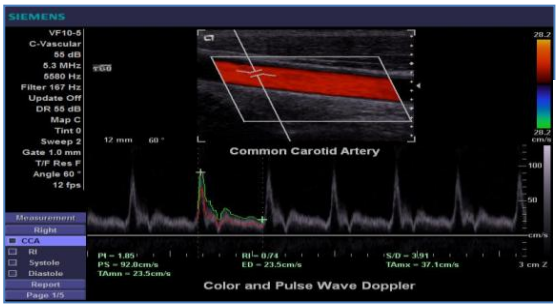
4) Benefits of taking part

The information that is gained from this study will allow an insight to acute arterial adaptations to an external cuff intervention and whether exercise can be mimicked by cuff pulsation technique. It will clarify the cause of change to arterial dilation whether it is the metabolic factors associated with exercise or the changes in blood flow. The information gained will be available to you as a participant, and upon request your results may be handed back to you and discussed in relation to your performance.

5) How data will be collected

Throughout this process ultrasound images using a linear probe will be used to collect FMD results, whilst an ECG will collect HR and a finometer will be used to measure BP, all of which are non invasive. The measurements will be collected from your upper arm.

6) How the data/research will be used



As a voluntary participant you will be allowing me to use your results to analyse

and include in a larger data set. Your results will be kept anonymous; your identity will not be identifiable outside the direct researchers.

Your rights as a participant

Your rights as a voluntary participant, gives you the opportunity to withdraw from the project at any time. This means that you hold the control of your participation. In addition you have the right to request your results, once testing is complete.

Protection to privacy

A great emphasis will be made to hide your identity within the project in all written electronic and any additional documents. Any information relating to your participation within this project will be kept anonymous and remain confidential according to the guidelines of the Data Protection Act (1998).

Contact

If any additional information is required to make an informed decision, feel free to contact me on the details bellow.

Sian Carrick

Cardiff School of Sport
Cardiff Metropolitan University
CF23 6XD
Email:st10001385@outlook.uwic.ac.uk

APPENDIX 2

CARDIFF METROPLOLITAN

INFORMED CONSENT FORM

CSS Reference No:

Title of Project: Can vascular structure and function change by altering brachial artery blood flow using an external pressure cuff pulsation technique

Name of Researcher: Sian Carrick

Participant to complete this section: Please initial each box.

1. I confirm that I have read and understand the information sheet dated (April 2012) for this evaluation study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that it is possible to stop taking part at any time, without giving a reason. ☐
3. I also understand that if this happens, our relationships with the Cardiff Metropolitan University, or our legal rights will not be affected ☐
4. I understand that information from the study may be used for reporting purposes, but I will not be identified. ☐
5. I agree to take part in this study on blood flow changes in exercise and cuff pulsations ☐

Name of Participant _____

Signature of Participant _____

Name of person taking consent_____

Signature of person taking consent_____

Date _____

APPENDIX 3

<u>Research Question:</u> Do changes in radial blood flow pattern caused by a pressure cuff pulsation result in simulation changes to vascular function as those induced by hand grip exercise.

Participant Information

Name: _____

Student ID no: _____

Identification: _____

Date of birth (dd/mm/yr): _____

Sport participates in: _____

Any upper limb injuries:

_____

_____

Time of day testing took place: _____

Cuff Pulsation Intervention **Date:** _____

Resting BP: _____ **Resting HR**: _____

Additional info

Anthropometric Measurements

Height: _____

Weight:

Visit 1: _____

Visit 2: _____

Visit 3: _____

Resting Blood pressure: _____

Resting Heart Rate: _____

APPENDIX 4

Name: _____

ID no: _____

Date: _____

Food Diary		**Training Diary**	
Day Before testing		**Day Before Testing**	
Breakfast			
Lunch			
Tea			
Snacks			
Morning of testing Day		**Morning of testing**	
Breakfast			
Lunch			
Snack			

UWIC RISK ASSESSMENT (RA99) - *(Hazards)* (V3/07)			*Page 1*
School / Unit and Area:	Cardiff Metropolitan University	Assessment Number:	1
Risk Assessment undertaken by: Recommended to be 2 or more people	Sian Carrick		
	Anna West		
Description of the work activity being assessed:	Ultrasound image collection on the Brachial Artery		
Persons Affected:	Staff [x] Students [x] Others [ ]		
Details of Others:			

HAZARD IDENTIFICATION Please provide details of the hazards associated with the area or task. EXAMPLES INCLUDE: Working at height, Manual Handling, Electricity, Fire, Noise, Contact with moving parts of machinery, Dust etc		RISK RATING - without Controls The Risk Rating (RR) and Degree of Risk are determined by multiplying the Severity (S) of injury by the Likelihood (L) of occurrence. Please see UWIC Risk Rating Matrix for details			
		S	**L**	**RR**	**Degree of Risk**
1	Side effect of Cuff Occlusion.	2	3	**6**	**Moderate**
2	Participant will be lying down for a long duration, dizziness might occur when they sit up.	1	2	**2**	**Low**
3	Cramp in the hand whilst holding the probe	1	3	**3**	**Low**
4	Tripping over loose cables	2	2	**4**	**Moderate**

Once all potential hazards have been identified and a Risk Rating has been applied, please go to page 2 and provide details of the control measures required to reduce the risk to an acceptable level.

CONTROLS TO BE APPLIED Examples Include: Elimination, Substitution for something less hazardous, Barriers or fixed guards, standard operating procedures and personnel protective equipment		Date Applied	RISK RATING - with Controls			
			S	L	RR	Degree of Risk
1	Explain in Full the side effects of the procedure, and give them the opportunity to withdraw from the protocol whenever they want.	January 2013	2	2	4	Moderate
2	Encourage the participant to sit up slowly and monitor their behaviour throughout the procedure.	January 2013	1	1	1	Low
3	Encourage the technician to take breaks when not scanning, move the fingers around when possible	January 2013	1	2	2	Low
4	Tape all cables down with tape, and ensure you know where they are all kept.	January 2013	2	1	2	Low
Date of first assessment:		January 2013				
Assessment review dates:						