The Relationship between Acute and Chronic Aerobic Exercise Response in Pre-hypertensive Individuals

by

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A thesis submitted in conformity with the requirements for the degree of Master of Science

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Abstract

Aerobic exercise is recommended as a lifestyle intervention to reduce blood pressure (BP) in individuals with elevated BP (SBP/DBP >120/80 mmHg). However, the BP response is highly variable after both acute (SBP/DBP: –27 to 9/-8 to 7mmHg) and chronic aerobic exercise (-20 to 9/ -11 to 11.3mmHg). We attempt to identify those who are resistant or responsive to training based on their responses to acute (one-bout) exercise. 17 prehypertensive (120 to 139/80 to 89mmHg) males and females (45-60yrs) underwent acute exercise assessments before and after an 8-week walking/jogging program. The magnitude of change in BP after acute exercise significantly correlated (r=.89, p < .01) with the magnitude of change in resting BP after the training. The antihypertensive mechanisms (total peripheral resistance, baroreflex sensitivity) for acute exercise were not correlated to those for chronic exercise. Central cardiovascular controls may link BP reductions after both acute and chronic exercise.
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Chapter 1 Introduction

1.1 Rationale

1.2 Primary Objectives

1.3 Secondary Objectives

1.4 Primary Hypothesis

1.5 Secondary Hypothesis

Chapter 2 Literature Review

2.1 Blood Pressure Response to Acute Exercise

2.1.1 Subject Characteristics and PEH

2.1.2 Acute Exercise Intensity, Duration, and PEH

2.1.3 Potential Reasons for the Observed Difference

2.1.4 Post Exercise Hemodynamic Response

2.1.5 The Mechanisms of Post Exercise Hypotension

2.1.6 Baroreceptors

2.1.7 Heart Rate Variability (HRV)

2.2 Blood Pressure Response to Chronic Exercise

2.2.1 Modes of aerobic exercise

2.2.2 Subject Characteristics and Blood Pressure Reduction

2.2.3 Exercise Training Frequency, Duration and Intensity on Chronic Blood Pressure

2.2.4 Mechanisms responsible for chronic blood pressure reduction

2.2.5 Baroreceptors’ Function

2.2.6 Heart Rate Variability (HRV)

2.3 The Interaction of Acute and Chronic Exercise Effects

Chapter 3 Experimental Design and Methods

3.1 General Study Design

3.2 Participants

3.3 Baseline Screening

3.3.1 Determination of Resting Blood Pressure

3.3.2 Exercise Stress Test

3.4 Acute Exercise Assessments (AEA)

3.5 Time Course of Changes in Resting Blood Pressure during Training

3.6 Measurements

3.6.1 Blood Pressure
List of Tables

Table 4.1: Anthropometric and cardiovascular descriptors of male and female study participants ................................................................. 39

Table 4.2: Blood pressure response to acute exercise ............................................ 40

Table 4.3: Blood pressure response to chronic exercise ......................................... 40

Table 4.4 Regression analysis of the magnitude of blood pressure reduction after chronic exercise and acute exercise response ................................................. 43

Table 4.5 Hemodynamic responses to acute exercises .......................................... 45

Table 4.6 Baroreflex sensitivity and heart rate variability responses to acute exercises. 46

Table 4.7 Hemodynamic responses to chronic exercise ........................................ 46

Table 4.8 Heart rate variability responses to chronic exercise ................................ 47

Table 4.9 Baroreflex sensitivity and arterial stiffness responses to chronic exercise ...... 48

Table 4.10 Correlations between acute and chronic antihypertensive mechanisms. ......... 48
Equation 1: Area under the Curve ................................................................. 35

\[ \text{AUC}_{30 \text{mmHg} \cdot \text{min}} = \sum_{n=1}^{30} \left( \frac{\Delta BP_n + \Delta BP_{n-1}}{2} \right) (t_n + t_{n-1}) \]
List of Figures

Figure 4.1 Resting Systolic Blood Pressure Response to Chronic Exercise ·······················41

Figure 4.2 Resting Diastolic Blood Pressure Response to Chronic Exercise ······················41

Figure 4.3 Systolic Blood Pressure Responses to Acute and Chronic Exercise ··················43

Figure 4.4 Diastolic Blood Pressure Responses to Acute and Chronic Exercise ···············44
List of Appendices

**Appendix A:** Supplemental Data ................................................................................................. 85

**Appendix B:** Supplementary Review ......................................................................................... 87

**Appendix C:** Study Timeline ....................................................................................................... 92

**Appendix D:** Weekly Training Log ............................................................................................. 92

**Appendix E:** Protocol for Acute Exercise Assessment ............................................................... 93

**Appendix F:** Par-Q ....................................................................................................................... 94

**Appendix G:** Rapid Assessment of Physical Activity ................................................................. 96

**Appendix H:** Recruitment Poster ............................................................................................... 100
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AI&lt;sub&gt;x&lt;/sub&gt;</td>
<td>Augmentation Index</td>
</tr>
<tr>
<td>AI&lt;sub&gt;x@75&lt;/sub&gt;</td>
<td>Augmentation Index at 75 heart beats per minute</td>
</tr>
<tr>
<td>AUC</td>
<td>Area under the curve for 30 minutes after acute exercise</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>BP</td>
<td>Blood Pressure</td>
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<tr>
<td>BPM</td>
<td>Beats per minute</td>
</tr>
<tr>
<td>BP&lt;sub&gt;peak&lt;/sub&gt;</td>
<td>Minimum 5 minute average SBP or DBP over the 30 minutes after acute exercise</td>
</tr>
<tr>
<td>BRS</td>
<td>Baroreflex Sensitivity</td>
</tr>
<tr>
<td>CIC</td>
<td>Cardiac Impedance Cardiography</td>
</tr>
<tr>
<td>CO</td>
<td>Cardiac Output</td>
</tr>
<tr>
<td>DBP</td>
<td>Diastolic Blood Pressure</td>
</tr>
<tr>
<td>HF</td>
<td>High Frequency</td>
</tr>
<tr>
<td>HFnu</td>
<td>High Frequency normalized units</td>
</tr>
<tr>
<td>HRV</td>
<td>Heart Rate Variability</td>
</tr>
<tr>
<td>HR</td>
<td>Heart Rate</td>
</tr>
<tr>
<td>Hypertension</td>
<td>SBP ≥130-139/DBP≥90mmHg</td>
</tr>
<tr>
<td>IC</td>
<td>Impedance Cardiography</td>
</tr>
<tr>
<td>LF</td>
<td>Low Frequency</td>
</tr>
<tr>
<td>LF/HF</td>
<td>Low Frequency to High Frequency Ratio</td>
</tr>
<tr>
<td>LFnu</td>
<td>Low Frequency normalized units</td>
</tr>
<tr>
<td>MSNA</td>
<td>Muscle Sympathetic Nerve Activity</td>
</tr>
<tr>
<td>PAR-Q</td>
<td>Physical Activity Readiness Questionnaire</td>
</tr>
<tr>
<td>PEH</td>
<td>Post Exercise Hypotension</td>
</tr>
<tr>
<td>Prehypertensive</td>
<td>SBP ≥120-139/DBP≥80-89mmHg</td>
</tr>
<tr>
<td>RAAS</td>
<td>Renin-Angiotensin-Aldosterone System</td>
</tr>
<tr>
<td>SBP</td>
<td>Systolic Blood pressure</td>
</tr>
<tr>
<td>SV</td>
<td>Stroke Volume</td>
</tr>
<tr>
<td>TP</td>
<td>Total Power</td>
</tr>
<tr>
<td>TPR</td>
<td>Total Peripheral Resistance</td>
</tr>
<tr>
<td>VET</td>
<td>Ventilatory Threshold</td>
</tr>
<tr>
<td>VLM</td>
<td>Ventral Lateral Medulla</td>
</tr>
<tr>
<td>VO&lt;sub&gt;2max&lt;/sub&gt;</td>
<td>Maximal Oxygen Consumption</td>
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1.1 Rationale

Hypertension (>140 mm Hg systolic and >90 mmHg) is a leading risk factor for cardiovascular disease, stroke, renal disease and mortality. Currently, one in five adult Canadians has hypertension, and the prevalence of hypertension is steadily increasing worldwide (Canadian Hypertension Education Program, 2008). It is anticipated that hypertension will afflict up to a third of the worldwide population by the year 2020 (Kearney et al., 2005). Thus, cost-effective treatment strategies are essential to prevent and treat this disease.

Aging is associated with an increase in resting blood pressure. The typical resting blood pressure range is 125/85 mmHg (SBP/DBP) to 130/85 mmHg (SBP/DBP) in the “young-old” population (40-59 years old) (Chobanian et al., 2003), and half of this population is at risk for hypertension. Therefore, it is important to employ a well tolerated, low cost intervention, such as exercise, as a way to reduce risk of hypertension in this population.

The category of prehypertension (120 to 139 mm Hg systolic or 80 to 89 mmHg) is identified by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (7th report) in an attempt recognize those at risk for hypertension (Chobanian et al., 2003). Management of prehypertension through lifestyle changes can prevent hypertension and cardiovascular diseases (Pescatello et al., 2004). Prehypertensives show excellent blood pressure adaptation responses to acute and chronic exercise by decreases of 14/9 mmHg (SBP/DBP) and 6/5 mmHg post exercise, respectively (Cornelissen & Fagard, 2005; MacDonald, 2002)

The current treatment guideline for prehypertension is primarily non-pharmacological lifestyle changes such as regular exercise. However, the range of blood pressure responses after exercise was highly variable. A quarter of the individuals with higher than normal blood pressure were observed to be non-responsive to exercise training (Hagberg & Brown, 1995). Prehypertensive individuals differ markedly in the magnitude of Post Exercise Hypotension (PEH), ranging from SBP –27 to 9 mmHg and DBP -8 to 7 mmHg (Kenney & Seals, 1993).
Chronic aerobic exercise also produces a wide range of reductions in resting SBP from -20 to 9 mmHg, and DBP -11 to +11.3 mmHg (Cornelissen & Fagard, 2005).

The wide range in blood pressure variability after acute and chronic exercise is due to different physiological responses (e.g. neural, hormone, vasodilator substances) (MacDonald, 2002). Currently, no study has made a clear link between the blood pressure responses of acute exercise to those of chronic exercise. Thus, in our study, we are attempting to relate the acute physiological response after exercise to the effects of chronic exercise. Identifying the characteristics of those individuals who exhibit minimal resting blood pressure reduction after chronic exercise is an important step in preventing hypertension.
1.2 Primary Objectives

The primary objective is to examine the relationship between acute (AEA1) and chronic exercise.

1. To relate acute exercise responses (blood pressure, hemodynamic, autonomic function, baroreflex) to the magnitude of change in resting blood pressure following chronic exercise.

2. To examine whether the blood pressure reduction after acute and chronic exercise result from similar mechanisms in males and females.

1.3 Secondary Objectives

The secondary objective of the study is to study the effects of chronic exercise training on physiological responses after acute exercise.

1. To determine how exercise training influences the magnitude of PEH in prehypertensive males and females

2. To examine whether the acute exercise anti-hypertensive mechanisms will respond differently before and after chronic exercise training in males and females.
1.4 Primary Hypothesis

1. A larger reduction in the magnitude of blood pressure (BP), total peripheral resistance (TPR), heart rate variability (HRV), baroreflex sensitivity (BRS) after acute exercise will be correlated with the larger reduction in the magnitude of resting blood pressure after 8 weeks of aerobic training.

2. TPR will decrease after acute and chronic exercise. HRV and BRS will be reduced after acute exercise, while they will increase with chronic exercise. Arterial stiffness is expected to decrease after chronic exercise. Additionally, a larger reduction in the magnitude of TPR, BRS and HRV after acute exercise will be correlated with a larger improvement in the magnitude of TPR, BRS and HRV after chronic exercise, respectively.

1.5 Secondary Hypothesis

1. The magnitude of blood pressure reduction after a bout of exercise will decrease with chronic exercise training.

2. Chronic exercise training will result in different antihypertensive mechanisms being employed after acute exercise. Based on a previous study, endurance trained males achieved PEH through a reduction in CO while sedentary males achieved PEH through a decrease in TPR. Meanwhile, endurance trained females and sedentary females both achieved PEH through a reduction in TPR. A similar trend will also be observed with the males and postmenopausal females (45-60 years old) in this study. After the training, HRV and BRS will not attenuate as much compared with the acute exercise prior to training.
Chapter 2  
Literature Review

2.1 Blood Pressure Response to Acute Exercise

The decrease in resting blood pressure after acute exercise is called post exercise hypotension (PEH). PEH was first documented in 1897 in athletes after 400 yard dash, but it was not until 1981 (Fitzgerald, 1981) that the scientific community began examining the effects of PEH in individuals with high blood pressure (MacDonald, 2002).

PEH has been observed after various types of aerobic exercise such as walking, running, leg ergometry, and arm ergometry (Forjaz et al., 2000; MacDonald, 2002; Pescatello et al., 2004). Exercise using a larger muscle mass (legs versus arm) did not affect the magnitude of PEH observed after aerobic exercise (MacDonald, MacDougall, & Hogben, 2000b). These findings provide evidence to support the notion that the magnitude of PEH may be independent of the type of aerobic exercise involved. Additionally, PEH occurs following other forms of exercise such as resistance, isometric, and interval exercise; however, the PEH magnitude is different from aerobic exercise. Resistance and isometric exercise (~3/4mmHg) have reported a smaller PEH than aerobic exercise (~14/9mmHg) (Millar, MacDonald, Bray, McCartney, 2009; MacDonald, 2002). The PEH magnitude after interval exercise is comparable with aerobic exercise, but the anti-hypertensive effect seems to last longer (>30 minutes) following interval exercise (Lacombe, 2010; Guimaraes et al. 2010). Higher resting blood pressure, as well as exercise duration and intensity, have been linked to a longer duration of PEH response (Forjaz et al., 1998; MacDonald, MacDougall, & Hogben, 2000a; MacDonald, 2002). In patients with elevated BP (>130/90 mmHg), PEH lasts up to 12 hours post exercise, but PEH has been reported to persist for approximately 90 to 100 minutes in individuals with normal BP (110-120/70-79mmHg). In general, the largest decrease of PEH takes place during the first 1 to 2 hours after exercise (Pescatello et al., 2004).

2.1.1 Subject Characteristics and PEH

PEH has been observed in both males and females, as well as in young, middle aged, and older adults. The magnitude of PEH has shown to be similar between gender and training status (sedentary vs. athletes) (MacDonald, 2002). However, the magnitude of PEH is greater
in older individuals (40-60 years old), compared to younger (20 to 39 years old) individuals (Kenney & Seals, 1993). Forjaz et al., (2000) reported that PEH is greater in subjects with higher initial resting blood pressure. The average magnitude of PEH is more pronounced (SBP/DBP 14/9 mmHg) in pre-hypertensive individuals (SBP/DBP: 120-129/80-89 mmHg) compared with the average magnitude of PEH (8/9 mmHg) seen in normotensive individuals (110-119/70-79 mmHg) (MacDonald, 2002). Since aging is associated with increased resting blood pressure, this may partially explain the greater magnitude of PEH in older individuals (Kenney & Seals, 1993). It has also been speculated that normal functional compensatory mechanisms such as the baroreflex may limit the degree of PEH in younger individuals. Moreover, lower weight and BMI as well as higher VO$_{2peak}$ have been correlated to greater PEH in both younger and older individuals (Forjaz et al., 2000).

2.1.2 Acute Exercise Intensity, Duration, and PEH

A great debate exists on whether higher exercise intensities are responsible for greater magnitudes of PEH in young and older populations with pre-hypertensives and hypertensives. MacDonald, MacDougall, & Hogben, (1999) found no difference in the magnitude of PEH (~8/5mmHg) following 30 minutes of cycle ergometry at 50% and 75% VO$_{2peak}$ in young individuals. Using an even wider range of intensity, Forjaz, Matsudaira, Rodrigues, Nunes, & Negrao, (1998) also observed no significant changes in PEH (~6/3mmHg) following 45 minutes at 30, 50, and 80% VO2max in younger (20-30 years old) normotensive individuals. Similarly, Pescatello, Fargo, Leach, & Scherzer (1991) observed no difference in PEH (~10/6mmHg) after older individuals (35-45 years old) cycled 30 minutes at 40% and 70% VO2 peak. Conversely, larger magnitudes of PEH in young and old have also been observed following high intensity exercise (70-80% VO$_{2max}$) (Jones, George, Edwards, & Atkinson, 2006; Quinn, 2000).

Conflicting data also exists regarding exercise duration and PEH. Forjaz et al., (1998) reported a greater and longer lasting PEH following longer duration (45 minutes) exercises compared with a shorter duration (25 minutes) exercises, while MacDonald, MacDougall, & Hogben (2000a) reported that exercise duration (10, 30, 45 minutes) did not significantly change the magnitude of PEH.
Recently, evidence suggested that the magnitude of PEH may be related to the total work done rather than intensity or duration. Jones et al. (2006) reported similar magnitudes of PEH (-5+/−3mmHg) when the subjects exercised at 70% VO\textsubscript{2peak} for 30 minutes and 40% VO\textsubscript{2peak} for during which produced the same total work. However, the magnitude of PEH was smaller (-1 +/- 7 mmHg) when subjects were prescribed a low exercise dose (30 minutes at 40%VO\textsubscript{2max}). A greater exercise dose (more work done) can possibly increase the magnitude of PEH but not in prolonged exercise (150 minutes) (Liu, Thomas, Banks, Busato, & Goodman, 2009). This was shown in our laboratory, by extending the exercise dose and PEH response curve using two intensities (55± 5% and 75%±5% VO\textsubscript{2max}) of prolonged exercise (150 minutes). The results show that the magnitude of PEH was similar for either exercise intensity, but was significantly greater in the older group (SBP/DBP mmHg: O-MI -12.3 ±6.3 / -6.6 ±6.1; O-HI -15.1 ±11 /-9.8 ±6.8) compared with the younger group (Y-MI -1.2 ±7.1 / -.11 ±5.8; Y-HI -5.7 ±9.4 /-2.2 ±8.34) p<.05. A dose-response of intensity for PEH was not present in prolonged exercise. However, older individuals showed a greater PEH response compared with younger individuals when given the same exercise dose.

In summary, PEH can be observed after exercising at 40-80% VO\textsubscript{2max} for 10-45 minutes. A larger exercise dose (high intensity and long duration) may result in a larger magnitude of PEH. Despite known gender differences in blood pressure regulation (e.g. androgens), there is no observed difference between men and women in PEH (Reckelhoff, 2001). However, older individuals may experience a greater PEH response compared with younger individuals.

### 2.1.3 Potential Reasons for the Observed Difference

The lack of consensus among these studies may be attributed to the different subject characteristics mentioned earlier or the techniques used to determine PEH. For example, some investigators reported PEH as the lowest point of blood pressure while others reported PEH as the average blood pressure post exercise (Padwal et al., 2008). Different methods in measuring baseline blood pressure can also influence the magnitude of PEH reported. The blood pressure determined at a doctor’s office maybe higher compared to average ambulatory blood pressure due to “white coat syndrome” and similar effects may also have occurred when blood pressure was measured by study investigators (Alpert et al., 2006). The time of the day can also influence the magnitude of post exercise hypotension. PEH is reported to be
larger when exercise is performed in the morning (Jones, George, Edwards, & Atkinson, 2008). Therefore, it is important to keep all measurements consistent, for example resting blood pressure or PEH should be taken during the same time of day to avoid inaccurate results.

2.1.4 Post Exercise Hemodynamic Response

There are several hemodynamic (ie, cardiac output, stroke volume, total peripheral resistance) changes after exercise which result in PEH (Figure 2.1). Vascular resistance decreases as a result of vasodilatation and this leads to increased venous pooling. The “muscle pump” is also absent during passive recovery and further increases venous pooling. Consequently, this results in decreased central venous pressure, cardiac filling and sometimes stroke volume (Halliwill, 2001).

![Figure 2.1 Schematic overview of hemodynamic changes during post-exercise hypotension in comparison with the resting state. A. Systemic vascular resistance is decreased by ~ 30%. B. The associated rise in blood flow through the vasodilated regions contributes to an increase in venous pooling of blood. C. The “muscle pump” that reduces the degree of venous pooling during exercise is absent during passive recovery from exercise. D. The increase in venous pooling, in conjunction with the loss of plasma volume associated with exercise, leads to a reduction in central venous pressure (~ 2 mm Hg supine) and cardiac filling pressure (preload). E. Despite this fall in cardiac preload, stroke volume is maintained due to the reduction in cardiac afterload and a probable increase in cardiac contractility. The net result of these influences on the blood vessels and heart is that cardiac output is elevated. Thus, post-exercise hypotension (F) results from a sustained drop in vascular resistance that is not completely offset by a rise in cardiac output. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle. Description and Image From: Halliwill: Exerc Sport Sci Rev, Volume 29(2).April 2001.65-70.](image-url)
The hemodynamic responses (CO, SV and TPR) are influenced by resting blood pressure, age and training status. MacDonald (2002) reported that CO is increased post exercise in normotensives, whereas CO is decreased in hypertensives. TPR has been shown to decrease following exercise across age groups (20-65 years old); due to alterations in neural activity and vasodilator substance. However, one study by Hagberg, Montain, & Martin (1987) reported that PEH in older hypertensives (60-69 years old) is the result of decreased CO while peripheral vascular resistance remained unchanged. In endurance-trained men (18-35 years old), PEH is the result of a reduced CO, whereas in sedentary men it was the result of vasodilatation (Senitko, Charkoudian, & Halliwill, 2002).

The different hemodynamic responses of achieving PEH suggest that different mechanisms (neural, hormone, vasodilator substance) are at play. Thus, in order to make the link between acute and chronic exercise adaptation, it is important to understand the mechanisms responsible for PEH and the reduction of blood pressure after exercise training.

2.1.5 The Mechanisms of Post Exercise Hypotension

The mechanisms that cause PEH are multifaceted and complex because a reduced mean arterial blood pressure is a result of the interaction between cardiac output and peripheral vascular resistance. Different PEH mechanisms may be influenced by gender, age and training status (MacDonald, 2002). Currently, the combination of changes in neural activity and vasodilator substances has been suggested to be the potential mechanism of PEH (Figure 2.2) (Halliwill, 2001).

**Autonomic Nervous Activity**

Studies have shown that the amount of sympathetic nerve activity controlling vasoconstriction attenuates post exercise. Specifically, a reduction of about 30% in the outflow of sympathetic vasoconstrictor nerve activity has been reported (Halliwill, 2001). Older individuals and hypertensives have been reported to have higher muscle sympathetic nerve activity (MSNA). However, the suppression of MSNA after exercise is accompanied by PEH (Kenney & Seals, 1993). Furthermore, Floras et al., (1989) reported that the amount of sympathetic nerve
discharge is decreased up to 60 minutes after exercise in prehypertensive subjects. On the contrary, Hara & Floras, (1992) found that MSNA was not changed after exercise in normotensive humans. This suggests that the occurrence of PEH in normotensive individuals may not be caused by a reduction in MSNA. The decreased MSNA may be caused by altered baroreflex control after exercise (see section 2.1.6), however further study is needed in this area (Fadel, 2008; Halliwill, 2001).

**Vasodilator substances**

Reviews by Halliwill (2001) and Kenney & Seals (1993) listed several possible vasodilators that cause PEH such as nitric oxide, prostaglandins, adenosine, potassium ions, hydrogen ions, increased carbon dioxide, oxygen and internal osmolarity changes. The interactions of these vasodilators are depicted in Figure 2.2. It may be difficult to identify a single substance responsible for PEH as evidence suggests that several vasodilators may work together (Kenney & Seals, 1993; Notarius, Morris, & Floras, 2006). These vasodilators also work at different time periods after exercise. For example, adenosine is identified as a vasodilator that accumulates in the interstitial space during exercise. Its functions include vasodilating the blood vessel, and indirectly inhibiting sympathetic discharge by inhibiting norepinephrine release presynaptically. Notarius, Morris, & Floras (2006) demonstrated that early PEH is attenuated when adenosine is blocked using caffeine. This study provides evidence to suggest that other vasodilators may influence PEH at different times post exercise.

The increases in blood flow and the shear stress occurring during exercise increases nitric oxide release, which in turn leads to endothelium dependent vasodilatation. However, blocking nitric oxide production did not prevent PEH in humans. A recent study by Lockwood et al., (2005) showed that histamine contributes to PEH by acting on the H1 receptors. H1 receptors are primarily located on the vascular endothelial cells and can cause vasodilatation through the formation of local vasodilators such as nitric oxide. This study shows that many factors work together contributing to the production of vasodilators. Future research is needed to extend the understanding of the mechanisms of PEH.
Figure 2.2 Schematic overview of neural and local control of vascular tone related to post-exercise hypotension. During post-exercise hypotension, diminished vasoconstrictor responses and vasodilation may be produced by a host of potential vasodilator substances acting via presynaptic (A) or postsynaptic (B) modulation of the [alpha]-adrenergic pathway or by direct effects on smooth muscle relaxation (C). *Description and Image From:* Halliwill: Exerc Sport Sci Rev, Volume 29(2).April 2001.65-70.

**Arterial Stiffness**

Central and peripheral arterial stiffness reflect the mechanical properties of blood vessels within our torso and limbs, respectively. Arterial stiffness increases with age and cardiovascular disease. Central arteries are more susceptible to arterial stiffening than peripheral due to higher content of collagen and elastin. Increased arterial stiffness can increase blood pressure by 1) preventing the arterial tree (aorta and major arteries) from absorbing the pressure generated during systole and 2) speeding reflection of the arterial pulse wave so that it occurs during systole (London & Guerin, 1999). Several studies reported that hypertensives have a higher central and peripheral arterial stiffness than normotensives (Nichols, 2005; Seals et al, 2008; Hamilton, Lockhart, Quinn, & McVeigh, 2007).

Arterial stiffness decreases after acute exercise are mostly caused by decreased vascular muscle tone through the change in neural (sympathetic activity), and regional factors (vasodilator substances) (Naka et al., 2003; Sugawara et al., 2004). Changes in arterial wall properties and improved function of endothelial cells are most likely to be the result of chronic exercise which will be discussed in section 2.2.4. Decreased vascular stiffness and increased vasodilation causes a decrease in TPR and this can result in PEH. Kingwell, Berry, Cameron, Jennings, & Dart, (1997) showed that acute exercise (30 minutes of cycling,
60% VO$_{2\text{max}}$) can induce decreases in central (aorta) and peripheral (femoral to dorsalis pedis arteries) arterial stiffness at 30 minutes after exercise. Similarly, Naka et al., (2003) reported a decrease in upper and lower limb arterial stiffness (measured by PWV) by ~23% compared to baseline. This lasted for 60 minutes before returning to baseline. Arterial stiffness is determined by the properties of the arterial wall, as well as the vascular smooth muscle tone (Sugawara et al., 2004). Interestingly, arterial stiffness did not exhibit a decrease in the healthy (physically trained and untrained) (Aizawa & Petrella, 2008) and elderly hypertensive (60-70 years old) after acute exercise (Tabara et al., 2007). Despite this, PEH was still observed in both studies. This indicates that different mechanisms (i.e. decrease of CO) may be responsible for PEH. Unfortunately, hemodynamic measures were not assessed in these two studies. It is also unclear whether pre-hypertensives showed similar results. See Appendix B.4 for methods in assessing arterial stiffness.

2.1.6 Baroreceptors

**Background and Theory**

The function of baroreceptors is to maintain systemic arterial pressure when our body is faced with perturbations. The baroreceptors achieve this by altering the balance between sympathetic and parasympathetic activity in the heart and peripheral vasculature (Fadel, 2008). The densest innervations of baroreceptors are located in the carotid sinus and the aortic arch; however baroreceptors have also been found in the subclavian artery and proximal parts of the coronary arteries (Fadel, 2008; La Rovere, Pinna, & Raczak, 2008).

It is well known that baroreceptors are responsible for regulation of short-term fluctuations in blood pressure. Recently, baroreceptors (especially the carotid sinus baroreceptor) were shown to contribute to long term blood pressure regulation (Filippone & Bisognano, 2007). This section will focus on baroreceptors’ acute effects on blood pressure. See the section 2.2.5 for chronic blood pressure regulation by baroreceptors.

Blood pressure decreases under sudden orthostatic stress (such as sitting to standing) and causes the baroreceptors in the carotid sinuses and aortic arch to decrease their firing rate. This results in the propagation of the afferent signals through the ninth (glossopharyngeal) and tenth (vagus) cranial nerves to the nucleus tractus solitarii of the medulla (Filippone &...
Bisognano, 2007). Ultimately, this results in increased sympathetic activity and vagal inhibition leading to tachycardia, and increased cardiac contractility, vascular resistance and venous return (La Rovere et al., 2008). The alteration of the balance between SNS and PNS allows our body to maintain optimal blood pressure.

**Baroreceptor at Rest**

A schematic illustration of the operating range of the carotid sinus baroreceptor for normotensive and hypertensive is depicted in Figure 2.3 top panel. The hypertensive show a “shift” of the baroreceptor towards the right to adjust for the higher arterial blood pressure but they also show a narrower operating range compared to normotensive (Fadel, 2008) (Figure 2.3, top panel). The gain curve (Figure 2.3, bottom panel) depicts the sensitivity of the baroreflex. This is an important index for the overall evaluation of baroreceptor function in the current literature. In hypertensives, the baroreceptors have been found to be less sensitive (show by gain curve) to changes in blood pressure (Filippone & Bisognano, 2007; Vasquez, Meyrelles, Mauad, & Cabral, 1997). The impairment of baroreflex sensitivity can be both a consequence and a cause of hypertension (Vasquez et al., 1997). Currently, no baroreflex stimulus response curve can be found for prehypertensive patients; however, it can be speculated that the baroreflex stimulus response curve and gain curve fall somewhere between the normotensive and hypertensive curves.

Figure 2.3. A schematic illustration of the baroreflex stimulus-response curve. The upper panel illustrates the carotid baroreceptor curve of normotensive compared to hypertensive individuals. The bottom panel illustrates the maximum baroreflex gains. The figure is adopted from Vasquez et al., (1997).
**Baroreceptor During and After Exercise**

The baroreceptor function is not shut off during exercise but “resets” to a higher operating point due to the increased blood pressure. The “resetting” of the baroreceptor would shift the normotensive curve to the right and upward. The shift is greater with higher exercise intensities. However, unlike the hypertensive baroreceptor curve, the operating range and baroreceptor sensitivity (maximal gain) are maintained during exercise (Raven, Fadel, & Ogoh, 2006).

Following exercise, baroreflex sensitivity can decrease for up to 60 minutes before returning to baseline. Higher intensity exercise (such as heavy resistance exercise) has been shown to attenuate baroreflex sensitivity for a longer period (60 minutes) compared with lower intensity exercise (30 minutes) (Niemela et al., 2008). In one study, baroreflex sensitivity has been shown to exceed the pre-exercise values at 60 minutes after exercise (Legramante et al., 2002). This increase in baroreflex sensitivity may be linked to chronic adaptation of baroreflex sensitivity.

It has also been speculated that the downward shift of the baroreflex to maintain a lower blood pressure after exercise can ultimately result in decreased sympathetic outflow from the central nervous system (hence PEH) compared to pre-exercise level (Halliwill, 2001). Currently, the exact mechanism involved is still unclear. Nevertheless, baroreceptors do play a role in mediating PEH because Chandler and Dicarlo et al. (1997) cited in MacDonald, (2002) reported that PEH was only observed in rats with intact baroreceptors. More research in this area is needed to understand the relationship between baroreceptors and sympathetic flow after exercise.

### 2.1.7 Heart Rate Variability (HRV)

**Background and theory**

The autonomic nervous system influences the heart rate through the parasympathetic (PNS) and sympathetic nervous activity (SNS). HRV provides a noninvasive method to evaluate the dynamic interaction and balance between the SNS and the PNS. The assessment of HRV is commonly done using time-domain (R-R interval) or frequency domain (LF, HF) approaches.
The HF component of HRV is associated with increased parasympathetic modulation, and an increase in LF power is associated with increases in both parasympathetic and sympathetic activity (Heart Rate Variability Task Force, 1996). The LF/HF ratio is a indicator of sympathovagal balance, allowing heart rate variability to be used as an index of autonomic responses. Higher LF/HF ratio reflects sympathetic predominance (Borresen & Lambert, 2008).

One of the main reasons that PNS and SNS reflect the HF and LF, respectively, is due to the 1-2 second time delay of sympathetic responses compared with vagal response. This delay reflects differences in signaling through the muscarinic and β₁ receptors (Berntson et al., 1997). Muscarinic receptors respond to the parasympathetic signal (acetylcholine) which activates the potassium channel via signal molecules located within the cell membrane. In contrast, β₁ receptor mediates the sympathetic signal (epinephrine) which requires second-messenger activation of a protein kinase in the cytosol. The second-messenger signal eventually sends a signal back to the membrane to change the ionic current in Phase 4 cardiac depolarization. The differences in the rate of receptor action appear to underlie more rapid heart rate change with vagal compared to sympathetic stimulation (Berntson et al., 1997).

Hypertension and aging are associated with decreased overall HRV and a higher LF/HF ratio (Barantke et al., 2008; Terathongkum & Pickler, 2004). In newly diagnosed hypertensives, HRV is reported to be significantly lower in women compared with men (Pavithran, Madanmohan, & Nandeesha, 2008). The HRV responses indicate that females may have an increased cardiac sympathovagal balance at baseline. However, no data exists on the difference of HRV between prehypertensive males and females.

**HRV During and After Exercise**

During exercise, HRV has been shown to decrease proportional to exercise intensity in both genders, as well as in young and old individuals. The large increase in sympathetic activity is mostly seen in exercise intensities above 50-60%VO₂max and ventilatory thresholds (Kaikkonen, Nummela, & Rusko, 2007).

HRV recovery after exercise is also dependent upon exercise intensity. Higher intensity can lead to a longer (1-12 hours) HRV recovery time, while lower intensity exercise is associated
with a shorter recovery time (Terziotti, Schena, Gulli, & Cevese, 2001). Fit normotensive individuals have shown to have a faster HRV recovery time (5-10 minutes) compared with less trained normotensive participants (90 minutes) while exercising at the first ventilatory threshold (Seiler, Haugen, & Kuffel, 2007). No studies have been reported regarding the effects of gender on post exercise HRV recovery after acute exercise in pre-hypertensives.

2.2 Blood Pressure Response to Chronic Exercise

A recent meta-analysis of 72 randomized controlled trials showed that chronic aerobic training induced significant net reductions in resting and daytime ambulatory BP by 3.0/2.4 (SBP/DBP) mmHg and 3.3/3.5mmHg, respectively (Cornelissen & Fagard, 2005). Blood pressure reduction after exercise training was not influenced by age (Fagard, 1999; Hagberg, Park, & Brown, 2000). Higher resting blood pressure is associated a more pronounced decrease in blood pressure. The average blood pressure decrease for prehypertensives is 6/5mmHg. However, blood pressure response after chronic aerobic exercise is on a continuum as there is a wide range of response in resting SBP -20 to 9 mmHg and DBP -11 to +11 mmHg (Cornelissen & Fagard, 2005)

Chronic resistance (dynamic and isometric) training have also been shown to decrease resting blood pressure by approximately 3/3 mmHg in individuals with high blood pressure (Collier et al., 2009; Pescatello et al, 2004). Currently, the American College of Sports Medicine has recommended resistance training to supplement aerobic training in the treatment of high blood pressure (Pescatello et al, 2004). A few studies have shown that sprint interval and interval exercise can also be used to lower blood pressure. Whyte, Gill, and Cathcart (2010) reported that chronic sprint interval training (4 to 6 repeats of 30-second Wingate anaerobic sprints for 2 weeks) can reduce resting blood pressure from 127/80 to 121/71 mmHg. Similarly, chronic interval training (4 x 4:3 min at 90/70% HR\textsubscript{max}, 3 x per week for 3 months) can lower resting blood pressure from 125/66 to 120/66 mmHg (Tjonna et al., 2009). Currently, it is unknown how effective interval or sprint interval exercise is compared with aerobic exercise. Future studies are warranted in this area.
2.2.1 Modes of aerobic exercise

The recommended aerobic exercise for pre-hypertensive and hypertensive patients is dynamic aerobic exercise (3-5 sessions per week, 20-60 minutes duration at 40-70% VO$_{2\text{max}}$) (Khan et al., 2008). The types of exercises include: walking, jogging, stationary bicycling, or any combination of these activities. Since no statistical difference was found between the types of aerobic exercise and chronic blood pressure reduction (Whelton, Chin, Xin, & He, 2002), the types of exercise employed in this study will be walking/jogging.

2.2.2 Subject Characteristics and Blood Pressure Reduction

Gender

Conflicting data exists on gender and the magnitude of blood pressure reduction with training in 30-45 years old individuals. (Hagberg et al., 2000) reported that hypertensive females have a greater reduction in blood pressure compared to that in males (SBP: 14.7 vs. 8.7 mmHg). Meanwhile, Kelley & Kelley (1999) reported that a greater blood pressure decrease in males (SBP/DBP -4/-3 mmHg) was observed than females (SBP/DBP – 2/-1). However, older men and post menopausal women (>50 years old) were reported to respond similarly to endurance training with similar changes in blood pressure (~SBP/DBP-8/8mmHg) (Braith, Pollock, Lowenthal, Graves, & Limacher, 1994).

Ethnicity and Genetics

Ethnicity and genetics both play a factor in blood pressure response to training. Hypertensive Asian and Pacific islanders (SBP: 11.7 mmHg) showed a greater reduction in resting systolic blood pressure with exercise training than Caucasians (SBP: 8.0 mmHg), while the magnitude of diastolic blood pressure is similar (DBP: 6.8 vs. 6.7) (Hagberg et al., 2000). Brandon & Elliott-Lloyd (2006) reported that African American women had a smaller reduction in blood pressure (SBP/DBP: -5.7/3.0mmHg) compared with Caucasian women (SBP/DBP: -11.3/3.6 mmHg) following a 16-week walking program. However, limited information is available on male African-American patients with hypertension or pre-hypertension.

The effect of genetics on the blood pressure response to exercise is still a relatively new field of research. Several genes have been identified as having an impact on blood pressure. The
most important of these genes are the angiotensin converting enzyme (ACE) II genotype, Lipoprotein lipase (LPL) HindII+/+ or +/- genotype. Individuals with these genotypes showed a greater decrease in BP (SBP/DBP: -10±3/-10±2mmHg) compared with similar hypertensives having the ACE DD and LPL HindIII-/- genotype (SBP/DBP: -5±3/-1.5±2mmHg) following 9 months of endurance exercise (Hagberg, Ferrell, Dengel, & Wilund, 1999). Future studies are necessary to elucidate the effects of ethnicity and genetics on blood pressure reduction after exercise.

2.2.3 Exercise Training Frequency, Duration and Intensity on Chronic Blood Pressure

The blood pressure response has been investigated with a wide range of exercise frequency (1-7 days per week) and duration (10-60 minutes). Jennings et al. (1991) and Whelton et al. (2002) reported that higher exercise frequencies per week (>5 times/week) and longer exercise duration per session (>60mins) did not produce a greater reduction in blood pressure in hypertensive patients compared with fewer bouts (3-4 times/week) and shorter exercise durations (30-60mins). This finding was later confirmed by Ishikawa-Takata, Ohta, & Tanaka (2003) showing that exercise frequency (1-2 or 3-4 or >5 times/week) did not affect the magnitude of decrease in blood pressure in hypertensives while the exercise intensity (50% VO$_{2\text{max}}$) was kept constant. The authors also reported that the magnitude of BP reduction was greater in the group who exercised 61 to 90 min/week (SBP/DBP: -12/-7 mmHg) than in the group who exercised 30 to 60 min/wk (SBP/DBP: -6.5/-6 mmHg). Exercising more than 120 min/week did not result a larger reduction in blood pressure compared with exercising 61 to 90 min/week. Currently, the Canadian Hypertension Education Program recommends similar aerobic exercise guidelines (four to seven days per week of aerobic exercise for 30-60 minutes) for pre-hypertensives and hypertensives (Khan et al., 2009). Thus, in our study, participants will be exercising four times per week for 30 minutes per session producing 120 minutes per week.

Exercise at an intensity less than 70% VO$_{2\text{max}}$ results in an approximately 50% greater reduction in blood pressure (SBP) compared to training at intensities greater than 70%VO$_{2\text{max}}$ (Hagberg et al., 2000). Fagard (2001) reported that exercise at low exercise intensity (40% VO$_{2\text{max}}$) did not influence blood pressure reduction compared to moderate exercise intensity
However, it has been shown that moderate intensity exercise (60-75% VO_{2\text{max}}) is required to increase in VO_{2\text{max}} (Gormley et al., 2008). Therefore, 65% VO_{2\text{max}} has been chosen as the exercise intensity in the current study.

A meta-analysis by Whelton et al. (2002) has shown that previous exercise training studies have employed programs varying in duration from 4 weeks to 54 weeks. The majority of the blood pressure reduction takes place during the first 10 weeks of training (Whelton et al., 2002). Meredith et al., (1990) reported that a decrease in resting blood pressure can occur as early as 1 week after aerobic training with no further significant reduction occurring during week 3 to 4. Thus, the beneficial effect of reduced blood pressure for pre-hypertensives is observed rapidly, which can be useful in motivating pre-hypertensive and hypertensive individuals to continue exercising (Hagberg et al., 2000). According to the operant conditional model, the immediacy of the blood pressure reduction associated with exercise may prevent extinction behavior (regular exercise), which occurs when the award (anti-hypertensive effects) does not follow the behavior (exercise) (Tucker, Sigafoos, & Bushell, 1998). The current training length selected for this study is 8 weeks to allow for chronic adaptation of blood pressure, the nervous system, vascular structure and renin-angiotensin-aldosterone system.

### 2.2.4 Mechanisms responsible for chronic blood pressure reduction

Mean arterial pressure (MAP) is the product of cardiac output (CO) and total peripheral resistance (TPR). A decrease in any one of these variables can cause a reduction in MAP. In a meta-analysis involving 72 trials, Cornelissen & Fagard (2005) reported that blood pressure reduction after chronic exercise is resulted from TPR (7.1%) reduction, which was not met by an increase in CO. The main mechanisms involved in these hemodynamic changes are the autonomic nervous system, vascular structure, endothelial function and the renin-angiotensin aldosterone system.

**Autonomic nervous activity**

The activation of sympathetic nerve activity (SNA) results in the release of (Smith & McFall, 2005) norepinephrine (NE), which mediates vasoconstriction and ultimately increases TPR.
The recording of efferent SNA in humans by microneurography shows that central SNA at rest is not changed after training in normotensive individuals (Carter, Ray, Downs, & Cooke, 2003; Ray & Carrasco, 2000). Currently, results regarding reductions in SNA activity remain inconclusive in hypertensive or prehypertensive individuals after training (Pescatello et al., 2004). However, a reduction (29%) of plasma NE after training has been reported in hypertensives (Cornelissen & Fagard, 2005; Dubbert, Martin, Cushman, Meydrech, & Carroll, 1994). Furthermore, the decrease of NE release rate is found to be associated with reduced blood pressure after training in older (63±7yrs) hypertensives (Brown, Dengel, Hogikyan, & Supiano, 2002). Additionally, evidence from changes in baroreflex sensitivity and HRV indicates that sympathetic nervous activity is decreased and parasympathetic is increased after exercise training (Hamer, 2006). A detailed description of exercise training and associated changes in baroreceptor function with HRV are in section 2.2.5 and 2.2.6 respectively.

Insulin also stimulates the sympathetic nerve activity in humans; thus, hyper-insulinemia and insulin resistance have been associated with hypertension and activation of SNA (Scherrer & Sartori, 1997; Scherrer & Sartori, 2000). Kohno et al. (2000) demonstrated a significant correlation between a reduction in arterial pressure, plasma NE and increased insulin sensitivity after 4 weeks of aerobic training in hypertensive subjects.

This evidence suggests that a change in autonomic nervous system activity (decreased SNA and increased PNA) plays a role in the reduction of blood pressure after training. However, there are multiple factors (i.e., baroreceptor, insulin sensitivity) influencing the activity of the autonomic nervous system.

**Vascular Structure**

Increased arterial stiffness results in a decreased ability for blood vessels to dilate, leading to increased TPR and systolic BP (Hamer, 2006). Cross-sectional studies have shown that fitness level was inversely related to arterial stiffness in middle-aged (38-57 years) and older (58-77 years) men and women (Tanaka et al., 1997; Tanaka et al., 2000; Vaitkevicius et al., 1993). Longitudinal training studies have shown a decrease in arterial stiffness observed with training. Aizawa, Shoemaker, Overend, Petrella, (2009) reported that following 24 weeks of
training (walking/jogging, 30 min, 4-6 times per week, 70-75% of HR\text{max}), the arterial stiffness (\beta stiffness index) of carotid artery decreased by 20% in prehypertensives. Similar improvements have also been shown in hypertensive individuals (Aizawa & Petrella, 2008). The shortest training program to show a decrease in both central and peripheral measures of arterial stiffness in male and female pre-hypertensives consisted of 4 weeks of endurance training (30 min, 3 times per week, 65% VO\text{2peak}) (Collier et al., 2008). However, in healthy young males, 6 days of aerobic training (cycling at 65\%VO\text{2peak}, 2 hours per day for 6 days) was sufficient to reduce arterial stiffness (CPWV: 5.9±.5 vs. 5.4 ±.8 m/s; PPWV: 9.7±.8 vs. 8.9±1.3m/s) (Currie, Thomas, & Goodman, 2009).

The decrease in arterial stiffness is a function of decreased sympathetic influence (mentioned earlier) and changes in vascular structure and composition. This includes reduced thickness of the intimal and medial arterial layers (Ben Driss, Benessiano, Poitevin, Levy, & Michel, 1997), increased lumen diameter (Miyachi et al., 2001) and aortic elastin content, and reduced calcium depositions (Matsuda, Nosaka, Sato, & Ohshima, 1993).

In addition, rarefaction of the microcirculation in a variety of tissues is associated with hypertension. It is possible that increased vascularisation of skeletal muscle following training may increase microcirculation, leading to reduced TPR (Feihl, Liaudet, & Waeber, 2009). However, further investigation is required in this area.

**Endothelial Function**

The endothelium produces several molecules (e.g., nitric oxide (NO), Endothelin-1(ET-1)) that stimulate the smooth muscle surrounding the blood vessels to vasodilate and vasoconstrict (Hamer, 2006). Exercise training is associated with improved endothelium-dependent dilation resulting in decreased TPR, and, ultimately, decreased blood pressure. Despite declining endothelial function with aging, chronic exercise training has been shown to be effective in improving endothelium-dependent vasodilatation. Endothelium-dependent vasodilatation in older men and women (55-65 years) has been reported to be comparable to that in healthy younger and middle-aged individuals after three months of aerobic training (DeSouza et al., 2000). Improved endothelium-dependent vasodilatation has been reported after as few as 7 days of endurance training in pigs (McAllister & Laughlin, 1997). However,
it is unclear whether this would also occur in pre-hypertensive humans. Since the time-course change of endothelial function is also unknown, more research in this area is needed.

Improvement of vasodilatation is associated with the chronic shear stress on the endothelial cells from exercise, which can then cause deformation and trigger an increase in the NOS gene expression and ultimately lead to enhanced bioavailability of NO (Manfredini et al., 2009). ET-1 (a vasoconstrictor substance) sensitivity has shown to decrease in endurance-trained individuals, which may also contribute to enhanced vasodilatation (Manfredini et al., 2009). Maeda et al., (2001) reported that following an 8 week training program, NO was found to increase in healthy men, while ET-1 decreased. All in all, endothelial function can be improved in both genders and across age groups. This can play a significant factor in the reduction of blood pressure.

**Renin-Angiotensin-Aldosterone System (RAAS)**

RAAS is regulated by the kidneys to control blood volume. This is particularly important because increased blood volume can increase blood pressure. RAAS regulates blood pressure by the secretion of the enzyme renin from the juxtaglomerular apparatus in the kidney to activate angiotensin I and II. Angiotensin II (AII) causes vasoconstriction of the blood vessels (increase in BP) and the release of aldosterone from the adrenal cortex. Aldosterone is a steroid hormone that stimulates the reabsorption of salt in the kidneys and thus increases blood (plasma) volume (Rush, Aultman, 2008).

Plasma volume increases in healthy normotensives (Convertino, 1991), while decreases in hypertensives after with chronic exercise training (Kiyonaga, Arakawa, Tanaka, & Shindo, 1985; Urata et al., 1987). The decreased plasma volume is caused by plasma renin reduction (20%) (Fagard & Cornelissen, 2007). However, the reduction in blood volume is not the only mechanisms responsible for long-term blood pressure reduction as some researchers did not observe a plasma volume reduction after endurance training in hypertensives despite a reduction in resting blood pressure (Hagberg et al., 1987; Tanaka et al., 1997). Aldosterone level has also found to decrease after 6 months of aerobic training in Caucasian participants, but not in African-American hypertensives (Jones et al., 2007). This decrease is correlated with reduction of blood pressure and TPR. No study has examined the effects of exercise on
renin and aldosterone level in prehypertensives. Recent evidence suggests the changes occurring with RAAS may relate to the function of baroreceptors (see section 2.2.5) (Lohmeier, Hildebrandt, Warren, May, & Cunningham, 2005). However, more study is still needed to further explore this area and confirm this hypothesis in prehypertensives.

2.2.5 Baroreceptors’ Function

Baroreceptors’ function in long-term blood pressure regulation has always been questioned. However, in the past decade, more evidence has been found to support the role of baroreceptors in long term blood pressure regulation. The carotid sinus baroreceptor has shown to be important in regulating long term blood pressure. This was established through observing increased chronic arterial blood pressure in patients with denervated carotid sinus (Smit et al., 2002).

Baroreceptors regulate chronic blood pressure mainly through the kidney and the posterior pituitary gland. For example, an increase in blood pressure or volume increases the carotid sinus baroreceptor firing rate, resulting in the activation of parasympathetic nuclei and the inhibition of sympathetic nuclei (Filippone & Bisognano, 2007). The diminished sympathetic outflow to the heart, kidneys, and peripheral vasculature and increased parasympathetic tone to the heart results in a fall in peripheral vascular resistance, heart rate, stroke volume, and blood pressure. The decreased renal sympathetic tone reduces the activity of the renin-angiotensin aldosterone system (RAAS), which results in a decrease in the retention of salt, water, and angiotensin II-mediated vasoconstriction (Lohmeier et al., 2005). Increased baroreceptor activity also results in decreased vasopressin production from the posterior pituitary, which results in the reduction of systemic vasoconstriction and renal water retention (Filippone & Bisognano, 2007). Conversely, a reciprocal effect on the autonomic nervous system would be observed if blood pressure or volume decreased (La Rovere et al., 2008).

**Baroreceptor Function after Chronic Exercise**

As mentioned in the Baroreceptor and Acute exercise section earlier (2.1.6), baroreceptor sensitivity (Maxgain), a measure of baroreceptor function, is reduced in individuals with chronic elevated blood pressure. In the first study that investigated the effects of endurance training on baroreflex sensitivity and blood pressure in borderline hypertension, Somers,
Conway, Johnston, & Sleight (1991) found that endurance training (4 months, 20 minutes per session, 3 to 4 times per week) increased baroreflex sensitivity, accompanied by the lowering of resting (day time ambulatory blood pressure) blood pressure; however, there was no evidence for a causal relation. In a similar but more recent study, Laterza et al. (2007) observed that an increase in baroreflex sensitivity was significantly correlated with reduced MSNA and BP in hypertensive patients. MSNA was normalized to a level similar to that of normotensives. This shows that baroreceptor function may play a role in controlling peripheral resistance; however the exact mechanisms are still unclear. Several other studies have also shown chronic aerobic training as an effective method for increasing baroreceptor sensitivity in males and females, young and old, using low to moderate intensities (30-70% VO$_{2peak}$; 3-5 days per week) (Hua, Brown CA, Hains, Godwin, & Parlow, 2009; Ueno & Moritani, 2003). However, one study by Loimaala, Huikuri, Oja, Pasanen, & Vuori, (2000) reported no change in baroreceptor sensitivity or HRV after 5 months of low (55% VO$_{2peak}$, 4-6 times per week, 30 minutes per session) or high intensity (75% VO$_{2peak}$, 4-6 times per week, 30 minutes per session) aerobic training. Unfortunately, resting blood pressure before and after training was not reported; thus, it remains inconclusive as to whether an increase in baroreflex sensitivity is always accompanied by a decrease in resting blood pressure.

Younger individuals (29±6 yrs) show higher baroreflex sensitivity (baroreflex gain) compared with older individuals (71± 3 yrs). With exercise training in older individuals, baroreceptor sensitivity (baroreceptor gain), along with resting blood pressure, showed a peak adaptation following 3-6 months. However, the baroreflex gain never achieved values equivalent to those for younger individuals even after a year of training (Iwasaki, Zhang, & Zuckerman, 2003). Nevertheless, the magnitude of the adaptation of these variables to identical training was similar between older and younger individuals. It was also shown that higher doses of exercise training did not lead to greater enhancement of baroreceptor changes in young and older individuals (Iwasaki et al., 2003; Okazaki et al., 2005). The earliest signs of an increase in baroreflex sensitivity to date was after 4 weeks (3 days per week, 30 minutes per session at 65% VO$_{2peak}$) of aerobic training in pre-hypertensive males and females (33-60 yrs old) (Collier et al., 2009).
There are two possible mechanisms responsible for the exercise induced increase in baroreceptor sensitivity. One is the increase in vessel wall compliance of the carotid artery, which affects the stretch-sensitive baroreceptors embedded in the carotid artery wall. The second is the neural alteration of the baroreflex-arc located in the nucleus tractus solitarius (Komine, Sugawara, Hayashi, Yoshizawa, & Yokoi, 2009; Filippone & Bisognano, 2007). Regular aerobic exercise in young men (19-27 yrs) increases arterial baroreflex sensitivity through changes in the neural component of the baroreflex arc and not by alterations in blood vessel wall compliance of the carotid artery (Komine et al., 2009). On the contrary, older individuals may improve baroreflex sensitivity through both neural (baroreflex arc) adaptation and a decrease in carotid arterial compliance (Hunt, Farquhar, & Taylor, 2001; Seals, 2003). Neural adaptation of the baroreceptors is speculated to take place first before changes to arterial vascular structure (ie, elastin, calcium deposition) (Komine et al., 2009). Thus, it may be possible that BRS was improved before the four weeks of training was completed (Collier et al., 2009). If this is the case, then the baroreflex can be a contributor of the initial reduction of blood pressure in the initial weeks of training.

2.2.6 Heart Rate Variability (HRV)

As mentioned earlier, high blood pressure is associated with decreased HRV. However, some studies have found that aerobic training decreases heart rate (Bonaduce et al., 1998; Sandercock, Bromley, & Brodie, 2005; Yamamoto, Miyachi, Saitoh, Yoshioka, & Onodera, 2001). However, in frequency domain, difference in total power (TP), HF, and LF due to training is less clear. Some studies reported HF (Sandercock et al., 2005) and LF (Iwasaki et al., 2003) to increase after training, while others reported a decrease in LF (Tulppo et al., 2003) or no change at all (Loimaala et al., 2000). A decrease in resting blood pressure after training did not always relate to an alteration in LF and HF power (Cornelissen, Verheyden, Aubert, & Fagard, 2009) and vice versa (Yamamoto et al., 2001).

Discrepancies between studies also make it difficult to determine which age groups have the greater HRV response to training. However, it has been found that heart rate variability (RR interval variability) was low in the sedentary seniors (71 ± 3 yrs) but was preserved in age-matched Master athletes (athletes who have been training for decades) compared with younger individuals (29±6 yrs) (Okazaki et al., 2005). This shows that regular exercise is able
to preserve the autonomic function. Sandercock et al. (2005) and Carter, Banister, & Blaber (2003) reported that younger individuals had a greater increase in HF compared with older individuals after undergoing similar exercise training. Conversely, Leicht, Allen, & Hoey, (2003) observed older individuals had a significant increase in HF, but younger individuals did not. Genovesi et al., (2007) showed that females had a greater improvement in HRV variability, while Sandercock et al., (2005) reported that there was no gender difference in HRV response to exercise training.

Inconsistent methodologies between studies may explain these inconclusive results; for example, body positions (supine/semi-supine), the duration of heart rate variability recordings (6 minutes to 24 hours), and differences in training duration (4 to 12 months), frequency (3 to 7 days) and intensities (70-90% of Heart rate max) can all affect HRV (Borresen & Lambert, 2008; Heart Rate Variability Task Force, 1996). Furthermore, the quantification of HRV measurement present challenges because it is highly variable between individuals. This variability has made it difficult to identify a normal range of HRV in different age and sexy groups for potential health care application. Nevertheless, some studies have tried to quantify normative values in a population study (Zhang, 2007) but normative HRV values have yet to be determined.

Despite the challenges with HRV measurements, a meta-analysis by Sandercock et al. (2005) found that the changes in RR interval and HF were greater in longer studies (>12 weeks) compared with shorter training studies (<12 weeks). However, there was a large increase in HF early in the training before 12 weeks, whereas RR interval tended to increase more uniformly. This may suggest that a higher vagal modulation is responsible for initial increases in RR interval, but factors such as changes in heart geometry may be responsible for further adaption. Additionally, in middle-aged subjects (61.2 ± 4.3 yr), greater improvements in vagal control were observed when more time was spent in moderate to high intensity activity or when daily energy expenditure was increased to 600 kcal/day (Buchheit et al., 2005).

Currently, HRV (RR interval variability) in middle-aged subjects (61.2 ± 4.3 yr) shows continued improvement with increased training dose and approaches the same magnitude in the young (29 ±6 yrs) at baseline after heavy doses of training for 1 year (Okazaki et al., 2005). The earliest change in HRV (increased HF) in pre-hypertensives was reported
following 4 weeks of aerobic training (30 min of treadmill, 3 days per week at 65\% VO_{2\text{peak}}) (Collier et al., 2009).

However, the time-course of the effects of training (3 times per week, 40 minutes per session at 60-70\% VO_{2\text{max}}) on reducing blood pressure reached significance in a week, with no further fall occurring during the subsequent eight training visits (Meredith et al., 1990). This is more rapid than the changes in HRV reported by Collier et al. (2009), and therefore suggest that HRV may change before 4 weeks, or that other mechanisms (i.e. endothelial function) are involved in the reduction of chronic blood pressure during the early phase of training.

### 2.3 The Interaction of Acute and Chronic Exercise Effects

There are few studies available examining the link between PEH and long term anti-hypertensive adaptation after exercise training. Haskell, (1994) has proposed patterns of acute exercise effects (Figure 2.4). Based on these patterns, several authors have tried to make the link between acute and chronic exercise.

Pattern 1) Exercise reduces risk factor (i.e. blood pressure) acutely and the effect of exercise dissipates overtime; therefore, no benefits are observed in the next session. This pattern may not apply to blood pressure response because a reduction in blood pressure is observed after three exercise sessions (Meredith et al., 1990)

Pattern 2) The acute effect accumulates over exercise sessions and this produces a greater effect.

Pattern 3) Exercise training increases exercise capacity which then allows the person to exercise for a longer period of time and this results in a greater acute effect.

A review by Thompson et al. (2001) suggested that some, if not all, of the hypotensive benefits associated with endurance training may be the result of the effects from acute exercise. The authors argued that a reduction in chronic blood pressure is seen in as little as three sessions of aerobic activity (Jennings, Kenny, & Sigal, 2002). Once the training stops,
however, the hypotensive effects subside quickly to pre-exercise training levels after only 1-2 weeks (Meredith et al., 1990). Thus, the immediacy by which blood pressure changes suggests the possibility of pattern 2 occurring. However, the longest PEH from an acute exercise last up to 12 hours before returning to pre-exercise level (MacDonald, 2002; Pescatello et al., 2004). The majority of the training studies have at least 24 hours, sometimes 46 to 72 hours, in between training sessions. According to the literature, even the longest response by our body to a single bout of exercise would subside after 24-48 hours (Figure 2.5). Therefore, this model cannot fully explain the link between acute and chronic exercise effects.

Pattern 3 links the acute and chronic exercise effects by suggesting that it is the increase in a person’s exercise intensity and duration that leads to a magnified PEH providing greater and longer lasting PEH (Hamer, 2006). Studies have shown that higher exercise intensity (Pescatello et al., 2004) and longer duration (Forjaz et al., 2000) may lead to a greater and longer lasting PEH. However, this is not reported by all studies (Hamer, 2006; MacDonald, 2002). Additionally, the progression of exercise frequency or intensity in exercise training studies did not appear to influence the chronic blood pressure effect (Iwasaki et al., 2003; Whelton et al., 2002). Therefore, it is unlikely that the chronic benefits of exercise training can be derived from the ability to exercise more vigorously (Hamer, 2006).

Additionally, it was demonstrated that chronic exercise trained individuals achieved PEH differently from sedentary individuals. PEH was achieved as a result of reduced cardiac
output, whereas vasodilatation was the primary mechanisms in sedentary men (Senitko et al., 2002). Other studies have shown that the reduction of chronic blood pressure is associated with decreased arterial stiffness, increased baroreflex sensitivity and endothelial functions (Hamer, 2006; Pescatello et al., 2004). These observations strengthen the hypothesis that chronic reduction of blood pressure is not only the result effect of the acute exercise response, but rather chronic adaptations.

Reductions in blood pressure due to training were seen during the initial weeks of the exercise regime (Meredith et al., 1990). The earliest adaptations which can be associated with the reduced BP may be baroreceptor and endothelial function. Improved baroreceptor function decreases sympathetic input. Enhanced endothelial function is associated with improved vasodilatation and causes a decrease in TPR. According to the timeline, they are one of the earliest to change with training (Figure 2.6).

Currently, no study has made a clear link between the acute and chronic exercise effects. As seen in Figure 2.5 and 2.6, many mechanisms are responsible for blood pressure regulation and all mechanisms change with exercise training. By studying the relationship between blood pressure after acute and chronic exercise, a clearer link may be established. For example, if individuals who do not exhibit acute effects of exercise (PEH) also do not show a reduction in chronic blood pressure, then this would lead to speculation about common mechanisms of action. Once the link of mechanisms responsible is understood clearly, we can then more confidently identify those exercise “responders” versus “non-responders”.
**Acute Exercise Response**
Based on: (30-45 minutes, 50-65% VO\textsubscript{2max})

**Figure 2.5:** Acute exercise effects after one bout of exercise. The color and the pattern of the lines are associated with the color and the pattern of label on the right hand side. The square-dot lines indicate uncertainty over the time course of the response.
Chronic Exercise Training Response
Based on: (3-4 times/week, 30-45 minutes, 50-65% VO$_{2\text{max}}$)

Figure 2.6: Chronic exercise effects after exercise training. The colour and the pattern of the lines are associated with the colour and the pattern of label on the right hand side. The square-dot lines indicate uncertainty over the time course of the response.
Chapter 3
Experimental Design and Methods

3.1 General Study Design

17 sedentary pre-hypertensive males (n=8) and females (n=9) ages of 45 to 60 years old were recruited. All subjects were non-smokers, free of cardiovascular diseases, diabetes and were not taking any medications. Written informed consent was obtained and PAR-Q was completed by all subjects. This study was approved by the University of Toronto ethics board and conformed to the Helsinki Declaration on the use of human subjects for research.

Prior to the study enrolment, all participants underwent an initial baseline screening to determine their resting blood pressure. Participants continued on only if their resting blood pressure was within the prehypertensive range (SBP from 120 to 139 and DBP from 80 to 89 mm Hg). An exercise stress test was then carried out to determine participants’ fitness level. Additionally, two acute exercise assessments (AEA) were administered before and after the training to assess physiological markers (blood pressure, baroreceptor sensitivity, heart rate variability, arterial stiffness) in response to acute exercise. An 8-week walking/jogging program (4 times per week at a heart rate equivalent to 65% VO\textsubscript{2peak}, 30 minutes per exercise session) was prescribed to all participants (Appendix C). Three out of the four training sessions were performed at the University of Toronto Athletic Center under the supervision of study investigators. The fourth session was performed by the participant unsupervised. All training sessions were recorded in the weekly training log (Appendix D). Additionally, all participants were assigned a heart rate monitor watch (Polar 810i) to ensure that they are exercising at the assigned intensity.

3.2 Participants

Participants were recruited through advertisements, word of mouth and physician referral. All participants recruited were untrained which was defined by a score of three or less using the Rapid Assessment of Physical Activity survey (Appendix G). The female participants recruited were postmenopausal (for at least 2 years) as they show a higher risk for hypertension and cardiovascular disease compared to premenopausal women (Wilmore, 2001). Also, the resting blood pressure has shown to be more stable in postmenopausal women due the lack of menstrual cycle.
3.3 Baseline Screening

Resting blood pressure, maximum oxygen consumption (VO_{2max}) and anthropometrics (BMI, waist-hip ratio) were determined at the baseline screening during participants’ first visit.

3.3.1 Determination of Resting Blood Pressure

Participants were asked to sit in a quiet room by themselves for 20 minutes, and an automated brachial blood pressure cuff (Tango, Suntech, NC, USA) took their blood pressure reading during the last 10 minutes. Blood pressure was taken every 2 minutes for a total of 5 readings. The highest and lowest readings were disregarded, and an average of the remaining three readings was used to determine resting blood pressure (Padwal et al., 2008). In order to ensure the resting blood pressure reliability at baseline, resting blood pressure measurements were carried out on two days; first during the baseline screening and second with the acute exercise assessment (AEA) 1. Similarly, two resting blood pressure measurements (at the end of week 8 and AEA2) were recorded after the chronic exercise.

3.3.2 Exercise Stress Test

A graded treadmill maximum oxygen consumption assessment was administered. Expired gases were collected and analysed using a calibrated metabolic cart (Moxus, AEI Technologies, IL, USA). Heart rate (HR) was measured using a heart rate monitor (Polar 810i). The subjects would select the treadmill speed, while the incline was increased by 2% every 2 minutes until the 8th minute, after which it was increased by 1% every minute (Shephard et al., 1968). Additionally, a 6-lead ECG (Biopack) was used to monitor cardiac activity to ensure the safety of the participants. VO_{2max} was determined either by the plateauing of VO_{2} values as exercise work rate increases, reaching the age-predicted maximum HR or achieving a respiratory exchange ratio of 1.15 or higher.

3.4 Acute Exercise Assessments (AEA)

Two acute exercise assessments (AEA) were carried out. AEA 1 referred to the exercise assessment performed within 2 to 3 days before the training and AEA 2 referred to the exercise assessment within 2 to 3 days after the training. AEA1 would address our primary objectives, which is the assessment of the relationship between acute and chronic exercise. AEA2 would
help answer the secondary objectives, which is whether acute exercise response will be altered after chronic exercise training.

Participants were required to abstain from caffeine for 12 hours and vigorous physical activity 48 hours prior to the AEAs. All AEAs were performed during late afternoon (5-9 pm) to avoid diurnal blood pressure variation. The AEA consisted of 5 stages (Arterial stiffness, Preparation, Data collection 1, Exercise, Data collection 2) and took 95 minutes (Appendix E). Arterial stiffness was measured using a tonometer during the initial 10 minutes. Afterwards, electrodes, finger cuffs, and brachial arm cuffs were applied to the participants during Preparation. Data collection 1 took 20 minutes, during which the participants remained in a seated position. The exercise portion on the treadmill matched the same intensity (heart rate which corresponds to 65±5% VO2max) and duration (30 minutes) as the training session in order to maintain consistency. Data collection 2 was similar to data collection 1 except the total collection time was 30 minutes.

3.5 Time Course of Changes in Resting Blood Pressure during Training

Resting blood pressure was measured using an automated sphygmomanometer (Tango, Suntech, NC, USA) at the end of weeks 1, 3, 5 and 8 to determine the response to training. The same protocol of determining resting blood pressure at baseline was used. However, the resting blood pressure was taken 48 hours after the previous exercise training session to avoid PEH response from the acute exercise. All measures of blood pressure were taken during late afternoon (5-9 pm) to avoid diurnal blood pressure variability.

3.6 Measurements

3.6.1 Blood Pressure

The Finometer MIDI (Model-2, Finapres Medical Systems BV, Arnhem, Netherlands) was used to record continuous beat to beat blood pressures from the right hand (third digit) at while fixed at heart level. In addition, brachial blood pressure was also recorded at two minutes interval using an automated sphygmomanometer (Tango, Suntech, NC, USA) at the left arm. The use of automated sphygmomanometer allows us to ensure the accuracy of our measurements and adjust for any Finometer drift associated with long recordings.
The decrease of blood pressure after acute exercise, known as PEH, was expressed as peak blood pressure decrease (-BP_peak) and area under the curve. -BP_peak decrease is the largest decrease from the pre exercise value (last 5 minutes during collection 1 of AEAs) in SBP or DBP post exercise during a five minute rolling average. Area under the curve is a trapezoid method used to quantify the area under the SBP or DBP curve (delta values). The post acute exercise blood pressure response was divided into 30 equally spaced periods and the sum of their trapezoids determined in equation 1.

Equation 1:

\[
\text{AUC}_{30\text{mmHg \cdot min}} = \sum_{n=1}^{30} \left( \frac{\Delta BP_n + \Delta BP_{n-1}}{2} \right) (t_n + t_{n-1})
\]

3.6.2 Cardiac output, stroke volume, Total Peripheral Resistance

Impedance Cardiography (IC) was used to measure hemodynamic variables (Cardiac output, stroke volume, and total peripheral resistance) before and after acute and chronic exercise. IC calculates the hemodynamic variables (SV, CO and TPR) by detecting the changing resistance or impedance ∆Z in the thorax that result from the cardiac cycles, respiratory activities and thoracic tissue resistance. The IC machine, Sobra CIC-1000 (Sorba Medical Systems, Brookfield, WI) has shown similar validity and reliability to methods such as thermodilution (Bogaard et al., 1997). Four electrodes were applied to 1) behind the left ear 2) left supraclavicular fossa 3) left mid-auxiliary line at the level of the xiphoid and 4) left mid auxiliary line in the region of the mid-pelvic bone.

3.6.2 Autonomic Function

Heart rate variability (HRV) was used to assess autonomic nervous system function. Heart rate was recorded using a three lead ECG and the data was sampled at 1000 Hz which was stored and analyzed using Labview (version 7.1, National instruments, TX, USA). All data collection and analysis were performed in according to the recommendation by the Task for Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology (Heart Rate Variability Task Force, 1996). The ectopic beats, or beats that are greater or less than
30% of the R-R interval of the average previous four R-R intervals will be identified and eliminated using sequential steps of algorithms (Kemper, Hamilton, & Atkinson, 2007). Kubios HRV (Biosignal Analysis and Medical Imaging Group, Kuopio, Finland) was used to analysis the five minute windows of RRI data extrapolated by Labview data. Fast Fourier transformation was applied in order obtain Mean RR, LF (.04-0.15Hz) and HF (.15-.50Hz) spectral components. Statistics performed on HRV were natural logarithm transformed and the HRV results are reported in raw units.

3.6.3 Baroreflex Sensitivity

Baroreflex sensitivity (BRS) was evaluated using the sequence method during a five minute interval. The ECG (obtained through CIC-1000) and the beat-to-beat blood pressure (obtained from Finometer) were recorded into Labview for storage and offline analysis. A custom program was used to identify three or more successive increases/decreases in blood pressure with corresponding increases or decrease in R-R intervals. For this experiment a lag of zero was chosen. The threshold value for sequence method is set to be 1 mmHg for beat-to-beat systolic blood pressure and 6 ms for RR interval (La Rovere et al., 2008). BRS was recorded during the AEAs at the last 6 minutes of collection 1 and 2.

3.6.4 Arterial stiffness

Arterial stiffness was assessed from the left radial artery using applanation tonometry (SphygmoCor, AtCor Medical, Sydney, Australia). This non-invasive method involves applying a hand-held tonometer to flatten or applanate an artery against an underlying structure (i.e. bones). The tonometer senses the intra-arterial pulse pressure that is transmitted through the arterial wall. This pressure wave was then saved and analyzed using the computer program SphygmoCor. A transfer function was used to generate a central arterial (aortic) wave form (Davies & Struthers, 2003; Nichols, 2005) from the average of 10 consecutive arterial wave forms. The augmentation index, normalized to a heart rate of 75 bpm was calculated as an index of arterial stiffness.
3.7 Statistical Analysis

The primary variables of interest were SBP and DBP after acute and chronic exercise. Sample size calculation was made for a correlation between magnitude of BP decrease after acute exercise and the magnitude of BP decrease after chronic exercise. The correlation coefficient was set to .65 with the alpha level set to .05 and the desired power set to .80. 17 participants were estimated to be needed.

An independent t-test was carried out to assess any sex related difference. If sex differences were detected, a mixed design repeated measure ANOVA was used to examine changes before and after exercise. However, if sex differences did not exist, a paired sample t-test was carried out. Furthermore, bivariate correlations were used to determine the predictor variables for the reduction of blood pressure after chronic exercise. Predictor variables included baseline measures and the physiological response after acute exercise. Only the statistically significant predictor variables were then entered into a stepwise multiple linear regression. Statistical significance was set at p≤.05.
Chapter 4
Results

The results are divided into two sections. The first section focuses on the blood pressure (BP) response after acute and chronic exercise. The second section focuses on the mechanisms responsible for the observed blood pressure response.

4.1 Descriptive Measures

Anthropometric and descriptive results are located in Table 4.1. Overall, 54 participants inquired about the study and 17 participants (8 male, 9 female) were recruited. 22 participants were disqualified because they did not meet the study’s specific requirement of age (6 participants), resting blood pressure (11 participants) or medical history (5 participants). Additionally, 15 participants dropped out due to personal reasons.

All recruited participants (17) completed the study and their adherence to the training sessions was greater than 80%. The average age of the male and the female subjects was 51 ± (2) and 55± (1) years old respectively. Baseline BMI and waist hip ratio classified both sex groups as overweight and as having a high risk for type 2 diabetes, hypertension and cardiovascular disease (Balady et al., 2000). At baseline, the waist-hip ratio was lower for the females than the males but BMI was found to be similar. After the training, only the male participants’ weight, BMI, and waist and hip circumference were significantly decreased.

VO$_{2\text{max}}$ and ventilatory threshold (VeT) were greater in the males than the females at baseline. The observed VO$_{2\text{max}}$ indicated the fitness levels of both sexes were estimated to be in the 40$^{th}$ percentile relative to their age-specific norms. After the training, VO$_{2\text{max}}$ and VeT were significantly improved in both sexes and their post-training VO$_{2\text{max}}$ classified them in the 50$^{th}$ percentile relative to age-specific norms (Balady, 2000). Increases in measures of aerobic fitness (VO$_{2\text{max}}$ and VeT) show the effectiveness of the training program. Resting blood pressure pre- and post-training was not different between the sexes (P<.05). The average baseline blood pressure for male (126 ± .94 / 81 ± 1.1 mmHg) and female (129 ± 2.5 / 80 ± 2.5 mmHg) subjects classified them as prehypertensive (Chobanian et al., 2003). No significant difference in resting blood pressure measurements was found between the initial screening and AEA1 (p>.05).
Table 4.1: Anthropometric and cardiovascular descriptors of male and female study participants (mean ± SE)

<table>
<thead>
<tr>
<th></th>
<th>Male (n=8) Pre Training</th>
<th>Male (n=8) Post Training</th>
<th>Female (n=9) Pre Training</th>
<th>Female (n=9) Post Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (m)</td>
<td>1.77± .24</td>
<td>1.77± .24</td>
<td>1.59± .24</td>
<td>1.59 ± .24</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>87.5± 4.7</td>
<td>86.0± 4.5</td>
<td>71.8± 4.8</td>
<td>72.4 ± 4.3</td>
</tr>
<tr>
<td>BMI</td>
<td>28.0± 1</td>
<td>27.4± 1</td>
<td>28.6± 1.9</td>
<td>28.8 ± 1.9</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>99.4± 4.6</td>
<td>97.4± 4.6</td>
<td>93.5± 4.3</td>
<td>92.8 ± 4.3</td>
</tr>
<tr>
<td>Hip(cm)</td>
<td>99.4± 3.7</td>
<td>97.3± 3.4</td>
<td>103± 3.5</td>
<td>103 ± 3.2</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>1.0± .32</td>
<td>1.0± .32</td>
<td>.90±.3</td>
<td>.89 ± .3</td>
</tr>
<tr>
<td>VO2max (ml/kg/min)</td>
<td>31.8±1.6</td>
<td>33.7±1.6</td>
<td>23.7 ±1.5</td>
<td>25.3 ±1.5</td>
</tr>
<tr>
<td>VeT (ml/min)</td>
<td>1831±171</td>
<td>1987±193</td>
<td>1065 ±56</td>
<td>1214 ±57</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>126±.94</td>
<td>120±1.8</td>
<td>129±2.5</td>
<td>122±3.2</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>81±1.1</td>
<td>75±1.1</td>
<td>80±2.5</td>
<td>75±2.0</td>
</tr>
</tbody>
</table>

*α* Significantly different between the sexes (p<.05)  
*¶* Significantly different after training within the sex group (p <.05)

### 4.2 Resting Blood Pressure Response to Acute Exercises

Two acute exercise assessments (AEA) were carried out. AEA 1 refers to the exercise assessment performed before the training and AEA 2 refers to the exercise assessment after the 8 weeks of training.

No significant interaction of gender and acute exercises (AEA1, AEA2) was observed for peak SBP (ΔSBP\text{peak}) and peak DBP decrease (ΔDBP\text{peak}), and AUC. The ΔSBP\text{peak}, ΔDBP\text{peak} decrease and AUC were not significantly different between the sexes. Therefore, analysis by combining the sexes was carried out (Table 4.2). See appendix A (Table A.1) for BP response by sex.

ΔSBP\text{peak} and AUCSBP significantly decreased after AEA 1 and AEA 2. However, the magnitude of ΔSBP\text{peak} was significantly smaller in AEA2 than AEA1. Additionally, a significant correlation was observed between peak SBP decrease and AUCSBP\text{30} after AEA 1 (r = .69, p<.05) and AEA 2 (r=.78, P<.05).

ΔDBP\text{Peak} and AUCDBP\text{30} significantly reduced after AEA1. The ΔDBP\text{Peak} and AUCDBP\text{30} response after AEA2 was significantly smaller compared with the response after AEA1. Moreover, ΔSBP\text{peak} was strongly correlated with ΔDBP\text{peak} decrease after AEA 1 (r=.71, P<.05) and AEA2 (r=.86, P<.05).
\( \Delta \text{SBP}_{\text{peak}} \) decrease (defined as the lowest 5 minutes BP post-exercise) occurred at a similar time during recovery in both sexes. During AEA1, \( \Delta \text{SBP}_{\text{peak}} \) occurred between 14 – 19 minutes for the male subjects and 13 – 18 minutes for the female subjects. During AEA 2, \( \Delta \text{SBP}_{\text{peak}} \) took place between 15-20 minutes for the male subjects and 13-18 minutes for the female subjects.

**Table 4.2: Blood pressure response to acute exercise (Mean ± SE)**

<table>
<thead>
<tr>
<th></th>
<th>AEA1</th>
<th>AEA 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \Delta \text{SBP}_{\text{peak}} ) (mmHg)</td>
<td>-7.2±1.2*</td>
<td>-4.2±1.9* Η</td>
</tr>
<tr>
<td>( \text{AUC}_{\text{SBP30}} ) (mmHg•min)</td>
<td>-97.3±29*</td>
<td>-71±29*</td>
</tr>
<tr>
<td>( \Delta \text{DBP}_{\text{peak}} ) (mmHg)</td>
<td>-4.2±1.0*</td>
<td>-0.21±1.2 Η</td>
</tr>
<tr>
<td>( \text{AUC}_{\text{DBP30}} ) (mmHg•min)</td>
<td>-27.8±32*</td>
<td>9.3±24 Ω</td>
</tr>
</tbody>
</table>

*Significantly different from baseline value p<.05
Ω Significantly different between AEA1 and AEA2 p<.05

### 4.3 Resting Blood Pressure Response to Chronic Exercise

Changes in resting BP during the training (at the end of week 1, 3, 5) and post training (week 8) are presented in Table 4.3. No significant difference in resting blood pressure measurements was found between week 8 and AEA2 (p>.05). See appendix A (Table A.2) for blood pressure response by sex. At the end of the training program, SBP and DBP significantly decreased by 7.0±1.4 mmHg and 5.2±1.2 mmHg, respectively. Blood pressure reduction was not significantly different between the sexes. Figures 4.1 and 4.2 illustrate blood pressure response for the combined sexes during and after training. See appendix A (Figure A.1, A.2) for individual BP response to chronic exercise.

**Table 4.3: Blood pressure response to chronic exercise (mean ± SE)**

<table>
<thead>
<tr>
<th></th>
<th>Week 1</th>
<th>Week 3</th>
<th>Week 5</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \Delta \text{Systolic Blood Pressure} ) (mmHg)</td>
<td>-1.0±1.6</td>
<td>-2.0±2.3</td>
<td>-4.5±1.7*</td>
<td>-7.0±1.4*</td>
</tr>
<tr>
<td>( \Delta \text{Diastolic Blood Pressure} ) (mmHg)</td>
<td>-1.1±1.5</td>
<td>-2.2±1.0</td>
<td>-3.8±1.3*</td>
<td>-5.2±1.2*</td>
</tr>
<tr>
<td>( \Delta \text{Heart Rate (BMP)} )</td>
<td>-3±1.8</td>
<td>-3±1.7</td>
<td>-4±1.6</td>
<td>-4±2.0</td>
</tr>
</tbody>
</table>

*Significantly different from baseline value (P<.05)
Figure 4.1: Resting systolic blood pressure (SBP) decreased throughout the 8 weeks. Significant reduction was achieved at week 5 and 8 ($p<.05$). Baseline SBP (SD): 128±6 mmHg; week: 127±8.6 mmHg; week3: 126±10 mmHg; week5: 123±8.3 mmHg; week8: 121±7.8 mmHg.

Figure 4.2: Resting diastolic blood pressure (DBP) decreased throughout the 8 weeks. Significant reduction was achieved at week 5 and 8 ($p<.05$). Baseline DBP (SD): 80±5.7 mmHg; week: 78±5.9 mmHg; week3: 79±6.2 mmHg; week5: 76±5 mmHg; week8: 75±4.7 mmHg.
4.4 Variables for Predicting Resting Blood Pressure response after Chronic Exercise

Bivariate correlations were used to determine the predictor variables for the magnitude of blood pressure reduction after chronic exercise. Subject’s baseline measurements and the physiological response after AEA1 were the dependent variables, while the magnitude of decrease in resting blood pressure after training was the independent variable.

The magnitude of resting SBP decrease after chronic exercise showed the strongest linear correlation with the magnitude of SBP decrease post-acute exercise, $r = .89$, $P < .001$, followed by AUC$_{SBP30}$, $r = .69$, $p < .05$, baseline waist size, $r = .66$, $p < .05$, and lastly BMI $r = .54$, $p < .05$.

The magnitude of resting DBP decrease after chronic exercise showed the strongest linear correlation with the magnitude of DBP decrease post acute exercise, $r = .78$, $P < .001$, followed by baseline resting DBP, $r = -.61$, $P < .05$ and AUC$_{DBP30}$ $r = .80$, $p < .05$

HRV (HF, LF, LF/HF ratio), arterial stiffness (AI$_x$, AI$_x@75$), TPR, HR, CO, SV, baseline SBP and BRS showed no significant correlation with the magnitude of either SBP or DBP decrease after chronic exercise.

4.4.1 Regression Analysis of Acute (AEA1) and Chronic Exercise Response

Multiple linear regression analysis was used to develop models for predicting the magnitude of SBP and DBP reduction after chronic exercise. The predictor variables used in the SBP model included post acute exercise $\Delta$SBP$_{peak}$, AUC$_{SBP30}$, baseline BMI, and waist size. The predictor variables used in the DBP model included post acute exercise $\Delta$DBP$_{peak}$, AUC$_{DBP30}$ and baseline DBP. A stepwise regression analysis was used for both models in selecting the best predictor variables. Basic descriptive statistics and regression coefficients are shown in Table 4.4. A collinearity analysis of the predictors were conducted and the tolerance was $>.2$ for all variables. The SBP and DBP model can be observed graphically in Figure 4.3 and 4.4.
**Table 4.4:** Regression analysis of the magnitude of blood pressure reduction after chronic exercise and acute exercise response (n=17)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Systolic Blood Pressure Model</th>
<th>Diastolic Blood Pressure Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>SE</td>
</tr>
<tr>
<td>ΔSBP peak post acute exercise</td>
<td></td>
<td>1.1</td>
</tr>
<tr>
<td>ΔDBP peak post acute exercise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept B</td>
<td>.92</td>
<td>1.2</td>
</tr>
<tr>
<td>F-ratio</td>
<td>61.0*</td>
<td></td>
</tr>
</tbody>
</table>

*The adjusted SBP r^2 = .79, *p<.001
*The adjusted DBP r^2 = .57 *p<.001

**Figure 4.3** The magnitude of change in systolic blood pressure (SBP) after acute exercise was significantly correlated with the magnitude of change in resting SBP after chronic training, r=.89, p<.05
4.4 The magnitude of change in diastolic blood pressure (DBP) after acute exercise was significantly correlated with the magnitude of change in resting DBP after chronic training, $r=.75$, $p<.05$.

**Figure 4.4** The magnitude of change in diastolic blood pressure (DBP) after acute exercise was significantly correlated with the magnitude of change in resting DBP after chronic training, $r=.75$, $p<.05$.

### 4.5 The Mechanisms of the Anti-hypertensive Effects After Acute Exercise

**Hemodynamics**

**AEA1:** The hemodynamic results are presented in Table 4.5. CO, SV, HR and TPR response were not different between the sexes after AEA1. HR significantly increased, while CO, SV, and TPR were not significantly changed after AEA1 with separate gender analyses. However, the TPR change was significant after combining the sexes, $p<.05$. Due to technical difficulties, all results for hemodynamic measures represent $n=7$ males and $n=7$ females.

**AEA2:** Significant interaction was observed between gender and the acute exercises (AEA1, AEA2) for TPR response only, $F= 5.1$, $P< .05$. The males exhibited a significant TPR decrease after AEA2. Meanwhile, the females exhibited a TPR increase ($p>.05$), which was significantly different from the TPR response observed in AEA 1. CO significantly increased by $1.1\pm 1.5$ L,
p<.05 in males, while CO decreased by -.72±.4, p>0.05 in females. HR was significantly elevated post exercise (AEA1, AEA2) in both sexes. SV decreased in females after AEA2, approaching significance, p=0.1.

Table 4.5 Hemodynamic responses to acute exercises (mean ±SE)

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AEA 1</td>
<td>AEA 2</td>
</tr>
<tr>
<td>ΔSBP (mmHg)</td>
<td>-7.0±1.4 *</td>
<td>-4±1.4 * H</td>
</tr>
<tr>
<td>ΔDBP (mmHg)</td>
<td>-4.8±1.86 *</td>
<td>2.2±1.6 H</td>
</tr>
<tr>
<td>ΔCO (l/min)</td>
<td>.68 ± .4</td>
<td>1.1±1.5 H</td>
</tr>
<tr>
<td>ΔSV (ml)</td>
<td>-2.4±5</td>
<td>4.2±5.8</td>
</tr>
<tr>
<td>ΔHR (bpm)</td>
<td>10±2.1 *</td>
<td>12±2.6 *</td>
</tr>
<tr>
<td>ΔTPR (dynes-sec/cm²)</td>
<td>-268±252</td>
<td>-380±190 *</td>
</tr>
</tbody>
</table>

*Significantly different from baseline value p<.05  
**Significantly different between AEA1 and AEA2 p<.05

**Baroreflex Sensitivity**

AEA1: BRS (--) significantly decreased, and no difference was found between groups. BRS (++) was not significantly changed in both sexes (Table 4.6).

AEA2: BRS (--) significantly decreased only in males, while BRS (++) was not significantly changed in both sexes. No significant interaction for BRS (++,--) was found between the sexes and the acute exercises (AEA1, AEA2).

**Heart Rate Variability**

AEA1: MeanRR, HF (ms²) and TP (ms²) were significantly decreased in both sexes (Table 4.6).

AEA2: MeanRR, HF (n.u.) and HF (ms²) were significantly decreased in both sexes. STDRR was significantly decreased in the females after AEA1 and AEA2. No significant interaction was found between sex and acute exercises (AEA1, AEA2) for meanRR, STDRR, LF, HF, TP and LF/HF. Additionally, no significant difference was found between sex groups for any of the HRV variables.
Table 4.6: Baroreflex sensitivity and heart rate variability responses to acute exercises (mean ±SE)

<table>
<thead>
<tr>
<th></th>
<th>Male AEA 1</th>
<th>Male AEA 2</th>
<th>Female AEA 1</th>
<th>Female AEA 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔBRS (--)</td>
<td>-2.0±.49 *</td>
<td>-1.9±.62 *</td>
<td>-1.3±.3*</td>
<td>-1±.23</td>
</tr>
<tr>
<td>ΔBRS (++)</td>
<td>-1.4±1.0</td>
<td>-1.4±.52</td>
<td>-.2±.96</td>
<td>-.9±.5</td>
</tr>
<tr>
<td>ΔMeanRR</td>
<td>-74±19 *</td>
<td>-113±21 *</td>
<td>-78±19 *</td>
<td>-116±21 *</td>
</tr>
<tr>
<td>ΔSTDRR</td>
<td>-7.9±3.6</td>
<td>-11±4.5</td>
<td>-6.7±2.6*</td>
<td>-10±3.2*</td>
</tr>
<tr>
<td>ΔLF (ms²)</td>
<td>-323±164</td>
<td>-155±121</td>
<td>-149±164</td>
<td>-91±121</td>
</tr>
<tr>
<td>ΔLF n.u.</td>
<td>6.6±8.3</td>
<td>9.4±3.5</td>
<td>3.5±8.4</td>
<td>14.7±3.5</td>
</tr>
<tr>
<td>ΔHF (ms²)</td>
<td>-46.1±37 *</td>
<td>-140±78*</td>
<td>-44±37*</td>
<td>-91±78*</td>
</tr>
<tr>
<td>ΔHF n.u.</td>
<td>-6.7±8.4</td>
<td>-9.4±3.5</td>
<td>-3.5±8.6</td>
<td>-14.7±3.5</td>
</tr>
<tr>
<td>ΔTP(ms²)</td>
<td>-546±232 *</td>
<td>-670±379</td>
<td>-547±231*</td>
<td>-293±379</td>
</tr>
<tr>
<td>ΔLF/HF</td>
<td>.3±2.2</td>
<td>2.5±2.4</td>
<td>3.2±2.2</td>
<td>6.3±6</td>
</tr>
</tbody>
</table>

* Significantly different from baseline value p<.05

4.6 The Mechanisms of the Anti-hypertensive Effects after Chronic Exercise

Hemodynamics

Hemodynamic variables at baseline and after chronic exercise are presented in table 4.7. No significance was found within and between sexes for any measures; however, TPR and HR were slightly reduced while SV slightly increased in both sexes.

Table 4.7 Hemodynamic responses to chronic exercise (mean ±SE)

<table>
<thead>
<tr>
<th></th>
<th>Male Pre Training</th>
<th>Male Post Training</th>
<th>Female Pre Training</th>
<th>Female Post Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPR (dynes-sec/cm-5)</td>
<td>2091±448</td>
<td>1822±675</td>
<td>2520±323</td>
<td>2262±462</td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>4.5±.70</td>
<td>4.6±.7</td>
<td>3.7±.73</td>
<td>3.9±.53</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>78±3.7</td>
<td>74±1.8</td>
<td>75±3.5</td>
<td>72±2.8</td>
</tr>
<tr>
<td>SV(ml)</td>
<td>57±11</td>
<td>62±10</td>
<td>49±5.8</td>
<td>51±6.5</td>
</tr>
<tr>
<td>CI (l/min/m2)</td>
<td>2.1±.38</td>
<td>2.1±.35</td>
<td>2.5±.35</td>
<td>2.0±.27</td>
</tr>
</tbody>
</table>
Heart Rate Variability

HRV data is presented in Table 4.8. The males had a higher LF/HF than the females at baseline (p< .05). After chronic training, the males had a higher LF (ms²) and LF (n.u.) than the females (p< .05). LF/HF in male participants was significantly reduced with training. There was no interaction between gender and exercise training for any of the HRV variables.

Table 4.8 Heart rate variability responses to chronic exercise (mean ±SE)

<table>
<thead>
<tr>
<th></th>
<th>Male Pre Training</th>
<th>Female Pre Training</th>
<th>Male Post Training</th>
<th>Female Post Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeanRR</td>
<td>778.6±35</td>
<td>790.9±35</td>
<td>810.4±30</td>
<td>796.0±30</td>
</tr>
<tr>
<td>STDRR</td>
<td>32.5 ± 4.4</td>
<td>26.7 ± 4.4</td>
<td>35.8 ± 4</td>
<td>27.0 ± 4.0</td>
</tr>
<tr>
<td>LF (ms²)</td>
<td>587.6±186</td>
<td>226.75±186</td>
<td>480.4±89</td>
<td>180±89.4</td>
</tr>
<tr>
<td>LF n.u.</td>
<td>81.2±7.3</td>
<td>68.9±7.3</td>
<td>80.1±4.3</td>
<td>66.4±4.2</td>
</tr>
<tr>
<td>HF (ms²)</td>
<td>86.9±46</td>
<td>115.5±46</td>
<td>176.6±81</td>
<td>114.5±81.2</td>
</tr>
<tr>
<td>HF n.u.</td>
<td>18.8±7.3</td>
<td>31.1±7.3</td>
<td>20.0±4.2</td>
<td>33.6±4.2</td>
</tr>
<tr>
<td>TP (ms²)</td>
<td>1141±285</td>
<td>919±285</td>
<td>1342±341</td>
<td>659±341</td>
</tr>
<tr>
<td>LF/HF</td>
<td>10.3±2.1</td>
<td>3.4±2.1</td>
<td>6.6±1.3</td>
<td>2.3± 1.3</td>
</tr>
</tbody>
</table>

* Significantly different within sex group p<.05
¶ Significantly different between the sexes p<.05

Baroreflex Sensitivity

BRS (+++) was observed to be significantly higher in the males than the females at baseline and post training. BRS (--) was not significantly different between the sexes. Moreover, BRS (++,--) did not improve with exercise training (Table 4.9)

Arterial Stiffness

Arterial stiffness data is presented in Table 4.9. AIx and AIx@75 were significantly greater in the females than in the males at baseline and post-training. After chronic exercise training, only the females exhibited a significant reduction in AIx@75.
Table 4.9 Baroreflex sensitivity and arterial stiffness responses to chronic exercise (mean ±SE)

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre Training</td>
<td>Post Training</td>
</tr>
<tr>
<td>BRS (--)</td>
<td>5.8 ± 1.0</td>
<td>5.8 ± .65</td>
</tr>
<tr>
<td>BRS (++)</td>
<td>6.3 ± .57</td>
<td>6.0±.59</td>
</tr>
<tr>
<td>AIx</td>
<td>14.6±2.4</td>
<td>14.4±2.0</td>
</tr>
<tr>
<td>AIx@75</td>
<td>16±2.1</td>
<td>14.8±2.8</td>
</tr>
</tbody>
</table>

* Significantly different within sex group p<.05
‡ Significantly different between the sexes p<.05

4.7 Relationship between Acute (AEA1) and Chronic Antihypertensive Mechanisms

The correlation between the magnitude of change in the antihypertensive mechanisms after acute exercise and the magnitude of change in the antihypertensive mechanisms after chronic exercise are presented in Table 4.10. Significant correlation was observed for LF (ms²), Total power (ms²) and LF/HF.

Table: 4.10 Correlations between acute and chronic antihypertensive mechanisms

<table>
<thead>
<tr>
<th>Variables</th>
<th>r</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>∆TPR acute vs. ∆TPR chronic</td>
<td>.36</td>
<td>P=.23</td>
</tr>
<tr>
<td>∆BRS(++) acute vs. ∆BRS(++) chronic</td>
<td>.42</td>
<td>P=.10</td>
</tr>
<tr>
<td>∆BRS(-- acute vs. ∆BRS(--) chronic</td>
<td>.20</td>
<td>P=.48</td>
</tr>
<tr>
<td>∆LF (ms²) acute vs. ∆LF(ms²) chronic</td>
<td>.88</td>
<td>P=.01*</td>
</tr>
<tr>
<td>∆HF (ms²) acute vs. ∆HF(ms²) chronic</td>
<td>-.25</td>
<td>P=.36</td>
</tr>
<tr>
<td>∆ Total (ms²) acute vs. ∆ Total(ms²)chronic</td>
<td>.75</td>
<td>P=.01*</td>
</tr>
<tr>
<td>∆LF/HF acute vs. ∆LF/HF chronic</td>
<td>.55</td>
<td>P=.02*</td>
</tr>
</tbody>
</table>

*Correlation is significant at the .05 level (2-tailed).
Chapter 5
Discussion

The main finding of this study was that a greater magnitude of blood pressure reduction after acute exercise (AEA1) was related to a greater magnitude of blood pressure reduction after chronic exercise, which supported our primary hypothesis. This blood pressure relationship could be valuable in identifying those individuals who may not respond effectively to chronic exercise. The antihypertensive effects after acute (AEA1) and chronic exercise were due to decreased TPR which was not met by an increase in CO. However, TPR reduction did not reach significance due to the variability of responses. Moreover, the autonomic function and arterial stiffness responded differently between the sexes after chronic exercise. The LF/HF was significantly decreased only in males suggesting an increase in vagal modulation, while arterial stiffness (AI$_x$@75) was significantly reduced only in the females. Furthermore, HRV (LF, TP, LF/HF) after acute exercise was the only variable that significantly correlated with HRV (LF, TP, LF/HF) after chronic exercise. Thus, we speculated the ventral lateral medulla (VLM), also known as the cardiovascular control center, may have a pre-existing set point to determine the blood pressure reduction after exercise. However, future studies are warranted in this area.

Finally, the acute exercise after training (AEA2) showed a smaller reduction in PEH than AEA1, which supported our secondary hypothesis number 1. The hemodynamics (CO, TPR) after AEA1 and AEA2 were observed to be different from the response of younger individuals (25-30 years old) reported by Senitko et al. (2002), which contradicted to our secondary hypothesis number 2. The females achieved PEH through a reduction in TPR in AEA2 while a slight decrease in CO was observed in AEA2. Meanwhile, the males achieved PEH through a reduction in TPR in both AEA1 and AEA2. These findings suggest that the mechanisms of PEH are influenced by exercise training, sex, and age. Future studies need to explore additional antihypertensive mechanisms such as endothelium function and arterial stiffness.

5.1 Blood Pressure Response to Acute Exercise

Two separate AEAs were carried out; AEA1 was performed prior to training and AEA2 was administered after the exercise training. PEH, defined as the peak blood pressure decrease (\(-BP_{peak}\)) and total effect (AUC$_{30}$), were observed after both AEA1 and AEA2. Additionally,
similar PEH was found between the sexes; therefore, statistical analysis for post exercise blood pressure response was performed by combining the sexes.

AEA1: The significant peak reduction of SBP (-7 mmHg) and DBP (-4 mmHg) after AEA1 was comparable to previous studies which had the similar doses of exercise prescription (Collier et al., 2009; Jones et al., 2006). In some studies, the magnitude of PEH was found to be greater due to higher exercise intensity or longer duration (MacDonald, 2002). Furthermore, SBP\text{peak} decrease was found to be significantly correlated with DBP\text{peak} (r=.71, P<.05) decrease and AUC\text{SBP30} (r = .69, p<.05). These correlations suggest that individuals with a greater SBP decrease also experienced a greater DBP decrease and a larger total effect.

AEA2: After the 8 weeks of aerobic training, the peak reduction of SBP (-4.6±.9 mmHg) and DBP (-.21±1.2 mmHg) were significantly smaller compared with AEA1. Moreover, only SBP\text{peak} reduction reached statistical significance. Pescatello, Guidry et al., (2004) reported that the magnitude of PEH is positively correlated with pre-exercise blood pressure value. Therefore, the lowering of resting SBP (121 ±1.9 mmHg) and DBP (75±1.1 mmHg) to almost normotensive values can decrease the magnitude of PEH (Forjaz et al., 2000; MacDonald, 2002). Despite the lower magnitude of PEH observed after the training, PEH was not significantly correlated to pre-exercise resting blood pressure (SBP: r=.31, p>.05; DBP: r=.21, p>.05). The lack of correlation observed could be caused by the small sample size (n=17) as Pescatello, Guidry et al. (2004) recruited 49 individuals. Nevertheless, individuals with a greater SBP decrease also experienced a greater DBP decrease and a greater total effect. This observation suggests that the reduction of peak SBP, DBP and the total effect are closely related in sedentary and moderately trained individuals.

5.2 Blood pressure response to Chronic Exercise

Resting blood pressure (SBP ± SE / DBP ± SE) was significantly decreased from 128 ± 1.5 / 80 ± 1.4 mmHg to 121 ± 1.9 / 75 ± 1.1 mmHg after chronic exercise training. A 5 mmHg reduction is clinically significant as it can decrease the risk of stroke by 40%, and decrease the risk of heart disease by 15-20% (Jones et al., 2008). The magnitude of blood pressure reduction found in this study was representative of the values of this age group (45-60 years old). Wilmore (2001) reported the average magnitude of SBP and DBP decrease ranged between 3-8 mmHg and 2-6 mmHg, respectively. Reduction of resting blood pressure was detected as early as one week
into the exercise training. However, the reduction of blood pressure became significant at the end of week 5 in our study. Meredith et al. (1990) have reported that no further reduction in blood pressure was observed after the third week of aerobic training in healthy young normotensive. The differences between our finding of continued decrease and Meredith et al.'s (1990) may be due to sample differences as younger individuals may present a different exercise adaptation pattern compared with older individuals. For example, younger individuals experienced higher testosterone, IGF-I, and strength gain than older individuals after 10 weeks of training (Kraemer et al., 1999). However, future studies investigating blood pressure adaptation response are warranted.

5.3 The Relationship between Acute and Chronic Blood Pressure Response

The variability of blood pressure response after exercise is a concern for managing high blood pressure (Cornelissen & Fagard, 2005; Hagberg & Brown, 1995). In this study, the post-exercise decrease in SBP and DBP ranged from -19 to 0 mmHg and -13 to 3 mmHg respectively after acute exercise (AEA1). Similarly, after chronic exercise, the magnitude of change in resting SBP and DBP varied from -14 to 0 mmHg and -17 to 7 mmHg, respectively. Recently, Hagberg et al. (2000) reported that 25% of the individuals with elevated blood pressure are non-responders to chronic exercise.

This is the first study to our knowledge that related the physiological changes after acute exercise (ΔTPR, ΔHRV, ΔBRS, ΔBP and AUC) to the magnitude of blood pressure reduction after chronic exercise. We found the magnitude of decrease in resting SBP after chronic training (8 weeks) can be best predicted based on peak SBP decrease after acute exercise. The regression analysis revealed that a large SBP peak decrease after acute exercise would also result in a large magnitude of resting SBP decrease after chronic exercise. The same relationship was also found between the peak DBP decrease after acute exercise and the magnitude of resting DBP decrease after chronic exercise.

The specific equations for predicting chronic blood pressure are listed below. The SBP and DBP prediction model accounted for 79% and 57% of variance, respectively. This suggested that there may be other factors such as genetics, diet and behavior that can influence blood pressure. The slope of the SBP (1.1 ± .14) model indicated that for every 1 mmHg decrease after acute
exercise, the SBP would decrease by 1.1 mmHg after chronic exercise. Similarly, every 1 mmHg DBP decrease after acute exercise would translate into .88 DBP decrease after chronic exercise. The intercept B in the SBP and DBP model indicated that blood pressure after chronic exercise was offset by .92 ± 1.2 and 1.5±1.2 mmHg, respectively.

\[ \Delta \text{Chronic SBP Reduction} = 1.1(\Delta \text{Peak SBP Reduction}) + 0.92 \]

\[ \Delta \text{Chronic DBP Reduction} = 0.88 (\Delta \text{Peak DBP Reduction}) - 1.5 \]

The relationship between acute and chronic blood pressure response can be a valuable tool in assessing an individual’s blood pressure variability. Importantly, the blood pressure relationships can help identify the non-responders so that additional diet and pharmacological intervention can be employed. Furthermore, this blood pressure relationship can also be used as a positive reinforcement for those who respond well to exercise training.

Previous studies predicting chronic blood pressure reduction were based on subjects’ pre-training health. Individuals with worse health, such as those with higher resting systolic blood pressure, were observed to have a greater reduction in systolic blood pressure after chronic training (Wilmore, 2001). However, this phenomenon has not always been observed (Lacombe, 2010; Liu et al., 2010). In this study, the magnitude of SBP after AEA1 was not correlated with baseline SBP \((r=.3, p>.05)\). Instead, we found that a person with a smaller baseline waist size or BMI resulted in greater resting blood pressure decreases. This observation was opposite to the principle of initial values - a person with a worse health profile (i.e., greater waist size or greater BMI) would result in greater improvements. Thus, we speculate that 1) the severity of the cardiovascular pathology and 2) genetic variation may have a greater influence on blood pressure reduction than just the principle of initial values.

Previous literature suggests the most serious cardiovascular pathology (hypertensive) and healthy individuals (normotensives) experience a smaller degree of blood pressure reduction (9/8mmHg) after acute exercise than individuals with moderate degree of cardiovascular pathology (perhypertensives, 14/9mmHg) (MacDonald, 2002). A similar trend was also observed with chronic exercise (Cornelissen & Fagard, 2005). These findings provide evidence that blood pressure reduction may not have a positive relationship with baseline health as described by the principle of initial values, but rather an inverted U relationship.
Additionally, genetic variability can also account for up to 30% of the variance in blood pressure response to exercise training (An et al., 2003). Genes such as angiotensin converting enzyme (ACE)II genotype, lipoprotein lipase (LPL) HindII+/+ or +/- genotype have been shown to give a greater decrease in blood pressure (SBP/DBP: -10/10 mmHg) compared with similar hypertensives having the ACE DD and LPL HindII-/- genotype (SBP/DBP: -5/-1.5 mmHg) following 9 months of endurance training (Hagberg et al., 1999). Augeri et al. (2009) reported that men with similar baseline blood pressure and BMI who were carriers of the eNOS C (786) allele responded more favorably to the antihypertensive effects of aerobic exercise than men with the eNOS T786T genotype. These data suggest that the principle of initial values may not always apply as genetic variability can have a profound influence on blood pressure. Future studies can incorporate the genetic variability and the severity of the cardiovascular pathology into the blood pressure prediction models constructed in this study.

5.4 The Mechanisms of the Anti-hypertensive Effects after Acute Exercise

Hemodynamic Response after AEA1

Previous literature has reported that the hemodynamic response post acute exercise varies depending on resting blood pressure, sex, and training status. Older hypertensives (>150/95mmHg) between the ages of 60-69 years old, achieved PEH through CO decrease while TPR was unchanged (Hagberg et al., 1987). Meanwhile, middle aged normotensives and prehypertensives (45-65 years old) achieved PEH through TPR reduction that was not completely offset by CO increase (MacDonald, 2002). In the present study, the hemodynamic responses observed after AEA1 was similar to findings with prehypertensive subjects. TPR was reduced by 12% and 15 % in the pre-hypertensive males and females, respectively. Elevated HR and a slight decrease in SV did not cause a significant increase in CO. Halliwill, (2001) reported that an increased vasodilation contributes to decreased TPR and thus venous pooling. This along with a loss of plasma volume associated with exercise can lead to a reduction in central venous pressure and SV. The increased heart rate, and venous pooling and decreased SV can result in unchanged CO (Halliwill, 2001; Senitko et al., 2002).
Hemodynamic response after AEA2

Exercise training has been shown to be able to alter the mechanisms of PEH in younger individuals (25-28 years old) due to chronic exercise adaptation. Senitko et al. (2002) reported that endurance trained males achieved PEH through a reduction in CO while sedentary males achieved PEH through decreased TPR. On the other hand, endurance trained as well as sedentary females both achieved PEH through a reduction in TPR. The effects of training on antihypertensive mechanisms in males and postmenopausal females (45-60 years old) have not been examined until this study.

Even though the participants in the present study were not as trained as the younger individuals in Senitko et al.’s (2002) study, sex related differences in the mechanisms of antihypertensive effects still persisted. In the present study, after AEA2 older males achieved PEH through a similar TPR response as AEA1. Specifically, the males exhibited a significant decrease in TPR by 20%. However, unlike AEA1, CO was significantly increased by 25% after AEA2. This increase contributed to the reduced magnitude of PEH in AEA2 relative to AEA1. The significant increase in HR combined with a slight elevation in SV (4.2 ±5.8ml) resulted in an increase in CO in males.

On the contrary, after AEA2 post-menopausal females achieved PEH via different mechanisms compared with AEA1. The major contributing factor to PEH was the reduction of CO by 20% relative to pre-exercise. TPR was found to have slightly increased by 9% relative to pre-exercise. The females’ TPR response was found to be significantly different from the males with exercise training. HR was significantly elevated after exercise in females after AEA2; however, the reduction of SV (16%), approaching significance (p=.1) contributed to the reduction of CO observed. These findings suggested that the mechanisms of antihypertensive effects in moderately trained prehypertensive males and females were different compared with younger trained males and females observed in (Senitko et al., 2002).

We hypothesize that the reduction in CO observed in the females after training is due to the greater fall in central venous pressure which can be due to CO redistribution from less compliant to more compliant vascular beds (Senitko et al., 2002). A reduction of cardiac contractility can also decrease CO, but this may not be likely since the exercise lasted only for 30 minutes at
moderate intensity and previous research has demonstrated no loss of contractility over that amount of time (MacDonald, 2002).

The elevated TPR after AEA2 in the females may be due to an increase in sympathetic vasoconstrictor outflow in order to compensate for the fall in CO. The increasing of LF and decreasing of HF observed in AEA2 compared with AEA1 may provide evidence for the increased sympathetic outflow in the females. Although not significantly different, the increased sympathetic outflow in the females was also found to be slightly higher when compared with the males. Therefore, the increased sympathetic vasoconstrictor outflow may explain the TPR response in the females after AEA2.

In addition to changes in TPR, decreased arterial stiffness after acute exercise can also decrease SBP. Unfortunately, arterial stiffness was not measured during acute exercise recovery in the present study. However, previous studies have shown that acute exercise (30 minute of cycling, 60% \( \text{VO}_2\text{max} \)) can induce decreases in central (aorta) and peripheral (femoral to dorsis pedis arteries) arterial stiffness 30 minutes after exercise (Kingwell et al., 1997). Similarly, Naka et al. (2003) reported a decrease in upper and lower limb arterial stiffness (measured by PWV) by ~23% compared to baseline. This lasted for 60 minutes before returning to baseline. Currently, it is unknown whether there are differences in the change of arterial stiffness after acute exercise in prehypertensive males and females (45-60 years).

**Autonomic Function after AEA1**

Heart rate variability (HRV) was used to assess the autonomic function after exercise. The increased HR and reduced HRV parameters (HF, LF, TP) suggest an increase in sympathetic and a decrease in parasympathetic modulation of the heart (Nolan, Jong, Barry-Bianchi, Tanaka, & Floras, 2008). Several other studies have also found a decrease in HRV after acute exercise (Rezk, Marrache, Tinucci, Mion, & Forjaz, 2006). However, Halliwill, (2001) reported a reduction in sympathetic outflow by 30% through the measurement of MSNA. The inconsistent findings of autonomic function after acute exercise can be due to the various measurement techniques (Heart Rate Variability Task Force, 1996; Millar, Rakobowchuk, McCartney, & MacDonald, 2009). Measuring autonomic activity using HRV provides a global assessment of sympathetic and parasympathetic contribution; thus, HRV may not be specific enough to detect
subtle changes in autonomic control. Meanwhile, MSNA can assess sympathetic nerve fibers of the lower leg, which is more sensitive compared with HRV.

The increased LF/HF suggests an increase in global sympathetic modulation which would cause an increase in vasoconstriction (Halliwill, 2001). However, a decrease in TPR was in fact observed in males after AEA 1 and AEA2 and in females after AEA1. Therefore, these results suggest that sympathetic outflow may not be as effective in contributing to vasoconstriction. (Halliwill, Taylor, & Eckberg, 1996) reported that the slope of sympathetic activity and vascular resistance was attenuated after exercise compared with the control, indicating less vasoconstriction with an increase in sympathetic activity. In addition to the alteration in autonomic function, the increase in local vasodilation caused by the production of vasodilator substances (nitric oxide, adenosine, prostaglandins) can also be a competing factor in the decrease of TPR (Halliwill, 2001; Halliwill et al., 1996). Studies have reported an increase in nitric oxide (NO) production after exercise and the majority of the reduction in TPR is attributed to vasodilator substances, as sympathetic vasoconstriction after exercise can only account for 30% of the vascular resistance response (Halliwill et al., 1996).

**Autonomic Function after AEA2**

Seiler et al. (2007) reported that individuals with higher fitness have a faster HRV recovery time than individuals with lower fitness while exercising at the first ventilatory threshold. In the present study, HRV was assessed at a similar time period post (10-15 minutes) AEA1 and AEA2. Our participants did not show any training related improvements in HRV recovery. A possible explanation of this observation can be attributed to the degree of the participants’ training status. In our study, participants improved their fitness level, but it was still much lower than the younger trained athletes in Seiler et al’s (2007) study, as their VO$_{2\text{max}}$ was above the 90% percentile relative to their age group.

**Baroreceptor sensitivity after AEA1**

Studies using the spontaneous methods to determine BRS have shown that it can be decreased up to 60 minutes after exercise (Niemela et al., 2008). Similarly, in the present study BRS (--) was significantly attenuated after the exercise in both sexes. Lowering BRS has been associated with altering the sympathovagal balance to be sympathetic dominant (Skrapari et al., 2007). A study
by Figueroa, Baynard, Fernhall, Carhart, & Kanaley (2007b) reported that reduced BRS post acute exercise was accompanied by an increased LF, and decreased HF. Therefore, the decrease in BRS observed in the present study may have contributed to increased sympathetic activity after AEA1.

**Baroreceptor sensitivity after AEA2**

BRS recovery after AEA2 was not significantly different from AEA1 in both sexes. To our knowledge, this is the first study to have examined the effects of endurance training on BRS recovery after acute exercise in middle aged prehypertensive males and postmenopausal females. Figueroa, Baynard, Fernhall, Carhart, & Kanaley (2007a) reported that chronic exercise (16 weeks) improved BRS recovery after acute exercise in middle aged obese women with and without T2DM. Our female participants did not experience a faster BRS recovery. Perhaps a longer training program (16 weeks) can result in improvements in BRS recovery after acute exercise.

5.5 The mechanisms of the Anti-hypertensive Effects after Chronic exercise

**Hemodynamic**

TPR and CO were not significantly different between the sexes at baseline. After the chronic training TPR was reduced to a similar (non-significant) extent in males (12%, p=.26) and females (10%, p=.29). The wide range of TPR variation (-62% to +60%) may have limited our ability to identify significance with the given sample size. CO at rest was not changed with training. Pre-training CO significantly correlated with post training CO response (r=.6, P<.05) suggesting that the variability of CO training response remained minimal. Our findings were consistent with a meta-analysis by Cornelissen & Fagard, (2005) involving 72 randomized trials which found that the decrease of blood pressure after chronic exercise was mainly due to the reduction of total peripheral resistance by 7.1%, while CO remained unchanged in individuals with high blood pressure. The reducing trend of HR and increasing trend of SV resulted in the unchanged CO. Similar findings were also observed in previous literature (Cornelissen & Fagard, 2005). The change in SV may result from improved cardiac function (altered diastolic function) (Levy, et al., 1993) or increased blood volume (Convertino, 1991).
**Arterial stiffness**

Our female participants (AI\(_x\)@75: 30.7 ±2.2) had significantly higher arterial stiffness at baseline than males (AI\(_x\)@75: 16±2.1), which agrees with previous research (Waddell, 2001). After chronic exercise, arterial stiffness (AI\(_x\)@75) significantly decreased in females (-22%) but not in males (-7.5%). Despite the greater AI\(_x\)@75 decrease in the females, they still had a significantly higher arterial stiffness than the males after training. Several studies have shown the higher AI\(_x\) in post-menopausal females may be related to hormonal status, as estrogen therapy can significantly reduce arterial stiffness in post-menopausal females (Nichols & Singh, 2002; Waddell, Dart, Gatzka, Cameron, & Kingwell, 2001).

Blood pressure is influenced by both TPR and arterial stiffness. As mentioned earlier, decreased TPR can result in decreased SBP, as well as DBP. However, decreased arterial stiffness leads to SBP decrease and DBP increase, which are caused by 1) the increasing of arterial dispensability and 2) the timing of the reflected arterial pause wave (London & Guerin, 1999).

The increased arterial dispensability allows for the arterials (aorta and major arteries) to absorb or “cushion” the pressure generated during systole which in turn lowers SBP. During diastole, the stored pressure in the arterials from systole recoils and squeezes the blood forward into the peripheral circulation, resulting in increased DBP (London & Guerin, 1999). Furthermore, decreased arterial stiffness can alter the timing of the reflected arterial pulse wave so that it does not occur during systole, which can augment SBP (London & Guerin, 1999).

In the present study, resting DBP decreased after chronic training despite the decrease in arterial stiffness. This observation suggests that 1) the degree of arterial stiffness decrease may not have been large enough to influence DBP; 2) the TPR reduction may have had a greater influence on DBP than arterial stiffness. Krstrup et al. (2010) also reported a significant reduction in SBP, DBP was accompanied by AI\(_x\) (Pre training 4.2+/−2.4, Post training −.9+/−2.5) decrease in premenopausal women (37±2 years old) after 16 weeks of aerobic training. Currently, limited numbers of studies have examined arterial stiffness using AI\(_x\) or AI\(_x\)@75 after long-term training in prehypertensive males and postmenopausal females (45-60 years). Future studies comparing gender differences after exercise training using AI\(_x\)@75 or AI\(_x\) are warranted.
**Autonomic function**

Autonomic function can influence the change in TPR and arterial (Waddell et al., 2001) stiffness through sympathetic and parasympathetic activity (Halliwill, 2001). Our HRV results suggested the female participants were more parasympathetic dominant at baseline than the males. However, the LF/HF ratio in males was significantly reduced by 36%, while a non-significant reduction was observed in the females (32%) following chronic exercise. These observations suggest a shift in autonomic nervous system control toward parasympathetic dominance in both sexes; however, the shift in control is more pronounced in the males than the females.

Interestingly, a greater improvement in vagal dominance did not result in a greater TPR and arterial stiffness reduction in the males. In fact, the females showed a greater reduction in arterial stiffness. This observation indicates that autonomic activity is not the sole mechanism responsible for changes in TPR and arterial stiffness. Based on evidence from chronic training studies, improvements in endothelial function and arterial remodeling can also result in a reduction in TPR and arterial stiffness (Currie, et al., 2009). Maeda et al. (2001) reported that following an 8 week training program, endothelial function was improved in humans. Vasodilator production such as nitric oxide increased and vasoconstrictor substance such as Endothelin1 was reduced. Favorable vascular remodeling of elastin and collagen content can take place with exercise training to decrease arterial stiffness. Additionally, increased lumen vessel diameter as result of chronic training can also decrease TPR (MacDonald, 2002; Halliwill, 2001).

**Baroreflex Function**

Previous studies have reported that post menopausal females have a blunted BRS compared to age-matched men (Laitinen et al., 1998). Similarly, BRS (++) was found to be significantly lower in the females compared with the males at baseline. Furthermore, BRS did not improve significantly in both sexes after the 8 week training despite the reduction in resting blood pressure. Collier et al. (2009) observed similar findings in pre-hypertensive males and females after 4 weeks of aerobic training. Loimaala et al. (2000) reported that BRS was not improved even after 5 months of endurance training in middle aged males. However, there are studies which have found improvements in BRS after 12 weeks of aerobic training in hypertensives (Hua et al., 2009) and older individuals (71+/- 3 years) (Iwasaki et al., 2003). BRS response after
exercise training remains inconclusive. However, this study suggests that resting blood pressure decrease can occur without BRS improvements in older males and post-menopausal females.

5.6 The Relationship between Acute (AEA1) and Chronic Exercise Response

There are few studies available examining the relationship between acute and chronic exercise. Our results indicate that some of the mechanisms between acute (AEA1) and chronic exercise were different. TPR was reduced after acute and chronic exercise in this study. However, sympathetic activity increased after acute exercise and decreased after chronic exercise. BRS also responded differently after acute and chronic exercise. Unfortunately, vasodilation was not measured in this study but previous studies reported a greater production of vasodilator substances following acute exercise (Halliwill, 2001). These findings suggest that the factors influencing TPR, such as autonomic activity and BRS, are different after acute and chronic exercise.

Currently, it is unclear why blood pressure after acute and chronic exercise correlated while most of the other mechanisms did not. Autonomic function (LF/HF, LF, TP) after acute exercise was the only mechanism found to be significantly correlated with autonomic function (LF/HF, LF, TP) after chronic exercise. Figure 5.1 illustrates the current understanding of blood pressure regulation. The ventral lateral medulla (VLM), also known as the central cardiovascular regulatory center is responsible for generating and maintaining the sympathetic vasomotor tone to regulate arterial blood pressure. The VLM is also the main site that integrates afferent signals from baroreceptors and chemoreceptor. Furthermore, the VLM is involved in water and salt intake by controlling ADH and vasopressin release (Cravo et al., 2009). Several studies have shown that a disruption to VLM by drug or by surgical intervention can disrupt the vasomotor tone and alter resting blood pressure (Bergamaschi, Campos, Schor, & Lopes, 1995; Cravo et al., 2009) (Ito, Komatsu, Tsukamoto, & Sved, 2001). Recent evidence from animal models reported that changes in neurotransmission within the VLM are related to acute and chronic hypertension (Cravo et al., 2009). Based on these findings about the VLM, we hypothesize that there may be a pre-existing set point in the VLM that ultimately determines the magnitude of blood pressure reduction after exercise.
Figure 5.1 Blood pressure is influenced by total peripheral resistance (TPR) and arterial stiffness. Autonomic function (sympathetic and parasympathetic) and local vasodilators (nitric oxide) can both have a direct impact on TPR and arterial stiffness. The ventralateral medulla (VLM), also known as the cardiovascular control center, directly influences autonomic function and can also modulate hormone release such as ADH and vasopressin. Baroreceptors are afferent sensors that send blood pressure information to the VLM to be processed (Cravo et al., 2009).

Since the VLM directly influences autonomic function (figure 5.1), this may be the reason we observed a correlation for autonomic function after acute and chronic exercise. Meanwhile, TPR is influenced through VLM and vasodilators (independently controlled from VLM); therefore, this may explain the lack of TPR correlation after acute and chronic exercise. The vasodilators (nitric oxide) are produced from the increased blood flow associated with exercise which stimulates the release of nitric oxide from the vascular endothelium (Halliwill, 2001). Currently, there is still much to be learned about the VLM and its influence on blood pressure. Future studies are needed to confirm our hypothesis that there is a pre-existing blood pressure set point in the VLM.

5.7 Limitations

A possible limitation of the study protocol was the length of the training program prescribed. Based on previous studies, resting blood pressure should reach peak reduction after 4 weeks of exercise training. However, this was not observed due to the wide range of blood pressure
responses. A longer study training prescription in the future can help confirm whether the reduction of blood pressure reached peak reduction after 8 weeks of exercise training.

A control group was not incorporated into the study due to the limited sample size. Nevertheless, studies containing a control group have shown that the reduction of blood pressure after acute and chronic exercises resulted from the exercise intervention (Lacombe, 2010; MacDonald, 2002, Cornelissen & Fagard, 2005). Adding a control group would strengthen the overall study design.

The limitation of an impedance cardiograph (IC) using the Kubicek formula is that it tends to overestimate low CO values and underestimate high CO values (Warburton, Haykowsky, Quinney, Humen, & Teo, 1999). This may lead to inaccurate absolute CO values (Bogaard et al., 1997). It has been shown that IC produces inaccurate readings when participants have structural defects of the heart (i.e., valvular disease, cardiac shunts, and atria fibrillation) (Ebert, Eckberg, Vetrovec, Cowley, 1984) and when undergoing strenuous physical activity (Warburton et al., 1999). In this study, IC was used to determine absolute CO but the initial screening of the participants ruled out any structural heart defects.

Several studies have shown that central and peripheral arterial stiffness respond differently with exercise training (Rakobowchuk et al., 2008; Rakobowchuk, Stuckey, Millar, Gurr, & Macdonald, 2009). However, only global arterial stiffness using AIx was assessed in this study. Future studies need to incorporate both central and peripheral arterial stiffness measurements after acute and chronic exercise.

HRV recording may be a limitation to the study as breathing frequency may influence HF (Heart Rate Variability Task Force, 1996). However, reliability studies have shown minimal HF difference between paced and spontaneous breathing (Bloomfield et al. 2001; Patwardhan et al. 1995). HRV was monitored throughout the post exercise recovery (30 minutes) in this study; thus, a paced breathing protocol could add additional stress or discomfort to the participant.

Diet was not controlled in this study, but participants were asked not to change their eating habits throughout the study. Diet can play a role in the reduction of blood pressure; however, this study has shown that even without diet intervention, exercise alone can reduce blood pressure significantly.
Resting blood pressure can be influenced by many external factors such as caffeine, amount of sleep, time of day and daily stress. Several attempts were made to control the external factors in this study. For example, participants were asked to measure their blood pressure only in the late afternoon. Caffeine and any strenuous exercise were avoided 8 hours and 24 hours prior to any assessment, respectively. Unfortunately, not every factor can be controlled. Stress from participants’ personal lives may have caused some of the blood pressure variations observed throughout the 8 weeks of training.
Chapter 6
Conclusion

Blood pressure response after acute exercise can be used to predict the blood pressure response after chronic exercise. An individual with a large decrease in resting blood pressure after acute exercise will also elicit a large decrease in resting blood pressure after chronic exercise. The SBP and DBP equation formulated to predict resting blood pressure after chronic exercise can be a useful tool in identifying exercise resistant vs. responsive individuals. However, future research is warranted in order to further improve the efficacy of the prediction model (See section 6.1).

The hemodynamics after acute (AEA1) and chronic exercise showed a similar trend of TPR reduction without a change in CO. Meanwhile, HRV and BRS responded differently after acute and chronic exercise. After acute exercise, HRV and BRS decreased; after chronic exercise, HRV increased while BRS remained unchanged.

Additionally, the antihypertensive effects after chronic exercise were achieved through different mechanisms between the sexes. Males exhibited a significant reduction in HRV, whereas females exhibited a significant decrease in arterial stiffness.

Furthermore, a relationship between the antihypertensive mechanisms (BRS, TPR) after acute and chronic exercise was not observed. Thus, we speculate that VLM, the cardiovascular control center, may have a pre-existing set point to determine the blood pressure reduction after exercise. Future studies assessing other blood pressure reduction mechanisms are warranted.

Finally, the two acute exercise assessments performed pre and post chronic exercise training showed different responses. AEA2 showed a smaller reduction in PEH than AEA1. The antihypertensive mechanisms after AEA1 were also different from AEA2. These findings suggest the exercise-related adaptations after chronic exercise can change the way our body achieves PEH.
6.1 Future Directions

1. This study has created a prediction method of blood pressure response after chronic exercise for prehypertensives. Future study needs to employ larger randomized trials with populations of different ethnic backgrounds. Studies have shown that certain ethnicities such as hypertensive Asian and Pacific islanders are more responsive to exercise training than Caucasians (Hagberg et al., 2000). Thus, a chronic blood pressure prediction model may be ethnicity-specific.

2. A longer study training prescription in the future can help confirm whether the reduction of blood pressure reached peak reduction after 8 weeks of exercise training. This can help increase the efficacy of the current blood pressure prediction model.

3. Anti-hypertensive effects after exercise result from multiple mechanisms. The most common mechanisms were examined in this study. Future studies need to incorporate measurements of arterial stiffness (central and peripheral), endothelium function, MSNA, and RAAS before and after acute and chronic exercise.

4. Genetic variations such as Angiotensinogen M235T polymorphisms or NOS3Gene polymorphisms have shown to influence blood pressure reduction after chronic exercise. It is unknown whether these individuals will also be resistant to PEH after acute exercise.

5. Treatment options for those exercise resistant individuals should also be explored. These areas can include diet interventions, behavior interventions, exercise dose (interval, supra-maximal exercise), and pharmacological interventions. For example, can a low sodium diet help those exercise resistant individuals lower their blood pressure? Can behavioral neurocardiac training with HRV biofeedback be beneficial for these exercise resistant individuals? Can interval or super-maximal exercise lower blood pressure for these exercise resistance individuals? Do exercise resistant individuals also resist pharmacological interventions?
References


## Appendix A: Supplemental Data

### Table A.1: Blood pressure response after acute exercise (mean ± SE)

<table>
<thead>
<tr>
<th>Combined sex</th>
<th>AEA1</th>
<th>AEA2</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔSBP (mmHg)</td>
<td>-7.2±1.2*</td>
<td>-4.2±0.9* Ω</td>
</tr>
<tr>
<td>AUC_{SBP30} (mmHg•min)</td>
<td>-97.3±29*</td>
<td>-71±29*</td>
</tr>
<tr>
<td>ΔDBP (mmHg)</td>
<td>-4.2±1.0*</td>
<td>-.21±1.2 Ω</td>
</tr>
<tr>
<td>AUC_{DBP30} (mmHg•min)</td>
<td>-27.8±32*</td>
<td>9.3±24 Ω</td>
</tr>
<tr>
<td>Male Participants</td>
<td>ΔSBP (mmHg)</td>
<td>-7.0±1.4*</td>
</tr>
<tr>
<td>AUC_{SBP30} (mmHg•min)</td>
<td>-89.6±31*</td>
<td>-26±41</td>
</tr>
<tr>
<td>ΔDBP (mmHg)</td>
<td>-4.8±1.86*</td>
<td>2.2±1.6 Ω</td>
</tr>
<tr>
<td>AUC_{DBP30} (mmHg•min)</td>
<td>-99±49</td>
<td>13.6±42 Ω</td>
</tr>
<tr>
<td>Female Participants</td>
<td>ΔSBP (mmHg)</td>
<td>-7.4±1.89*</td>
</tr>
<tr>
<td>AUC_{SBP30} (mmHg•min)</td>
<td>-104±40*</td>
<td>-29±50</td>
</tr>
<tr>
<td>ΔDBP (mmHg)</td>
<td>-3.7±1.05*</td>
<td>-2.4±1.7</td>
</tr>
<tr>
<td>AUC_{DBP30} (mmHg•min)</td>
<td>-46.5±35</td>
<td>5.4±28</td>
</tr>
</tbody>
</table>

*Significantly different from baseline value, P<.05
Ω Significantly different between AEA1 and AEA2, P<.05

### Table A.2: Blood pressure response with chronic exercise (mean ± SE)

<table>
<thead>
<tr>
<th></th>
<th>Week 1</th>
<th>Week 3</th>
<th>Week 5</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔSBP (mmHg) for combined sex</td>
<td>-1.0±1.6</td>
<td>-2.0±2.3</td>
<td>-4.5±1.7*</td>
<td>-7.0±1.4*</td>
</tr>
<tr>
<td>ΔDBP (mmHg) for combined sex</td>
<td>-1.1±1.5</td>
<td>-2.2±1.0</td>
<td>-3.8±1.3*</td>
<td>-5.2±1.2*</td>
</tr>
<tr>
<td>ΔHR (BMP) for combined sex</td>
<td>-3±1.8</td>
<td>-3±1.7</td>
<td>-4±1.6</td>
<td>-4±2.0</td>
</tr>
<tr>
<td>ΔSBP (mmHg) for male (n=8)</td>
<td>.6±2.2</td>
<td>-1.5±1.3</td>
<td>-3.4±2.0</td>
<td>-6.4±1.7*</td>
</tr>
<tr>
<td>ΔDBP (mmHg) for male (n=8)</td>
<td>1.0±1.5</td>
<td>-1.4±1.6</td>
<td>3.9±2.3</td>
<td>6.2±1.5*</td>
</tr>
<tr>
<td>ΔHR (BMP) for male (n=8)</td>
<td>-2.4±1.5</td>
<td>-4.0±1.9</td>
<td>-3.8±1.6</td>
<td>-4.5±3.0</td>
</tr>
<tr>
<td>ΔSBP (mmHg) for female (n=9)</td>
<td>-1.4±1.8</td>
<td>-2.4±4.2</td>
<td>-5.5±2.7</td>
<td>-7.6±2.3*</td>
</tr>
<tr>
<td>ΔDBP (mmHg) for female (n=9)</td>
<td>-1.1±2.6</td>
<td>-2.89±1.4</td>
<td>3.8±2.2</td>
<td>-4.4±1.8*</td>
</tr>
<tr>
<td>ΔHR (BMP) for female (n=9)</td>
<td>-2.4±3.2</td>
<td>-1.3±2.9</td>
<td>-4.1±1.6</td>
<td>-3.8±3.0</td>
</tr>
</tbody>
</table>

*Significant relative to baseline value, P<.05
Figure A.1: Individual resting systolic blood pressure response (SBP) to chronic exercise. SBP recordings are standardized to baseline SBP by dividing the resting SBP at each time point (week 1, 3, 5, 8) by baseline SBP.

Figure A.2: Individual resting diastolic blood pressure response (DBP) to chronic exercise. DBP recordings are standardized to baseline DBP by dividing the resting DBP at each time point (week1, 3, 5, 8) by baseline DBP.
Appendix B: Supplementary Review

B.1 Review of the Finometer Measures

The Finometer model-2 measures blood pressure through the volume clamp method developed by Penaz (1973). This method works by clamping the middle phalanx using an inflatable finger cuff between the first and second distal phalangeal joints. Then the cuff detects the arterial blood volume using infrared photoplethysmography (light source). Every time the blood volume increases during systole, the amount of light detected decreases. Conversely, the opposite occurs when blood volume decreases during diastole. The data of the arterial diameter size is then sent to a servo which changes the pressure inside the inflatable cuff accordingly in order to maintain a constant diameter with every heart beat. In order to match the cuff pressure to intra-arterial pressures at the finger, the artery needs to be “unloaded”. The Finometer reaches the transmural pressure of zero (unloaded artery) by using a calibrating algorithm called “Physiocal”. The “Physiocal” is applied periodically during the continuous blood pressure recording (Finapres Medical Systems, 2005).

The blood pressure at the finger is not equivalent to the blood pressure at the brachial. Therefore, the Finometer has a built-in waveform filter to correct this. This filtering consists of applying a transfer function, however, there are still minor differences between brachial and finger pressure (Finapres Medical Systems, 2005). Regardless, a study has shown that the Finometer was reliable in providing relative blood pressure measurements in normotensive, hypertensive, and obese individuals (Elvan-Taspinar et al., 2003). It has also been reported by Schutte, Huisman, Van Rooyen, Oosthuizen, & Jerling (2003) that the Finometer was reliable in measuring both short term and long term changes in blood pressure when participants were asked to ingest caffeine or vitamin supplements. In our study, only relative beat-to-beat blood pressure recordings are needed to calculate BRS and PEH.

B.2 Review of the Impedance Cardiography Measures

Impedence Cardiography (IC) calculates the hemodynamic variables (SV, CO and TPR) by detecting the changing resistance or impedance $\Delta Z$ in the thorax that result from the cardiac cycles (emptying and filling of the heart), respiratory activities (changing the amount of air in the thorax) and thoracic tissue resistance (difference in the density of muscles, bones, connective tissues). IC operates using the concept of Ohm’s law, which states that resistance or $\Delta Z$ is equal
to voltage divided by current. IC applies an alternating current (.05mA) through the electrodes attached to the human thorax and through that, the fluctuating $\Delta Z$ is detected (Sorba Medical Systems, 1996). IC then calculates the derivatives of $\Delta Z$ to find the $dZ/dt$ waveform (figure 7). $dZ/dt$ waveform is associated to different events during the cardiac cycle. IC is able to derive CO, SV and TPR using mathematical equations by matching $dZ/dt$ waveform to the ECG recording (Sorba Medical Systems Manual, 1996; Bogaard et al., 1997).

![Figure B.1](image)

**Figure B.1**: The three waves of Z, $dZ/dt$ and ECG are matched in terms of time. Adapted from Sorba Medical Systems Manual (1996)

Stroke volume is calculated using the Kubicek equation (listed below), which is under the assumption that 1) the thorax is a cylinder, which is from the base of the neck to the xiphoid process 2) the electrical current distribution in the cylinder is homogeneous. 3) the resistivity of blood during the cardiac cycle is constant 4) the maximal change in impedance x left ventricular ejection time (LVET) is proportional to the systolic pulsatile change in aortic blood volume (Kubicek, Karnegis, Patterson, Witsoe, & Mattson, 1966; Kubicek et al., 1970).

$$SV=p \times (L/Z_0)^2 \times dZ/dt_{(max)} \times LVET$$
P= resistivity of blood (135Ω/cm)

L= mean distance between inner electrodes

Z₀ = basal thoracic impedance (Ω)

dZ/dt_{max} = maximum rate of decrease in Z during systole which represents the velocity of blood ejected from left ventricle

LVET: left ventricle ejection time at the point from B to X on the dZ/dT waveform.

Cardiac output is determined by multiplying the stroke volume by the heart rate.

Total peripheral resistance (TPR) is calculated by the following equation (Sorba Medical Systems Manual, 1996):

\[
TPR \text{ (dynes-sec/cm}^5) = \text{mean arterial pressure (MAP) x 80/CO}
\]

MAP is calculated after entering the blood pressure obtained from the automated blood pressure cuff (Tango).

**Validity, Reliability and Limitations**

Several studies have compared the validity of IC’s hemodynamic measures to other known methods such as thermodilution. The SV measured by IC showed a correlation coefficient of .9 with thermodilution (Bogaard et al., 1997). IC has also shown to be reliable (r=.96) in healthy subjects with IC measures taken on separate days (McFetridge & Sherwood, 1999).

However, the limitation of IC using the Kubicek formula is that it tends to overestimate low CO values and underestimate high CO value (Warburton et al., 1999). This may lead to inaccurate absolute CO values and therefore it has been recommended that IC should be used to obtain relative CO changes only (Bogaard et al., 1997). It has been shown that IC produces inaccurate readings when participants have structural defects of the heart (ie: valvular disease, cardiac shunts, and atria fibrillation) (Ebert et al. 1984) and when undergoing strenuous physical activity (Warburton et al., 1999).

**B.3 Review of the Baroreflex Sensitivity**

Varieties of invasive and non-invasive techniques have been developed to assess BRS (Raven et al., 2006). Techniques that are used in animal models include: surgical isolation of the
baroreceptors, surgical denervation of the baroreceptor, pharmacological manipulation of the systemic vasculature and acute electrical or chemical blockade of the baroreflex’s neural afferents. Techniques used to examine BRS in humans include: pressure neck collar, pharmacological injection of phenylephrine (adrenergic vasoconstrictor) and nitroprusside (powerful vasodilator) and use of computer based mathematical analysis (La Rovere et al., 2008; Raven et al., 2006). In our study, noninvasive and cost effective, computer based BRS analysis will be used. Two approaches have been used: 1) sequence method and 2) spectral method. Short-term (10 minutes) sequence method will be employed to collect and analyze BRS. The sequence method assesses BRS by analyzing spontaneous beat-to-beat fluctuations of arterial pressure and heart rate (La Rovere et al., 2008). The sequence method is based on the identification of three or more consecutive beats in which progressive increases or decreases in systolic blood pressure are followed by progressive lengthening or shortening in RR interval. The baroreflex sensitivity is obtained by calculating the slopes of the regression line relating to changes in systolic pressure to changes in RR interval. All calculated slopes are then finally averaged to determine BRS (La Rovere et al., 2008; Parati et al., 1988). The time sequence has shown to significantly correlate with baroreflex sensitivity assessed with the phenylephrine method (sequence: \( r = 0.50, P < 0.001 \)) (Watkins, Grossman, & Sherwood, 1996) in borderline hypertensives (Watkins et al., 1996). The advantages of using sequence method include 1) the automatic and standardized computation, which allows one to eliminate some of the intra and inter-subject measurement variability; 2) the ability to measure the increasing and decreasing arterial pressure values which accounts for the asymmetry of baroreceptor response.

B.4 Review of the Arterial Stiffness

The changes in arterial stiffness can be an indicator of vascular health (Hamilton, Lockhart, Quinn, & McVeigh, 2007). There are three types of noninvasive arterial stiffness measurements: 1) systemic arterial stiffness which is assessed by augmentation index; 2) regional stiffness (i.e. a segment of the arterial tree) which is recorded through plus-wave velocity, 3) local stiffness (i.e. a small segment of a blood vessel) which is measured by ultrasound or magnetic resonance imaging (Hamilton, Lockhart, Quinn, & McVeigh, 2007). In this study, augmentation index (AIx) was used.
The measuring of arterial stiffness is based on the recording of blood pressure waves produced by the left ventricle and the arterial blood vessels. The contraction of the left ventricle results in the production of blood pressure waves travelling distally (incident wave). Waves are also reflected back to the heart (reflected wave) from the resistance produced by the peripheral blood vessels. The incident and reflected waves form arterial pressure waves, which will be recorded to undergo pulse wave analysis (PWA) in the determination of $\text{AI}_x$ (Hirata, Kawakami, & O'Rourke, 2006; Nichols, 2005).

$\text{AI}_x$ is determined by applying a hand-held tonometer to flatten or applanate an artery against an underlying structure (i.e. bones). The tonometer will sense the intra-arterial pulse pressure that is transmitted through the arterial wall. This pressure wave is then saved and analyzed using the computer program SphygmoCor. In this study, Augmentation index $\text{AI}_x$ will be used as the index for arterial stiffness (Nichols, 2005).

$\text{AI}_x$ is reported as a percent and is calculated by dividing augmentation pressure (AP) by pulse pressure (pp). ($\text{AI}_x = \frac{\text{AP}}{\text{PP}} \times 100$). AP is determined by the difference between the first systolic peak ($p_1$: peak flow) and the second systolic peak ($p_2$: peak pressure). In a healthy and compliant artery, the reflected wave returns during diastole which result in negative ($P_1 > P_2$) or zero ($P_1 = P_2$) AP. However, in a stiffer vessel, the reflected wave returns earlier and interrupts the systole resulting in the augmentation of the peak pressure (Papaioannou et al., 2004). SphygmoCor then applies a validated transfer function, calibrated using peripheral blood pressure, to calculate the central aortic pressure and waveform from the radial pulse pressure waveform (Davies & Struthers, 2003; Nichols, 2005). PWA using applanation tonometry has shown good intra-inter-operator reproducibility (Wilkinson et al., 1998). One of the advantages of applanation tonometry is that it is a quick and simple measurement to collect, which is suitable for the data collection process carried out in this study. However, the transfer function (a generalized mathematical algorithm) has been criticized for its inability to account for individual vascular composition differences. Regardless, studies have demonstrated that no significant variation is observed between normal adults (i.e., absent from any abnormal heart function) (Nichols, 2005).
### Appendix C: Study Timeline

<table>
<thead>
<tr>
<th>Week #</th>
<th>Tasks at each Week</th>
</tr>
</thead>
</table>
| 1      | Recruit participant  
           Resting Blood pressure assessment  
           VO_{2max} assessment              |
| 2      | Acute exercise assessment |
| 3      | Training week 1      |
| 4      | Training week 2      |
| 5      | Training week 3      |
| 6      | Training week 4      |
| 7      | Training week 5      |
| 8      | Training week 6      |
| 9      | Training week 7      |
| 10     | Training week 8      |
| 11     | Post training exercise assessment  
           VO_{2max} assessment  
           Resting blood pressure assessment |
Appendix E: Protocol for Acute Exercise Assessment

Time (minutes):

- Measure arterial stiffness (10 min)
- Set up for CIC 5 min
- Collection 1 (15 mins):
  1) Continuous BP
  2) Brachial BP
  3) HRV
  4) CO, TPR, SV
  5) Baroreflex sensitivity
- Exercise (30 mins):
  Exercising at a heart rate and intensity that corresponds to 65% VO2max
- Reset (5 mins)
- Collection 2 (30 mins):
  1) Continuous BP
  2) Brachial BP
  3) HRV
  4) CO, TPR, SV
  5) Baroreflex sensitivity
Appendix F: Par-Q

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

1. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?

2. Do you feel pain in your chest when you do physical activity?

3. In the past month, have you had chest pain when you were not doing physical activity?

4. Do you lose your balance because of dizziness or do you ever lose consciousness?

5. Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?

6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?

7. Do you know of any other reason why you should not do physical activity?

---

**YES** to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

**NO** to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active — begin slowly and build up gradually. This is the safest and easiest way to go.

- take part in a fitness appraisal — this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/84, talk with your doctor before you start becoming much more physically active.

**PLEASE NOTE:** If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professionals. Ask whether you should change your physical activity plan.

---

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

**I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction.**

---

**Signature of participant**

**Date**

**Signature of parent (if participant under the age of majority)***

**Witness**

---

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.

---

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94
PAR-Q & YOU

Get Active Your Way, Every Day—For Life!

Choose a variety of activities from these broad groups:

- Aerobic
- Resistance
- Stretching
- Active games
- Formal activities

Get active your way—build physical activity into your daily life...

- at home
- at school
- at work
- at play
- on the way
- through active living!

Starting slowly is very important. Be safe and consult your health professional. For a copy of this guide, contact Health Canada or visit our website at www.par-q.com

For more information, please contact:

Canadian Society for Exercise Physiology
202-188 Somerset Street West
Ottawa, ON K2P 0J2
Tel. 1-877-551-3755 • FAX (613) 204-8088
Online: www.cssep.ca

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Supported by: Health Canada

Physical Activity Readiness Questionnaire—PAR-Q
(revised 2002)

Time needed depends on effect

- Immediate
- Short-term
- Long-term

Benefits of regular activity:

- Improved health
- Increased fitness
- Improved balance
- Improved overall health
- Improved mood
- Improved sleep
- Improved communication
- Improved cognitive function

Health risks of inactivity:

- Poor health
- Increased risk of cardiovascular disease
- Increased risk of diabetes
- Increased risk of osteoporosis
- Increased risk of obesity

PAR-Q was developed by the British Columbia Ministry of Health. It has been revised by an Expert Advisory Committee of the Canadian Society for Exercise Physiology chaired by Dr. N. Goodall (2002).

Available in French at www.quebec-cps.sante.gouv.qc.ca/parq/rapport/index.html

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Fitness and Health Professionals May Be Interested in the Information Below:

The following companion forms are available for doctors’ use by contacting the Canadian Society for Exercise Physiology (address below):

The Physical Activity Readiness Medical Examination (PARmed-X) — to be used by doctors with people who answer YES to one or more questions on the PAR-Q.

The Physical Activity Readiness Medical Examination for Pregnancy (PARmed-X for Pregnancy) — to be used by doctors with pregnant patients who wish to become more active.

References:


Appendix G: Rapid Assessment of Physical Activity

How Physically Active Are You?

An assessment of level and intensity of physical activity

University of Washington Health Promotion Research Center
(3/27/06) © Copyright 2006
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Contact: James P. LoGerfo, MD, MPH, logerfo@u.washington.edu
Rapid Assessment of Physical Activity

**Physical Activities** are activities where you move and increase your heart rate above its resting rate, whether you do them for pleasure, work, or transportation.

The following questions ask about the amount and intensity of physical activity you usually do. The intensity of the activity is related to the amount of energy you use to do these activities.

**Examples of physical activity intensity levels:**

<table>
<thead>
<tr>
<th>Light activities</th>
<th>Walking Leisurely</th>
<th>Stretching</th>
<th>Vacuuming or Light Yard Work</th>
</tr>
</thead>
<tbody>
<tr>
<td>* your heart beats slightly faster than normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* you can talk and sing</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderate activities</th>
<th>Fast Walking</th>
<th>Aerobics Class</th>
<th>Strength Training</th>
<th>Swimming Gently</th>
</tr>
</thead>
<tbody>
<tr>
<td>* your heart beats faster than normal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* you can talk but not sing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vigorous activities</th>
<th>Stair Machine</th>
<th>Jogging or Running</th>
<th>Tennis, Racquetball, Pickleball or Badminton</th>
</tr>
</thead>
<tbody>
<tr>
<td>* your heart rate increases a lot</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* you can’t talk or your talking is broken up by large breaths</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### How physically active are you? *(Check one answer on each line)*

<table>
<thead>
<tr>
<th></th>
<th>Does this accurately describe you?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>I rarely or never do any physical activities.</td>
</tr>
<tr>
<td>2</td>
<td>I do some <strong>light</strong> or <strong>moderate</strong> physical activities, but not every week.</td>
</tr>
<tr>
<td>3</td>
<td>I do some <strong>light</strong> physical activity every week.</td>
</tr>
<tr>
<td>4</td>
<td>I do <strong>moderate</strong> physical activities every week, but less than 30 minutes a day or 5 days a week.</td>
</tr>
<tr>
<td>5</td>
<td>I do <strong>vigorous</strong> physical activities every week, but less than 20 minutes a day or 3 days a week.</td>
</tr>
<tr>
<td>6</td>
<td>I do 30 minutes or more a day of <strong>moderate</strong> physical activities, 5 or more days a week.</td>
</tr>
<tr>
<td>7</td>
<td>I do 20 minutes or more a day of <strong>vigorous</strong> physical activities, 3 or more days a week.</td>
</tr>
<tr>
<td>8</td>
<td>I do activities to increase muscle <strong>strength</strong>, such as lifting weights or calisthenics, once a week or more.</td>
</tr>
<tr>
<td>9</td>
<td>I do activities to improve <strong>flexibility</strong>, such as stretching or yoga, once a week or more.</td>
</tr>
</tbody>
</table>

ID # ____________________________

Today's Date ____________________
Scoring Instructions

RAPA 1: Aerobic

To score, choose the question with the highest score with an affirmative response. Any number less than 6 is suboptimal.

For scoring or summarizing categorically:

Score as sedentary:

1. I rarely or never do any physical activities.

Score as under-active:

2. I do some light or moderate physical activities, but not every week.

Score as under-active regular – light activities:

3. I do some light physical activity every week.

Score as under-active regular:

4. I do moderate physical activities every week, but less than 30 minutes a day or 5 days a week.

5. I do vigorous physical activities every week, but less than 20 minutes a day or 3 days a week.

Score as active:

6. I do 30 minutes or more a day of moderate physical activities, 5 or more days a week.

7. I do 20 minutes or more a day of vigorous physical activities, 3 or more days a week.

---

RAPA 2: Strength & Flexibility

I do activities to increase muscle strength, such as lifting weights or calisthenics, once a week or more. (1)

I do activities to improve flexibility, such as stretching or yoga, once a week or more. (2)

Both. (3)

None (0)
Appendix H: Recruitment Poster

GET FIT and GET HEALTHY NOW
An Exercise and Blood Pressure Study
Volunteers needed

STUDY PURPOSE
Our study is attempting to evaluate how our body responds to 8-week exercise training. Regular exercise is known to lower blood pressure and risk for hypertension; however, about one quarter of the population do not respond to the lowering effects of blood pressure after exercise. We are particularly interested in finding ways of identifying these “non-responders” early on, so that alternative methods can be used for them to prevent hypertension.

Participant Requirements
- Men and Post-menopausal women with resting blood pressure 120-139/80-89mmHg
- Aged 45-60 years old
- Not undergoing exercise training
- Non-smokers who are currently not on any cardiovascular medication
- Free from any history of cardiovascular disease, diabetes and chronic inflammatory disease

Benefits for the participants
- Increase your fitness in a safe, supervised training environment
- Gain knowledge about exercise training and health
- FREE membership at the Athletic Center at U of T.
- FREE personalized training plan designed to meet your fitness goals
- Making a large contribution to exercise science

Study Requirements
- Significant time commitment (on-site training and laboratory assessments)
- 8 weeks of walking/jogging training (4 exercise sessions per week, 30 minutes per session, exercise at 65% of your maximum effort)
- Follow-up assessment will take place 2 weeks after the completion of 8 weeks of training
- Non-invasive testing of cardiac output, total peripheral resistance, blood pressure, baroreflex sensitivity and heart rate variability
- Maximal exercise testing (VO2max)

Please Contact:
- sam1.liu@utoronto.ca
- scott.thomas@utoronto.ca
Cardiovascular Regulation Laboratory: 416-978-0762

UNIVERSITY OF TORONTO
FACULTY OF PHYSICAL EDUCATION AND HEALTH
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