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An Investigation of the Effects of Seven Days of Physical Training on Cardiac Output and the Relationship between Cardiac Factors

by

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled "An Investigation of the Effects of Seven Days of Physical Training on Cardiac Output and the Related Factors" submitted by Matthew Black in partial fulfilment of the requirements for the degree of Master of Science.

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Abstract

The effects of 7 days of combined endurance and resistance training on peak oxygen consumption, cardiac output, maximum heart rate and power during an incremental test, and specific blood parameters were assessed. Ten well trained cyclists (mean age 24.9±1, mean $\dot{V}O_2max$ 4.61L·min^{-1}) were tested at baseline and after 7 days of training. During the training, subjects also performed a daily incremental power output test to volitional fatigue where heart rate, peak power and peak lactate were recorded. Compared to baseline, 7 days of training did not alter cardiac output at any exercise intensity. Training resulted in a significant decrease in heart rate at rest and all exercise intensities except 66 watts, while stroke volume at rest, 265 watts and peak exercise intensity was 11.3, 10.6 and 9.1% higher post-training, respectively. Despite the increase in maximum stroke volume, peak oxygen consumption and power output remained unchanged following training. Training resulted in a 6.9% increase in plasma volume, with no change in glutamine, glutamate or alpha-1-antitrypsin. A significant decrease in peak heart rate was found after 2 days of training, and the decrease in peak heart rate persisted until the end of training. No change in peak power or peak lactate was found throughout the training cycle. Therefore, 7 days of combined endurance and resistance training appears to increase stroke volume in well-trained cyclists without increasing peak oxygen consumption or peak power output, presumable because of the decrease in peak heart rate.

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$\dot{V}O_2$ max:	Maximum oxygen consumed during an incremental exercise test to volitional fatigue
MAP:	Maximum aerobic power achieved during an incremental exercise test to volitional fatigue
VT2:	Second ventilatory threshold
$\dot{Q}$:	Cardiac output
HR:	Heart rate
SV:	Stroke volume
$(a-\bar{v})O_2$	Calculated difference between arterial and venous oxygen contents, as estimated from $\dot{V}O_2/\dot{Q}$
PV:	Plasma volume
Hb:	Hemoglobin concentration
Hct:	Hematocrit concentration
C_2H_2:	Acetylene
He:	Helium
N:	Nitrogen
O_2:	Oxygen

V_E = minute ventilation

P_{ECO2} = mixed expired CO_2 partial pressure

P_{IC2H2} = inspired C_2H_2 partial pressure

λ = C_2H_2 blood-gas partition coefficient

P_{ACO2} = end-tidal CO_2 partial pressure

P_{AC2H2} = end-tidal C_2H_2 partial pressure (He corrected) back extrapolated to breath 1

α_1-AT:	Alpha-1-antitrypsin.
Gm:	Glutamine
Ga:	Glutamate
CO:	Carbon monoxide
ICG:	Indocyanine Green Dye
EB:	Evans Blue Dye

Chapter 1. Introduction

1.0 Background

The ability of an endurance athlete to generate and maintain the highest level of power output is an integral component of success. Several factors affect this ability, including physiological, biomechanical and psychological characteristics. While a certain magnitude of each of these factors is undoubtedly innate, physical training acts as a powerful stimulus for improvements in each factor. The ability to precisely monitor changes in response to physical training is a critical component in the quest to increase the performance of the human body. As such, sports scientists continue to develop and improve methods for monitoring changes that occur with training.

Sustained muscular activity requires optimal functioning of the body's ability to take up, deliver and utilize oxygen. As energetic requirements increase during increasing intensity of exercise, oxygen consumption ($\dot{V}O_2$) increases to meet these demands. The linear relationship between $\dot{V}O_2$ and power output (Astrand and Ryhming, 1954) provides a useful index of global change in the physiological and biomechanical components (Figure 1.0). A decrease in the slope or y-intercept of the relationship suggests improvements in mechanical efficiency. The decrease in the slope or y-intercept of the relationship has positive consequences for the competing athlete, since, for any given $\dot{V}O_2$, the more efficient athlete will be able to produce a higher power output. Physical training can also increase the magnitude of maximum oxygen uptake ($\dot{V}O_2max$) (Ekblom et al., 1968), extending the relationship between $\dot{V}O_2$ and power output. Assuming efficiency is similar,

the increased power of the oxidative system will allow for a greater external power output at $\dot{V}O_2max$.

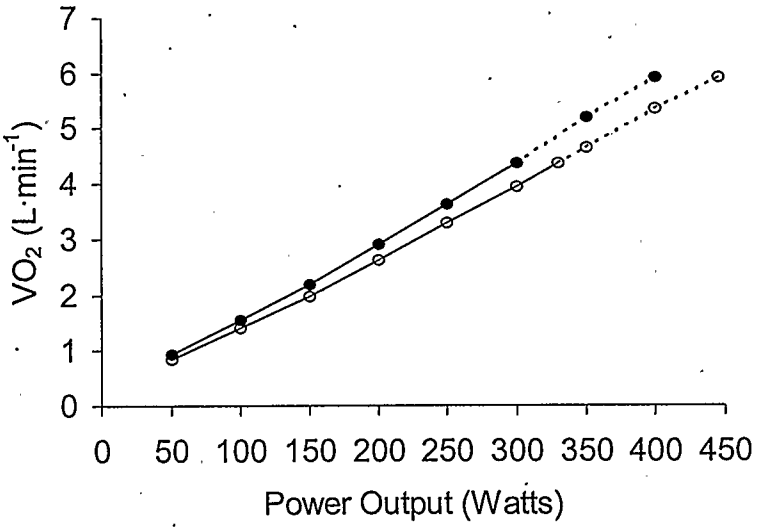

Figure 1.0. The linear relationship between oxygen consumption and power output (data from Astrand & Rodahl, 1986). A decrease in the slope or intercept of the relationship allows the athlete to produce a higher power output for the same oxygen consumption (open circles). Similarly, increasing the maximum oxygen consumption allows the athlete to produce higher power outputs, and this improvement is augmented when mechanical or physiological efficiency is improved (broken line, open circles).

The increase in $\dot{V}O_2$ with increasing exercise intensity represents a close coupling between central (oxygen delivery) and peripheral components (skeletal muscle metabolism). Cardiac output ($\dot{Q}$) increases oxygen and substrate delivery while maintaining thermo-neutrality, while the periphery increases the rate of oxidative ATP production. The increase in oxygen and substrate delivery is accomplished by redistributing blood flow to the active tissues while increasing $\dot{Q}$ by six times or more than resting $\dot{Q}$ (Rowell, 1986).

Effective coupling of oxygen delivery and use is accomplished through increasing $\dot{Q}$ linearly with $\dot{V}O_2$ (Ekblom et al., 1968) via increasing heart rate (HR) and stroke volume (SV) (Ekblom et al., 1968). Early research demonstrated that SV plateaus during exercise at approximately 40% of $\dot{V}O_2max$ (Astrand et al., 1964). Consequently, above 40% $\dot{V}O_2max$, increases in $\dot{Q}$ were primarily achieved through increasing HR (Astrand et al., 1964). However, recent evidence has shown that well-trained athletes are capable of increasing SV up to maximum exercise intensities (Gledhill et al., 1994; Di Bello et al., 1996; Warburton et al., 1999c; Ferguson et al., 2001; Zhou et al., 2001). As a result, trained athletes appear to increase $\dot{Q}$ through the entire range of exercise intensities by increasing both HR and SV.

Extensive research has shown an increase in SV and decrease in HR for any given power output or $\dot{V}O_2$ following endurance training in untrained and trained subjects (Ekblom et al., 1968; Ekblom et al., 1973; Ehsani et al., 1978; Péronnet et al., 1981; Mier et al., 1996; Mier et al., 1997; Wilmore et al., 2001). Increases in SV can be achieved by altering cardiac morphology (increasing cardiac dimensions), increasing contractile properties of the heart and altering extra-myocardial factors that affect ventricular filling or emptying (Blomqvist and Saltin, 1983).

In a meta-analysis of longitudinal echocardiographic studies, Péronnet et al. (1981) reported the main alteration in cardiac morphology following endurance training was an increased end-diastolic volume of the ventricle. Early research with isolated cardiac fibers

found a length-dependence of cardiac muscle fiber force development (Patterson et al., 1914). When the volume of the ventricle at end-diastole is increased, elongated myocytes can produce more tension when they contract. This relationship has been identified as the Frank-Starling mechanism. As a result of the Frank-Starling mechanism, under conditions of equal afterload, increasing the end-diastolic volume of the ventricle (preload) results in increased SV. An increase in end-diastolic volume can be achieved through a reduction in HR (i.e. increased diastolic filling time), an increase in ventricular compliance (Woodiwiss and Norton, 1995), pericardial compliance (Stray-Gundersen et al., 1986) or an increase in ventricular filling pressure secondary to increased blood volume (Convertino et al., 1991) or altered venous capacitance (Tyberg, 2002).

Improvements in intrinsic contractile performance of the heart also result in increased SV. Several cross-sectional studies have shown improved ventricular contractile function in trained subjects compared to sedentary subjects (Gledhill et al., 1994; Seals et al. 1994). Several longitudinal studies have shown an increase in ventricular contractility following exercise training (Krzeminski et al., 1989; Diffee et al., 2001; Wisloff et al., 2001). Training-induced improvements in systolic function have been explained by increased calcium sensitivity (Diffee et al., 2001; Wisloff et al., 2001).

Due to its ease of measurement, the HR response to exercise may be useful for evaluating change in the heart's response to exercise training. Astrand and Ryhming (1954) developed an exercise test based on the HR at 50% $\dot{V}O_2max$ to predict $\dot{V}O_2max$. Changes in HR at a specific workload are generally thought to reflect changes in SV, and as such a decrease in

HR at submaximum workloads can be used to predict increases in $\dot{V}O_2max$ and power output. The relationship between cardiac factors (HR and SV) and $\dot{V}O_2$ is defined with the Fick equation;

$$\dot{V}O_2 = \dot{Q} \cdot (a\text{-}\bar{v})O_2$$

Where:

$\dot{V}O_2$ = Oxygen consumption ($ml \cdot min^{-1}$)

$\dot{Q}$ = Cardiac output ($ml \cdot min^{-1}$) = HR · SV

HR = Heart rate ($beats \cdot min^{-1}$)

SV = Stroke volume ($ml \cdot beat^{-1}$)

$(a\text{-}\bar{v})O_2$ = Difference between arterial and venous O_2 content ($ml \cdot 100\ ml^{-1}$)

Evaluation of the Fick equation suggests changes in HR may represent a complex interaction between systemic oxygen delivery and use. As such, changes in the HR response to exercise may reflect changes in: 1) SV 2) $\dot{Q}$ 3) peripheral oxygen extraction and 4) mechanical efficiency.

Recently, several non-invasive measures of $\dot{Q}$ have been validated which allow determination of SV during intensive exercise (Barker et al., 1999; Warburton et al., 1999b). The non-rebreathing acetylene (C_2H_2) method of Barker et al. (1999) provides a

method for simultaneously measuring $\dot{Q}$ and $\dot{V}O_2$, and provides a means for evaluating the source of change in the HR response to exercise.

1.1 Statement of the Problem

Following 3 – 7 days of intense training in national level endurance athletes, the linear relationship between HR and power output has been observed to change (S. Norris, personal communication). However, no studies have evaluated the specific source of change in this relationship that occurs with training of a similar duration. In addition, no studies have examined the change in the slope component of the HR versus power output relationship that has been observed following intense training periods in well-trained athletes.

1.2 Statement of the Research Hypothesis

This study tested the hypothesis that 7 days of high-volume and high-intensity training would increase $\dot{Q}$ at any given workload when compared to pre-training. It was expected that a decrease in the slope and y-intercept of the HR versus power output would occur, and these changes would inversely reflect changes in SV. Based on the multitude of variables affecting SV, it was anticipated that changes in HR and SV would be caused by mechanisms apart from an increase in plasma volume.

Chapter 2. Literature Review

2.0 Changes in $\dot{V}O_2$ max following Short-term Endurance Training

It has been established that the change in $(a-\bar{v})O_2$ is minimal following short-term training (Rowell, 1986), and improvements in $\dot{V}O_2$max are the result of increased maximum $\dot{Q}$. Consequently, increases in $\dot{V}O_2$max may provide a useful index of increases in maximum $\dot{Q}$. $\dot{V}O_2$max can increase with training of relatively short duration. Gaesser and Poole (1988) noted an 8% increase in $\dot{V}O_2$max in healthy sedentary males following three weeks of training. Following ten days of training for two hours/day at 60% $\dot{V}O_2$max, a 4% increase in $\dot{V}O_2$max was found in moderately active male subjects (Green et al., 1991).

Changes in $\dot{V}O_2$max in well-trained athletes following short-term training are variable. Smith et al. (1999) found a 5% increase in $\dot{V}O_2$max following four weeks of intensive training in well-trained athletes. Hedelin et al. (2000) reported a 5% decrease in $\dot{V}O_2$max in well-trained canoeists following an intensive six-day training camp. The specific source for the decrease in $\dot{V}O_2$max was not identified. However, Hedelin et al. (2000) noted a significant decrease in maximum HR, suggesting a possible chronotropic limitation to $\dot{V}O_2$max following 6 days of intense training. Although the authors did not report the correlation between changes in maximum HR and $\dot{V}O_2$max, Hedelin et al. (2000) did report a correlation ($r = 0.79$) between the reduction in maximum HR and run time to exhaustion. Similarly, Jeukendrup et al. (1992) reported a significant reduction in

$\dot{V}O_2max$, maximum HR and time trial performance following 2 weeks of intensified training. In contrast, Costill et al. (1988) found no change in swimming performance or $\dot{V}O_2max$ despite a reduction in maximum HR following 10 days of increased training volume and intensity.

It appears that the changes in $\dot{V}O_2max$ following exercise training are dependent on the training status of the subject, as well as the duration and intensity of the training stimulus. In addition, markedly increased training volume and intensity in well-trained athletes can negatively impact a subject's $\dot{V}O_2max$ in the short term.

2.1 Exercise Training and Cardiac Output

In addition to higher $\dot{V}O_2max$ in endurance athletes, evidence supports a greater maximum $\dot{Q}$ in elite endurance athletes when compared to their untrained counterparts (Gledhill et al., 1994; Krip et al., 1997; Zhou et al., 2001). Furthermore, the research consensus to date suggests that this difference is mediated through exercise training. Ekblom et al. (1968) reported an 8% increase in maximum $\dot{Q}$ in sedentary subjects following 16 weeks of endurance training. Spina et al. (1992) demonstrated a 12% increase in maximum $\dot{Q}$ following 12 weeks of endurance training. It appears that the increase in maximum $\dot{Q}$ can occur following training of shorter duration as well. Mier et al. (1997) reported a 12% increase in maximum $\dot{Q}$ in sedentary subjects following 10 days of intense

endurance training. Unfortunately, no studies to date have evaluated changes in maximum $\dot{Q}$ in well-trained athletes following intense training of similar duration.

The effect of training on submaximal $\dot{Q}$ appears variable. Several authors have reported a significant decrease in $\dot{Q}$ at the same submaximal power output following training (Andrew et al., 1966; Ekblom et al., 1968; Wilmore et al., 2001), while other authors have found no change (Barnard, 1975; Mier et al., 1996). The decrease in submaximal $\dot{Q}$ has been attributed to an improvement in mechanical efficiency following training which results in a reduced $\dot{V}O_2$ at any given workload (Ekblom et al., 1968; Wilmore et al., 2001). However, Ekblom et al. (1968) also noted a decrease in $\dot{Q}$ at 1 and 2 liters of $\dot{V}O_2$ post-training. The authors suggested the decrease in $\dot{Q}$ at the same $\dot{V}O_2$ may reflect a more effective distribution of $\dot{Q}$ to the working musculature or improved extraction of oxygen from arterial blood. Unfortunately, little evidence exists regarding the effect of training on submaximal $\dot{Q}$ in well-trained endurance athletes.

2.2 Changes in Stroke Volume with Training

There is a compelling body of evidence suggesting that the increase in maximum $\dot{Q}$ with training is achieved through increases in SV. Ekblom et al. (1968) reported a 13% increase in maximum SV in sedentary subjects following 16 weeks of endurance training, and Spina et al. (1992) found a 16% increase in maximum SV in sedentary subjects following 12 weeks of endurance training. Research has shown that similar improvements

can be achieved following shorter training cycles. Mier et al. (1996) found a 10% increase in SV at 50% of the pre-training $\dot{V}O_2max$ following 10 consecutive days of training, and in a similar study, Mier et al. (1997) reported a 15% increase in maximum SV after 10 consecutive days of endurance training. Given the limited data on well-trained athletes, it is difficult to speculate on the effects of such a short training stimulus on SV. However, it has been suggested that maximal improvements in SV are achieved following interval training at intensities requiring $\dot{V}O_2max$ (Cox et al., 1986).

2.2.0 Mechanisms for Increased Stroke Volume: Altered Preload

Exercise training can increase SV by increasing left ventricular end-diastolic volume leading to improved use of the Frank-Starling mechanism. An acute increase in the left ventricular end-diastolic volume may occur in response to an increase in central venous pressure. Increases in central venous pressure can be achieved via an increased volume of fluid in the vasculature (Berne & Levy, 2001). Mier et al. (1997) demonstrated a 4.6% increase in left ventricular end-diastolic dimension following 10 days of exercise training which induced a 6.3% increase in total blood volume. The authors found a strong relationship between the training-induced increase in blood volume and the training-induced increase in SV ($r = 0.85$). This data suggests an enhanced myocardial shortening secondary to increased filling pressure and the Frank-Starling mechanism.

A strong relationship between the increase in blood volume and SV has been found following artificially induced hypervolemia. Kanstrup and Ekblom (1982) induced hypervolemia (12.6%) via infusion of a plasma expander in moderately trained athletes and

found a 5 $b \cdot min^{-1}$ decrease in HR at any submaximal workload, while SV was significantly increased. Warburton et al. (1999c) induced hypervolemia in elite cyclists and found a significant increase in SV during exercise. These findings provide strong support for an increase in SV through increased preload via hypervolemia. However, while Hopper et al. (1988) found similar results in untrained subjects, the same expansion in trained subjects did not result in any significant changes in SV. These data may suggest a potential upper limit in the ability of the ventricles to accommodate increases in blood volume. However, it is difficult to ascertain if this effect is a consequence of artificially induced hypervolemia rather than training-induced hypervolemia.

There is evidence that supports an increase in blood volume (hypervolemia) following training. The magnitude of hypervolemia appears dependent on the training state of the athlete and the intensity/duration of training. The greatest effect was noted by Green et al. (1990), who reported a 20% increase in plasma volume following 3 days of prolonged duration training (2 $hrs \cdot day^{-1}$) in moderately active subjects ($\dot{V}O_2max = 48.5\ ml \cdot kg^{-1} \cdot min^{-1}$). Mier et al. (1997) found a 8.8% increase in plasma volume in sedentary subjects following 10 days of cycling 1 $hr \cdot day^{-1}$. Similar increases in plasma volume (11.6%) were found following 3 days of intermittent intensive exercise in active subjects ($\dot{V}O_2max$ = 53 $ml \cdot kg^{-1} \cdot min^{-1}$) (Green et al., 1984). Well-trained runners experienced a 4.4% increase in plasma volume following two days of high-intensity training (Richardson et al., 1996).

While increases in total blood volume may in part explain the increase in SV that occurs following training, alterations in venous capacitance may also affect central venous

pressure. Flamm et al. (1990) showed a redistribution of blood volume from the legs and abdomen to the heart and lungs during exercise of increasing intensity. At $\dot{V}O_2max$, heart blood volume was 124% of baseline, while lung volume increased to 150% of baseline (Flamm et al., 1990). An alteration in the redistribution of blood to the central circulation may provide a stimulus for increasing end-diastolic volume.

2.2.1 Mechanisms for Increased Stroke Volume: Altered Contractility

Although many authors suggest increases in SV following endurance training are mainly due to increases in end-diastolic volumes and use of the Frank-Starling mechanism, several authors have shown improved ventricular contractility in endurance-trained and resistance-trained athletes. Jenson-Urstad et al. (1998) compared elite runners and moderately active controls and found greater ventricular contractility in elite runners. Similar findings were reported by Gledhill et al. (1994) in comparing elite cyclists to untrained controls. Specifically, the rate of ventricular emptying at a heart rate of 190 $b \cdot min^{-1}$ was 20% greater in elite cyclists. Fisman et al. (2002) compared endurance-trained and resistance-trained subjects and found similarly heightened levels of systolic function when compared to untrained subjects. Mier et al. (1997) noted a trend ($P = 0.06$) for left ventricular end-systolic diameter to decrease following 10 days of endurance training. Decreases in end-systolic volumes can be attributed to enhanced contractility of the myocardium or a reduction in afterload. Wisloff et al. (2001) found a 20% increase in contractility of isolated rat myocytes following 4 weeks of endurance training. Krzeminski et al. (1989) found increased ventricular contractility during exercise in subjects following 4 weeks of exercise training. It has been suggested that improvements in systolic function

may be explained by increased calcium sensitivity (Diffee et al., 2001; Wisloff et al., 2001). The above studies suggest that improvements in SV following exercise training may be mediated through preload-independent increases in ventricular contractility.

2.2.2 Mechanisms for Increased Stroke Volume: Altered Afterload

Marked reductions in total peripheral resistance following exercise training provide an essential mechanism for increasing SV (Blomqvist and Saltin, 1983). Decreases in total peripheral resistance are achieved by alterations in the size of the capillary bed and changes in arteriolar structure and function (Blomqvist and Saltin, 1983). Short-term alterations in afterload are generally attributed to alterations in flow-mediated vasodilation and arterial compliance. Drexler et al. (1996) found a significant increase in flow-mediated vasodilation in the trained forearm following 4 weeks of unilateral dynamic exercise training. These changes have been attributed to alterations in endothelial function or nitric oxide release (Huonker et al., 1996). Increases in flow-mediated vasodilation result in an increase in the size of the vascular bed and reduction in afterload.

Increases in arterial compliance also induce reductions in ventricular afterload. Mohiaddin et al. (1989) found greater total arterial compliance in endurance-trained athletes compared to sedentary controls. Cameron et al. (1994) reported a significant increase in systemic arterial compliance following 4 weeks of endurance training in sedentary subjects. Based on the findings of the study, Cameron et al. (1994) concluded that exercise training induces blood-pressure independent increases in systemic arterial compliance which appear to result from alterations in the intrinsic compliance of arteries. In addition, the authors found

a linear relationship between the change in systemic arterial resistance and changes in $\dot{V}O_2max$ following training. The strong relationship between arterial compliance and $\dot{V}O_2max$ suggests a reduction in arterial compliance allows for increased $\dot{Q}$, presumably via increased SV.

2.3 Changes in Heart Rate with Training

The HR response to exercise changes with an individual's physical training status. Several authors have identified a decrease in HR at any given power output following training (Hedelin et al., 2000; Green et al., 1990). Following periods of intense short-duration training, this shift has been attributed to an enhanced inotropic state as a result of acute increases in SV secondary to increases in plasma volume (Hedelin et al., 2000). The authors found a strong correlation ($r = -0.8$ to -0.9) between the increase in plasma volume and decrease in HR at submaximal workloads following six days of a dramatic increase in training load. However, a significant correlation was not found between the increase in plasma volume and the decrease in maximum HR. The authors attributed the decrease in maximum HR following training to peripheral fatigue, and noted a decrease in maximum lactate at maximum HR. However, it has been suggested that reductions in maximum HR following periods of intense training may be due to altered beta-adrenergic receptor responsiveness (Douglas et al., 1998) or density (Werle et al., 1990). However, no studies have evaluated whether acute reductions in maximum HR result in decreased maximum $\dot{Q}$.

While a decrease in exercising HR at any given workload is generally well recognized, few studies have evaluated changes in the slope of the HR versus power output relationship.

Sunagawa et al. (1985) evaluated differences in the slope of the HR versus $\dot{V}O_2$ relationship (i.e. O_2 pulse) and found that physically inactive children demonstrated a higher slope when compared to physically active children. Since the maximal HR was not significantly different between the untrained and trained subjects, the authors concluded that the trained subjects had an enhanced cardiac reserve, presumably via increased SV. The authors also found a significantly higher slope of the HR versus $\dot{V}O_2$ relationship for a group of children with various heart diseases when compared to the active and inactive groups. The authors suggested that this data may be useful in identifying a decrease in cardiac function during exercise. During a condition of decreased inotropic state, $\dot{Q}$ is preserved via an increased HR. Evaluation of changes in HR versus $\dot{V}O_2$ rather than HR versus power output allows the investigators to eliminate the possibility of changes in mechanical efficiency as a source of altered metabolic cost.

2.4 Measures of Training Stress

The process of exercise training serves to impose a stress of sufficient magnitude to induce an adaptive response and a subsequent higher level of functioning. It has been suggested that the adaptive process reflects a balance between the response to training loads and the corresponding recovery (Smith and Norris, 2000). While several blood markers have been suggested for monitoring training stress, Rowbottom et. al. (1995) suggested plasma glutamine (Gm) can be used as a marker of positive and negative adaptive states. Specifically, an increase in Gm reflects a positive adaptive state while a decrease in Gm reflects a negative adaptive state or overtraining (Rowbottom et al., 1995).

Keast et al. (1995) reported a 22% decrease in Gm following 5 days of intensive training, and a 48% decrease following 10 days of intense training. Smith and Norris (2000) found an 11% decrease in Gm in elite athletes during intense training periods when compared to a rested state. Smith and Norris (2000) suggested that a decrease in Gm occurs when the volume of training exceeds the athlete's capacity to adapt. In the same study, Smith and Norris (2000) found a significant increase in plasma glutamate (Ga) concentration during intensive training periods, and suggested elevations in Ga may occur in response to high-intensity training periods. As such, monitoring Gm and Ga concentrations may provide useful insight into the ability of the athlete to tolerate training loads.

The measurement of alpha-1-antitrypsin (α_1-AT) has been suggested for measurement of exercise-induced inflammation and tissue injury (Smith and Roberts, 1994). Roberts and Smith (1989) reported a 9% increase in α_1-AT in untrained subjects 24 hours after completing a 30 second supramaximal test. Following one week of high-intensity training no change in α_1-AT was found, suggesting α_1-AT may provide a useful marker for evaluating the inflammatory response to a training regimen. Given this data, the use of α_1-AT may provide an additional marker for monitoring the extent and type of stress that occurs in response to training.

2.5 Measures of Cardiac Output

Numerous techniques, both invasive and non-invasive, can be used for the measurement of $\dot{Q}$ (Warburton et al., 1999a; Warburton et al., 1999b). Each methodology

has its own limitations which are dependent on the subject being evaluated, the research setting, the type of exercise being performed and the range of exercise intensities over which $\dot{Q}$ is to be measured. The following sections address the main advantages and disadvantages of several techniques used in an exercise setting.

2.5.0 Invasive Measures

The direct Fick and dye-dilution methods are considered the gold standards of $\dot{Q}$ measurement, and provide accurate and reliable measures of $\dot{Q}$ during rest and steady-state exercise (Warburton et al., 1999a). However, both methods contain considerable risks due to the required cardiac catheterization. Consequently, the use of these methods in a research setting is rarely feasible (Warburton et al., 1999a). Similar limitations are inherent in the thermodilution technique. In addition, the validity of the thermodilution technique has been questioned due to assumptions regarding heat loss from the coolant before injection and coolant loss in the circulation (Mackenzie et al., 1986). Due to these limitations, several non-invasive measures of $\dot{Q}$ may be more useful in the exercise-physiology research setting.

2.5.1 Non-invasive Measures

CO_2 Rebreathing

CO_2 rebreathing has been used extensively during exercise due to its non-invasiveness and ability to give accurate measures of $\dot{Q}$ during exercise (Wigle et al., 1979; Warburton et al., 1999b). The main drawback of the CO_2 rebreathing technique is

that it requires steady state exercise for the accurate determination of $\dot{Q}$. Consequently, this method is inappropriate for an incremental exercise test where $\dot{Q}$ determinations near $\dot{V}O_2max$ are required.

Doppler Echocardiography

Doppler echocardiography provides another non-invasive measure of $\dot{Q}$ during exercise. Shaw et al. (1982) reported a coefficient of variation of 9 to 15% during submaximal exercise in a group of healthy subjects. During maximal exercise this value was similar (14%). Excellent reproducibility using the same technician was also found when comparing several serial measurements ($r = 0.98$). However, several sources of inaccuracy have been noted in the use of Doppler echocardiography as a measure of $\dot{Q}$ (Espersen et al., 1995). Assumptions in the angle between the transducer beam and blood flow may be inappropriate, leading to inaccurate measures of blood flow velocity. In addition, transducer placement will affect the reliability of echocardiographic determinations of $\dot{Q}$. The most notable limitation during exercise testing is the effect of movement artifact on determination of $\dot{Q}$. Consequently, the use of Doppler echocardiography during an incremental test to $\dot{V}O_2max$ may not provide satisfactory results.

Single-Breath Constant-Exhalation C_2H_2 Method

The recent integration of rapid response infrared C_2H_2 analyzers into metabolic carts allows a method of determining $\dot{Q}$ without the use of rebreathing techniques. This is

beneficial since it eliminates the increase in arterial PCO_2 and changes in arterial PO_2 that may occur with rebreathing techniques (Barker et al., 1999). Zenger et al. (1993) reported a high correlation between the constant-exhalation C_2H_2 method and direct Fick measurements ($r = 0.92$). However, some subjects were not able to perform the constant-exhalation manoeuvre, which affects the accuracy of the measurement. It is likely that the required breath-hold manoeuvre and subsequent constant-exhalation becomes increasingly difficult as ventilation rate increases. As a result, this method appears limited to submaximal testing intensities.

Open-Circuit Acetylene-Uptake Method

Recently, Barker et al. (1999) proposed a method utilizing open-circuit C_2H_2-uptake. As with the other foreign gas techniques, open-circuit C_2H_2-uptake is based on the principle of mass conservation, which states that the rate of alveolar-capillary diffusion of a soluble gas is proportional to capillary blood flow (Barker et al., 1999). In normal subjects, capillary blood flow is equivalent to $\dot{Q}$. During the open-circuit C_2H_2 technique the subject breathes a gas mixture (1% C_2H_2, 5% He, 20.9% O_2, balance N) through a one-way valve. Expired C_2H_2 and He are measured with the use of a mass spectrometer, while ventilation and $\dot{V}O_2$ are measured with a metabolic cart. Following correction for mixing with the ratio of inspired and end-tidal He, end-tidal C_2H_2 partial pressure is back-extrapolated to breath 1 to account for the recirculation of C_2H_2 back to the lungs in venous blood (Barker et al., 1999). Since the end-tidal C_2H_2 partial pressure will be dependent on the solubility of C_2H_2 in the blood, a solubility coefficient is used to correct for differences in solubility. End-tidal C_2H_2 (breath 1) is then used to calculate $\dot{Q}$ based on the following formula;

$$\dot{Q} = [V_E \cdot P_{ECO2} \cdot (P_{IC2H2} - P_{AC2H2}) / \lambda \cdot P_{ACO2} \cdot P_{AC2H2}]$$

Where:

V_E = minute ventilation ($L \cdot min^{-1}$ BTPS)

P_{ECO2} = mixed expired CO_2 partial pressure

P_{IC2H2} = inspired C_2H_2 partial pressure

λ = C_2H_2 blood-gas partition coefficient

P_{ACO2} = end-tidal CO_2 partial pressure

P_{AC2H2} = end-tidal C_2H_2 partial pressure (He corrected) back extrapolated to breath 1

Barker et al. (1999) compared this technique to direct Fick and found no significant differences between the two methods. A linear relationship between $\dot{Q}$ and $\dot{V}O_2$ existed using both methods, and the regression line was nearly identical using the Fick ($\dot{Q}$ = 4.71 $\dot{V}O_2$ + 5.63) and C_2H_2-uptake ($\dot{Q}$ = 4.71 $\dot{V}O_2$ + 5.60) methods. However, accuracy of the technique may be limited when ventilation-perfusion mismatching occurs. Another limitation to the method is the need to determine λ for each individual, since considerable variation in this measure occurs between subjects (Barker et al., 1999). However, the authors noted that determination of λ is less important when comparing mean data. In addition, Barker et al. (1999) found no significant change in λ following test-retest 7 days apart, suggesting a constant value for λ can be used to ensure repeatable results. Given these limitations, Barker et al. (1999) noted the open-circuit technique was more comfortable for the subjects than C_2H_2-rebreathing techniques, and allows measurement of

$\dot{Q}$ up to maximum exercise intensity without discomfort. Using a similar open-circuit C_2H_2-breathing technique established by Johnson et al. (2000), Bell et al. (2003) reported a coefficient of variation of 6-8% in tests done 2 days apart. The authors reported the greatest variability in the open-circuit C_2H_2-breathing technique during lower-intensity exercise, with the least variability during near-maximal exercise intensities.

While several non-invasive measures of $\dot{Q}$ are available that minimize the risks and costs associated with invasive techniques, each non-invasive method also has its limitations. Doppler echocardiography appears limited by increasing movement artefact with increasing exercise intensity. Although some studies have partially rectified this problem by momentarily stopping exercise while the measurement is taken, this method introduces a variety of possible errors that will negatively affect the relationship between cardiac factors. The use of carbon dioxide rebreathing, while well established, does not allow determination of $\dot{Q}$ during non-steady state exercise. Another limitation to rebreathing techniques lies in the potential subject discomfort, particularly in response to increasing arterial CO_2 levels. Due to the difficulty in performing the constant-exhalation C_2H_2 technique in the face of increasing ventilation, this method also appears limited to submaximal if not sub-anaerobic threshold intensities. As a result, the open-circuit C_2H_2-uptake method presents the fewest limitations for an incremental test to $\dot{V}O_2max$. Recognizing the limitations inherent in the method, the open-circuit C_2H_2 method provides an accurate and reliable measure of $\dot{Q}$ during an incremental test to $\dot{V}O_2max$ without

altering arterial carbon dioxide or oxygen content. Furthermore, simultaneous measurements of $\dot{Q}$ and $\dot{V}O_2$ can be performed.

2.6 Measures of Blood Volume

Training induced increases in blood volume are frequently considered an important stimulus for increases in SV. As such, the measurement of blood volume following requires a reliable and affordable technique. The following sections outline the advantages and disadvantages of the most feasible methods for determination of blood volume.

2.6.0 Estimation of Changes using Hemoglobin and Hematocrit

Acute alterations in blood volume are generally recognized to reflect changes in plasma volume rather than red blood cell volume. As such, Dill and Costill (1974) reported a method for the determination of changes in plasma volume using measurement of hemoglobin (Hb) and hematocrit (Hct);

$$PV_1 = 1 - Hct_1$$

$$PV_2 = 100 \cdot (Hb_1/Hb_2) - [100 \cdot (Hb_1/Hb_2) \cdot Hct_2]$$

$$\Delta PV = (PV_2 - PV_1) / PV_1$$

Where:

PV_1, PV_2 = Plasma volume before (1) and after (2)

Hct_1, Hct_2 = Hematocrit fraction before (1) and after (2)

Hb_1, Hb_2 = Hemoglobin concentration before (1) and after (2)

The main limitation lies in the assumption that red cell volume remains constant before and after the training intervention. As such, any training that may lead to red cell destruction or synthesis may affect the prediction of changes in plasma volume. However, under conditions where red cell volume remains constant, the estimation of changes in plasma volume in this manner provides a relatively inexpensive and simple procedure.

2.6.1 Carbon Monoxide Rebreathing

During the carbon monoxide (CO) rebreathing technique, the subject breathes a specific quantity of CO for approximately 15 minutes. The main advantage of this method is that carbon monoxide labelled erythrocytes are unlikely to leave the circulation, as may occur in other dilution techniques. Using CO-rebreathing, Christensen et al. (1993) found the coefficient of variation was 6.2%. However, it has been speculated that there may be a loss of carbon monoxide to cytochrome heme and myoglobin. In addition, leakage of gas from the rebreathing apparatus may introduce another source of error. The main limitations of the technique involve the increase in carboxyhemoglobin levels and intricate rebreathing apparatus.

2.6.2 Dye-Dilution Techniques

The principle of dye-dilution is based on the theory of mass conservation, and can be described by the following equation;

$$V = M1/C2$$

Where:

V = volume after dye injection

M1 = injected amount of dye

C2 = concentration of dye in the sample taken

After injection into the bloodstream, the dye (e.g. Evans Blue, Indocyanine Green) binds with albumin, and mixes in the bloodstream during circulation. The validity of the mass conservation principle requires that the injected dye remains in a closed system. However, following binding with albumin a small component of the dye-albumin complex leaves the blood at a very slow rate. This loss of dye violates the principle of mass conservation. Consequently, the rate of dye-albumin disappearance must be corrected for by taking multiple blood samples after full mixing has occurred (Foldager & Blomqvist, 1991).

Foldager and Blomqvist (1991) performed three successive determinations of plasma volume through injection of Evans Blue (EB) dye and found no significant differences between the three values. Similar reliability was found by Mier et al. (1996), who reported a coefficient of variation of 2.1%. Using Indocyanine Green dye (ICG), Haller et al. (1993) found no significant difference between tests. Schad et al. (1987) compared plasma volume determinations using EB and ICG and found no significant difference between the methods. While EB and ICG have both been used extensively, ICG is advantageous in that it is cleared rapidly from the blood. Henschen et al. (1993) reported a half-life of 187 seconds, resulting in an exponential decay of $21\% \cdot min^{-1}$. In addition, ICG is eliminated exclusively through the liver, with no extrahepatic uptake, urinary excretion or metabolic transformation (Henschen et al., 1993).

2.7 Conclusion

Research suggests that short-term exercise training can alter $\dot{V}O_2max$, however, the direction of response appears dependent on the training status of the individual and the duration of the training stimulus. Previous findings suggest that training cycles of 6-14 days duration in well-trained endurance athletes results in either a decrease in $\dot{V}O_2max$ or no measurable effect, while training cycles of 21 days have been reported to increase $\dot{V}O_2max$ in similarly trained subjects. The source of change in $\dot{V}O_2max$ following short-term intense training has not been identified, although changes in cardiac output have been suggested as the most plausible explanation. Changes in cardiac preload, afterload and contractility have been reported following four weeks of endurance-exercise training, which may provide potential mechanisms for increases in stroke volume and subsequently cardiac output. However, decreases in maximum heart rate following intense training have also been demonstrated, suggesting an adaptive limit to short-term increases in maximum cardiac output. More research is needed to determine the effect of intense training cycles on the cardiac output response to exercise in well-trained athletes.

Chapter 3: Methodology

3.0 Sample Size

Changes in the $\dot{Q}$ response of well-trained athletes to incremental exercise following 7 days of training have not been studied in the past. Considerable research indicates that an increase in $\dot{Q}$ following plasma volume expansion is necessary to compensate for the reduced arterial oxygen content. Consequently, the sample size for the present study was based on the change in peak $\dot{Q}$ found by Warburton et al. (1999c) following an acute 8% expansion of plasma volume in similarly trained subjects. The significance level (α) was set at 0.05. The minimum sample size required to detect a 1 $L \cdot min^{-1}$ change in peak $\dot{Q}$ using a two-sided $\alpha = 0.05$ and a power of 0.80 was 9. For details of the sample size calculation see Appendix D.

3.1 Subjects and Ethics Approval

Subjects were recruited from the university community through a poster outlining the details of the study. Age requirements were between 18-35 yrs and a $\dot{V}O_2max$ above 60-$ml \cdot kg^{-1} \cdot min^{-1}$ was required for inclusion in the study. Informed consent was obtained from each subject. Ethical approval for the study was obtained from the University of Calgary Conjoint Health Research Ethics Board.

3.2 Laboratory Setting

All testing was conducted in the Human Performance Laboratory at the University of Calgary. Ambient temperature was maintained between 19 and 22°C for each testing

session to minimize changes in skin blood flow. Testing personnel were the only people permitted in the laboratory during testing to minimize alterations in HR caused by disturbances.

3.3 Pre-Screening Procedures

All subjects were pre-screened according to the American College of Sports Medicine guidelines (ACSM, 1998) to exclude any respiratory or cardiovascular disorders. The upper limits for resting HR and blood pressure were 95-bpm and 145/95 mmHg respectively. All subjects signed an informed consent form (Appendix A).

3.4 Testing Schedule

3.4.0 Overview

The testing schedule consisted of 3 periods (Figure 3.0). Completion of the study protocol required 15 days, 3 of which involved testing and 7 of which involved combined strength and endurance training.

Period 1 Day 0	Period 1 Day 7	Period 2 Day 8	Period 2 Day 9	Period 2 Day 10	Period 2 Day 11	Period 2 Day 12	Period 2 Day 13	Period 2 Day 14	Period 3 Day 15
$\dot{V}O_2$ max	PV Hb/Hct α_1-AT Gm/Ga $\dot{V}O_2$ peak $\dot{Q}$	Hb/Hct	Hb/Hct	Hb/Hct	Hb/Hct	Hb/Hct	Hb/Hct	Hb/Hct	PV Hb/Hct α_1-AT Gm/Ga $\dot{V}O_2$ peak $\dot{Q}$
		Cycle (2 hr)	Cycle (2 hr)	Cycle (2 hr)	Cycle (2 hr)	Cycle (2 hr)	Cycle (2 hr)	Cycle (2 hr)	
			Weights (45 min)		Weights (45 min)		Weights (45 min)		

Figure 3.0. The testing and training protocol. $\dot{V}O_2$ max, 8-12 minute incremental exercise test with gas collection to volitional fatigue; $\dot{V}O_2$ peak, 20-30 minute incremental exercise test with gas collection to volitional fatigue; $\dot{Q}$, measurements of cardiac output during the $\dot{V}O_2$ peak test via acetylene breathing.

3.4.1 Period 1: Pre-Testing

Objectives: Obtain baseline measures of $\dot{V}O_2max$, plasma volume, Hb, Hct, α_1-AT, Gm, Ga, and $\dot{Q}$.

$\dot{V}O_2max$: All subjects performed an initial $\dot{V}O_2max$ protocol. Subjects exercised on a cycle ergometer (Monark 828E, Monark Exercise AB, Vansbro, Sweden). Power output was increased by 44 watts every two minutes until one workload beyond the second ventilatory threshold. The second ventilatory threshold was identified by attainment of at least two of the following: 1) the second non-linear increase in ventilation with increasing workload, 2) a respiratory exchange ratio between 0.98 and 1.02 and 3) the point where ventilation increased disproportionately to carbon dioxide production (Wasserman and Whipp, 1983). After the second ventilatory threshold was reached, power output was increased 22 watts·min^{-1} until volitional fatigue. Expired gases were collected through a three-way non-rebreathing valve and directed to an online metabolic measurement cart (TrueMax 2400 Metabolic Measurement Cart, Parvo Medics, Inc., Sandy, Utah) for determination of ventilation rates and $\dot{V}O_2$. HR was continuously monitored via telemetry (Polar Vantage XL, Polar Electro, Finland). The primary purpose of this test was to ensure that the subjects met the inclusion criteria $\dot{V}O_2max$ of 60 ml·kg^{-1}·min^{-1}.

Plasma Volume: Plasma volume (see Appendix C for detailed procedure) was determined between 07:00 and 09:30 hours on the day prior to the first day of training. Subjects reported the biochemistry laboratory in the Human Performance Laboratory where an 18-

gauge catheter was inserted into the antecubital vein of one arm. After 30 minutes in the supine position, a 25-ml blood sample was withdrawn. Thirteen ml of this sample was distributed into appropriate vacutainers for the determination of Hb, Hct, α_1-AT, Gm and Ga. The remainder of the sample was used for the creation of a calibration curve. The Hb/Hct and α_1-AT vacutainers were analyzed by the Calgary Laboratory Services. Determination of Gm and Ga concentrations was performed by a trained biochemist in the Human Performance Laboratory.

Following the initial blood sampling, approximately 5 ml of ICG dye was injected through a 21 gauge butterfly needle into the antecubital vein of the opposite arm. The exact mass of dye was determined by weighing the syringe prior to and immediately after injection. Four minutes following injection of the dye, 3-ml blood samples were withdrawn from the catheter at 30-second intervals for 10-12 samples. All blood samples were immediately put on ice. At the end of the procedure blood samples were centrifuged at 3000 RPM for 10 minutes. Following this the plasma was separated from the cell component of the blood, mixed equally with a 120 $g \cdot L^{-1}$ polyethylene glycol solution, centrifuged again and filtered into micro-cuvettes. The absorbance of each sample was then determined in duplicate at wavelengths of 805 and 900 nm using a spectrophotometer (DU-62 Spectrophotometer, Beckman Instruments Inc., Fullerton, California). The mean absorbance at 900 nm was subtracted from the mean absorbance at 805 nm to account for differences in plasma turbidity. Corrected absorbance was plotted against time and an exponential regression was fitted and back-extrapolated to time = 0. Preparation of the standard curve was done in a similar manner, except a known volume of dye was mixed with a known volume of plasma

to achieve concentrations of 0.625, 1.25, 2.5 and 5.0 $mg \cdot ml^{-1}$. The linear regression equation from the standard concentration vs. absorbance curve was used to convert the absorbance at time = 0 to a concentration. Using the mass of injected dye and the theoretical concentration at time = 0, the volume of plasma was estimated.

Cardiac Output: Following the determination of plasma volume subjects were instructed to eat a light meal and report back to the laboratory two hours later for measurement of $\dot{Q}$. All $\dot{Q}$ measurements were performed using a modification of the C_2H_2 uptake technique as described by Barker et al. (1999). Subjects breathed through a three-way non-rebreathing valve. A mass spectrometer (Perkin-Elmer 1100, MA Tech Services, Inc., St. Louis, Missouri) was used to analyze end-tidal and inspired gas concentrations collected through a sampling line in the mouthpiece. The analog output from the mass spectrometer was collected through a National Instruments input/output box which used a 100 Hz cut-off frequency low-pass R-C filter on each channel to filter the signal. The input/output box was connected to a CPU via an analog-to-digital converter (National Instruments, Austin, Texas). Labview software (National Instruments, Austin, Texas) was used to convert the digital voltage signal to a concentration. During the measurement of $\dot{Q}$, end-tidal and inspired gas concentrations were saved at 50 Hz in ASCII text format. Mixed expired gasses were collected and analyzed with a Parvomed 2400 metabolic measurement cart. Inspired air was directed though a 4-way valve which allowed switching between room air and a 200 L bag containing 0.7% C_2H_2, 5% He, 20.94% O_2 and balance N. Between $\dot{Q}$ determinations the intake valve was set to allow inspiration of normal room air. During $\dot{Q}$

determination the 4-way valve was switched to have the subject breathe the C_2H_2 gas mixture.

Resting $\dot{Q}$ was determined with the subject sitting on the cycle ergometer. After 1-2 minutes of gas collection the 3-way valve was switched to have the subject breathe the C_2H_2 gas mixture. When inspired and expired He concentrations reached equilibrium, 15 to 20 additional breaths were acquired before the measurement was considered complete. Subjects were then asked to begin cycling at 90 RPM and the resistance was set to achieve a power output of 66 watts. Once C_2H_2 was sufficiently eliminated from the lungs and blood (identified by an end-tidal C_2H_2 concentration $\leq 0.03\%$) the $\dot{Q}$ measurement was repeated. This was repeated at 132, 198, 265 watts. Peak $\dot{Q}$ was measured when the subject indicated that he could continue no more than 30 seconds.

After all tests were completed, each ASCII text file was analyzed for end-tidal and inspired gas concentrations using Matlab (The Mathworks, Natick, Maine). Matlab was used to monitor changes in He, C_2H_2 and CO_2. End-tidal gas concentrations were identified using the second derivative of the concentration vs. time relation. To account for differences in breathing patterns the program was modifiable to identify end-tidal and end-inspiration concentrations. These end-points were typically between 20 and 100 ms before the maximum of the second derivative. For the He and C_2H_2 channels, Matlab automatically graphed the differences between inspired and expired gas concentrations. An exponential regression pattern was fit to the He data to identify the point where inspired-expired difference was less than 5% of the original difference. This point in time was used to

identify full-mixing of He and C_2H_2 in the lung. After this point the C_2H_2 differences were plotted against breath number. A linear regression was fit to this data and back-extrapolated to breath 1 to identify the theoretical C_2H_2 difference at breath 1. End-tidal carbon monoxide was identified at the same point as end-tidal C_2H_2, and the average end-tidal carbon dioxide for the duration of the $\dot{Q}$ test was automatically calculated. The values of the C_2H_2 difference at breath 1 and average end-tidal carbon dioxide in conjunction with data from the metabolic cart (minute ventilation and mixed expired carbon dioxide) were used to calculate $\dot{Q}$.

3.4.2 Period 2: Training Intervention

Objective: To provide a training stimulus of sufficient magnitude to induce hypervolemia and a transient decrease in performance capacity.

Training Overview

Subjects reported to the Human Performance Laboratory between 06:00 and 08:30 for the next 7 consecutive days. Prior to exercising each day a venipunture blood sample was procured and analyzed by Calgary Laboratory Services for Hb and Hct. The main component of the training intervention consisted of approximately 2 hours daily on a cycle ergometer at power outputs 70 – 150% of the maximum power achieved during daily incremental exercise tests. Training outside of this protocol was discouraged. On the afternoons of training days 2, 4 and 6 athletes reported to the Fitness and Lifestyle Centre at the University of Calgary where they completed a weight-training circuit three times.

Cycle Training Session

1. On each day, the subjects warmed-up during an incremental cycling test from rest to volitional fatigue. Subjects pedalled at 90 RPM and power output was increased every 2 minutes by 44 watts. Heart rate was monitored continuously and the last 10-second average of each workload was recorded. The maximum HR achieved was also recorded. Subjects were given approximately 10 minutes of active recovery at 25 watts following the completion of the incremental test. After the third minute of recovery a fingertip lactate sample was taken and recorded.
2. After 10 minutes of recovery, subjects completed one repetition of 3 minutes in duration on the cycle ergometer at each of the following intensities; 100%, 95%, 90%, 85% and 80% of the maximum power achieved in the incremental cycling test. Three minutes of active recovery at approximately 25 watts was performed between each repetition. The maximum HR achieved during each repetition was recorded. After completing the fifth repetition, subjects were given 8 minutes active recovery at 25 watts.
3. Following 8 minutes of recovery, subjects completed 5 repetitions of 20 seconds duration at approximately 150% of the maximum power achieved during the incremental test. Between each repetition subjects cycled at 25 watts for 1 minute and 40 seconds. Following the final repetition subjects cycling at 25 watts for 8 minutes.
4. The final 20 minutes of exercise consisted of cycling at the first ventilatory threshold (as estimated from the first $\dot{V}O_2$max test).

Weight Training Session

On training days 2, 4 and 6, subjects completed three weight training circuits consisting of 11 exercises. Subjects performed approximately 12 repetitions in 45 seconds, after which they were given 15 seconds to move on to the next exercise. After the 11 exercise stations were completed, subjects walked 200 meters prior to beginning another circuit. The resistance was set by the researcher to achieve failure by 12-15th repetition. The number of repetitions and the corresponding resistance were recorded by the researcher.

3.4.3 Period 3: Post-Testing

Objectives: To measure potential changes in plasma volume, Hb, Hct, α_1-AT, Gm, Ga, and $\dot{Q}$.

On the day after the seventh day of training subjects reported to the Human Performance Laboratory between 07:00 and 08:30. This testing session was conducted in the same format as the pre-training testing (described in section 3.4.1).

3.5 Statistical Analysis

A two-way analysis of variance (ANOVA; time x intensity) was used to detect differences in $\dot{V}O_2$, $\dot{Q}$, HR, SV, O_2pulse, $(a-\bar{v})O_2$. The Chow test (Dillon and Goldstein, 1984) was performed by hand to identify the effect of training on the following relationships: 1) $\dot{Q}$ vs. power output and $\dot{V}O_2$, 2) HR vs. power output and $\dot{V}O_2$, 3) SV vs. power output and $\dot{V}O_2$, 4) O_2pulse vs. power output and $\dot{V}O_2$ and 5) $(a-\bar{v})O_2$ vs. power output and $\dot{V}O_2$. Briefly, the Chow test compares the residual sums-of-squares from

the individual data pools with the residual sums-of-squares of the pooled data to determine if the regressions are different (Dillon and Goldstein, 1984). If the Chow test showed the pre- and post-training relationships to be significantly different, an ANOVA was performed to determine if the slope or y-intercept was different. If significant differences were noted the Tukey Honest Differences post-hoc test was used to determine where the relationships differed. A dependent-measures t-test was used to identify differences between plasma volume, α_1-AT, Gm, Ga, and the Gm-Ga ratio. Except for the Chow test, the statistics software STATISTICA (Statistica for Windows, Statsoft Inc., Tulsa, Oklahoma) was used for all data analysis.

Chapter 4: Results

4.0 Subjects: Ten male subjects completed all testing and training sessions. One subject who volunteered did not meet the $\dot{V}O_2max$, and was subsequently removed from the study. The mean (SD) age, height and weight of the subjects were 24.9 (3.2) yr, 177.7 (8.7) cm, and 73.9 (7.7) kg, respectively. Performance data from the preliminary $\dot{V}O_2max$ test are presented in Table 4.0.

Table 4.0. Parameters from the pre-training incremental exercise test.

$\dot{V}O_2$ ($L \cdot min^{-1}$)	$\dot{V}O_2$ ($ml \cdot kg^{-1} min^{-1}$)	VT2 ($L \cdot min^{-1}$)	HR ($beats \cdot min^{-1}$)	MAP (watts)
4.61	62.99	3.56	194.6	379.3
(0.02)	(0.2)	(0.4)	(13.6)	(35.3)

Values represent mean ± SE ($N = 10$). $\dot{V}O_2$ = absolute peak oxygen consumption and peak oxygen consumption normalized for body weight; VT2 = oxygen consumption at the second ventilatory threshold; HR = maximum recorded heart rate; MAP = maximum power output at exhaustion.

4.1 Training Load

Cycling: Daily cycling volume was calculated from the product of time and power output. The mean daily cycling work (SD) was 816 (112) $KJ \cdot day^{-1}$. No significant differences were found between the training days.

Weight Training: Weight training volume was calculated from the product of distance and total mass lifted. The weight training work (SD) on training days 2, 4 and 6 was 102 (19), 114 (22) and 117 (24) KJ, respectively. Weight training volume on days 4 and 6 was significantly greater ($P<0.05$) than day 2.

Total Training Load: The mean total training load (SD) was 863 (114) $KJ \cdot day^{-1}$. Subjects performed significantly ($P<0.05$) more work on training days 2, 4 and 6.

4.2 Heart Rate and Blood Lactate Response to Training

An incremental exercise test to exhaustion was performed during each day of training. A positive linear relationship between exercising HR and power output was found (Figure 4.0).

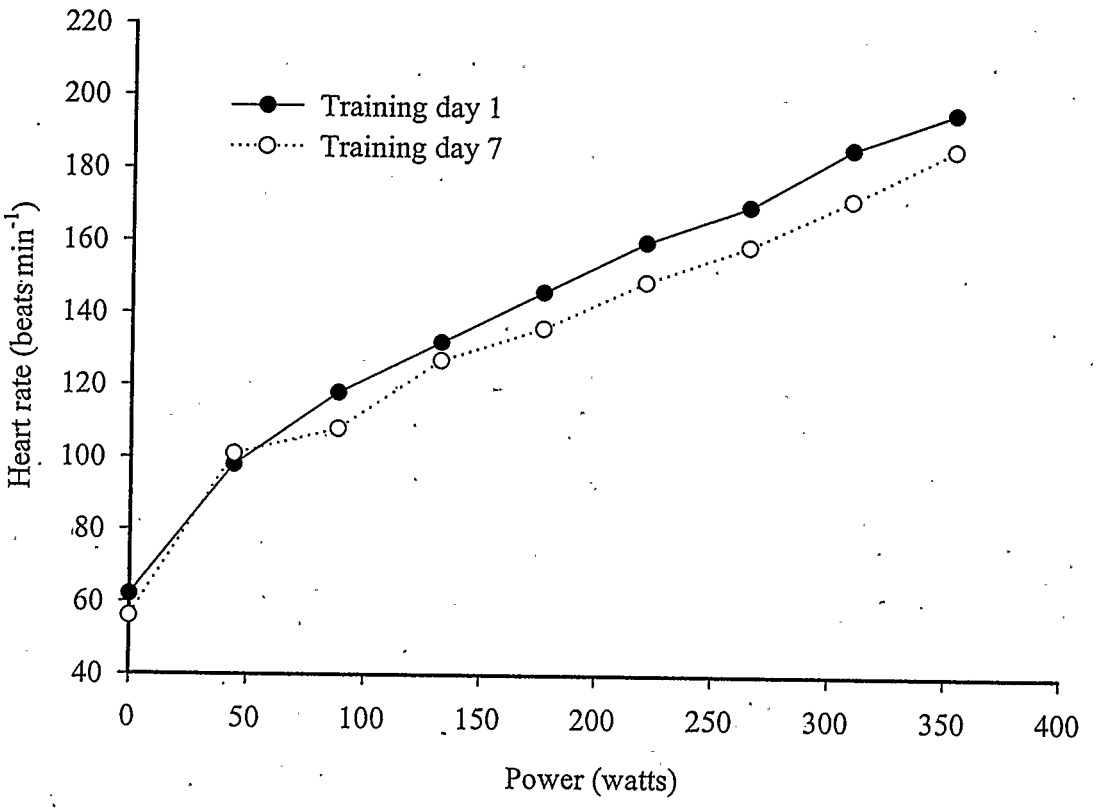

Figure 4.0. Data from a representative subject showing the changes in the heart rate response to increasing exercise intensities on the 1st and 7th day of training. Mean data for all subjects is shown in Table 4.1.

The HR and blood lactate response from each test are presented in Table 4.1. Using HR versus power output data from 88 watts to the last completed workload, a linear regression model was fit to each HR versus power output relationship. These relationships were then compared between training days. When compared to the first day of training, the slope of

the relationship was significantly lower ($P<0.05$) on the 3rd, 4th, 6th and 7th day of training. No significant differences were found in the intercept of this relationship. Likewise, when compared to the first day of training, the maximum HR achieved during the incremental test was significantly lower on training days 3-7 ($P<0.05$). The greatest decrease in maximum HR (7 beats·min^{-1}) when compared to training day 1 was found on training day 7 ($P<0.05$). No differences were found between training days 2-7. There was no difference in the maximum power achieved or post-test blood lactates following each test throughout the 7 days.

Table 4.1. Regression parameters and blood lactate concentrations from the daily training (T1-T7) incremental heart rate versus power output tests.

Day	Slope (b·min^{-1}·W^{-1})	Intercept (b·min^{-1})	HRmax (b·min^{-1})	MaxP (W)	BLa (mM)
T1	0.2906	81.5	186.7	387.9	12.51
	(0.02)	(2)	(4)	(16)	(0.7)
T2	0.2753	82.4	182.9	387.5	11.92
	(0.02)	(3)	(4)	(15)	(0.8)
T3	0.2695*	84.7	180.5*	378.8	11.59
	(0.02)	(2)	(4)	(14)	(1.0)
T4	0.2683*	84.7	180.2*	378.8	12.59
	(0.01)	(3)	(4)	(14)	(0.7)
T5	0.2741	83.0	181.1*	383.2	13.06
	(0.01)	(3)	(3)	(13)	(0.6)
T6	0.2696*	83.9	182.2*	391.9	12.77
	(0.01)	(3)	(3)	(14)	(0.7)
T7	0.2704*	81.9	179.6*	378.6	12.44
	(0.01)	(3)	(4)	(14)	(0.6)

Values represent mean ± SE ($N = 10$). Linear regressions were based on the average heart rate during the last ten seconds of each completed workload, excluding rest and 44 watts. HRmax, highest heart rate achieved during the incremental test; MaxP, final workload attained; BLa, blood lactate concentration three minutes after the incremental test finished. Symbol * denotes significant differences from training day 1 ($P<0.05$).

4.3 Cardiorespiratory Measures: Relationships with Power Output

Oxygen Consumption: Expired gases were analyzed continuously for the duration of the $\dot{Q}$ test (Figure 4.1). Mean $\dot{V}O_2$ over the duration of $\dot{Q}$ measurement at each workload is shown in Table 4.2. There was a significant main effect of intensity ($P<0.001$), but no significant effect of time ($P=0.438$) or time by intensity interaction ($P=0.743$). A positive linear relationship was found between $\dot{V}O_2$ and power output before training ($y = 0.01006x + 0.714$, $r^2=0.98$) and after training ($y = 0.01006x + 0.741$, $r^2 = 0.96$). These relationships were not significantly different from each other.

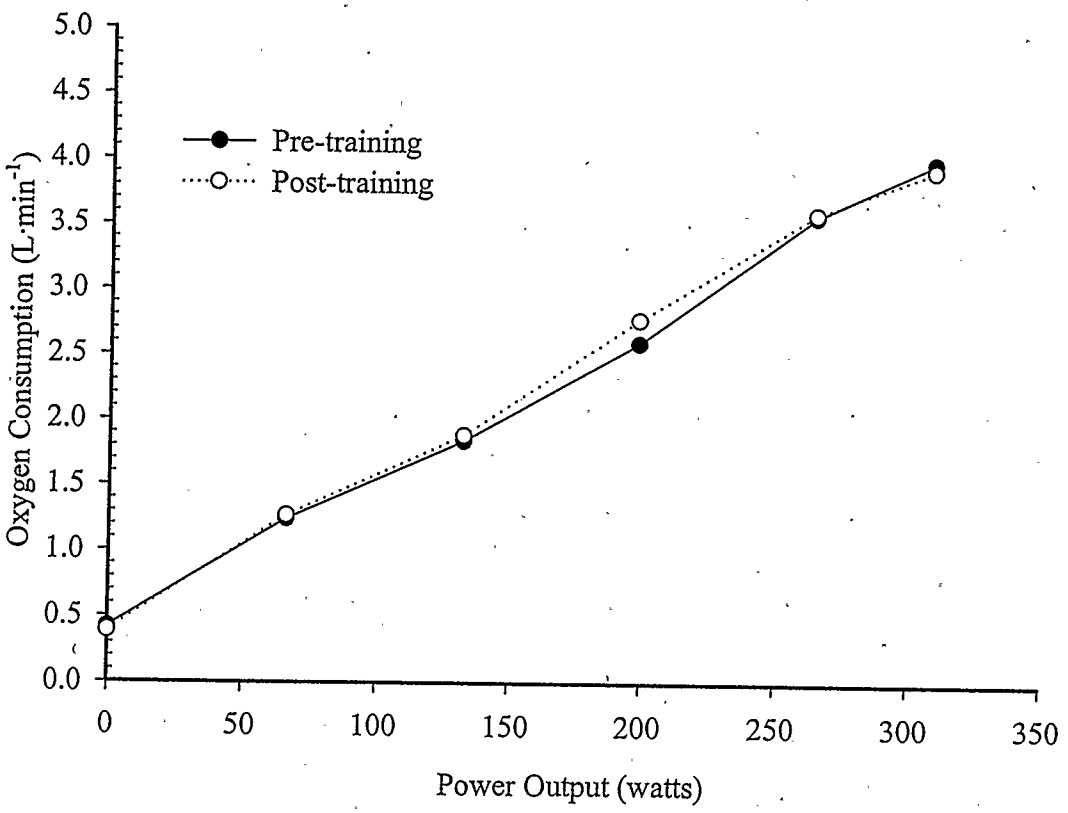

Figure 4.1. Data from a representative subject showing the linear increase in oxygen consumption with increasing power output before and after 7 days of training. Mean data for all subject is shown in Table 4.2.

Table 4.2. Oxygen consumption during cardiac output measurement before and after 7 days of training. Values represent mean ± SE (N = 10). NE, non-exercising.

	Pre		Post	
Power (watts)	$\dot{V}O_2$ ($L \cdot min^{-1}$)	$\dot{V}O_2$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	$\dot{V}O_2$ ($L \cdot min^{-1}$)	$\dot{V}O_2$ ($ml \cdot kg^{-1} \cdot min^{-1}$)
NE	0.43 (0.02)	5.9 (0.2)	0.50 (0.02)	6.1 (0.3)
66	1.37 (0.03)	18.6 (1.)	1.38 (0.05)	18.8 (1.)
132	2.03 (0.04)	27.6 (1.)	2.06 (0.04)	28.1 (1.)
198	2.74 (0.05)	37.3 (1.)	2.79 (0.04)	38.0 (1.)
265	3.42 (0.05)	46.7 (2.)	3.47 (0.06)	47.2 (2.)
351	4.20 (0.13)	56.9 (2.)	4.19 (0.18)	56.6 (2.)

Cardiac Output, Heart Rate and Stroke Volume: There was a significant main effect of intensity (P<0.001) but not time (P=0.297) on $\dot{Q}$. There was a significant time-by-intensity interaction effect (P<0.01). A significant interaction effect was only found when intensities above 198 watts were included in the analysis. There was a trend for $\dot{Q}$ to be higher at 265 watts and peak power following training. A positive linear relationship between $\dot{Q}$ and power output was found pre-training ($y=0.05886x+7.991$, $r^2 = 0.89$) and post-training ($y=0.06501x+6.992$, $r^2= 0.90$). These relationships were not significantly different from each other.

There was a significant main effect of intensity (P<0.001) and time (P<0.01) on HR (Table 4.3). There was a significant time-by-intensity interaction effect (P<0.05). Resting HR was 9.3% lower post-training (P<0.05). During exercise, HR was approximately 5% lower at all intensities except 66 watts, where no significant difference was found post-training (Figure 4.2). A significant decrease (P<0.05) in the intercept of the HR versus power output

relationship (Pre = 0.281x + 89.75, r^2 = 0.79; Post = 0.263x + 86.95, r^2 = 0.83) was evident post-training.

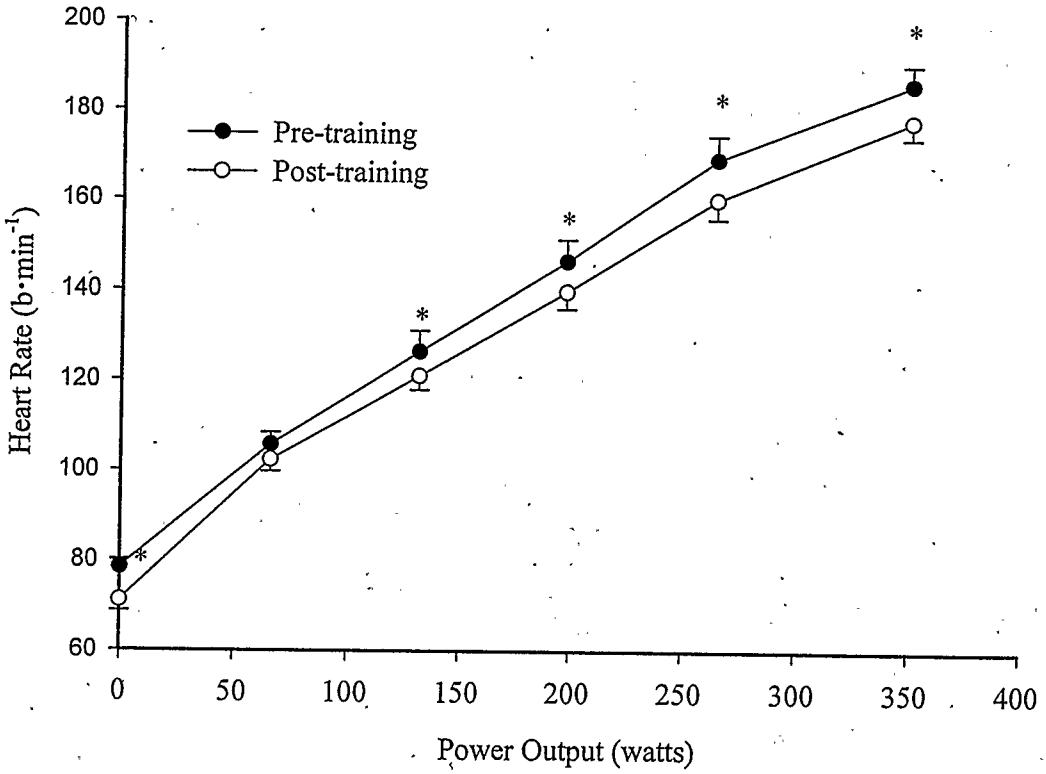

Figure 4.2. The heart rate response to incremental exercise before and after 7 days of training. Symbol * represents a significant difference post-training when compared to pre-training. Bars represent ± SE (N = 10).

A significant main effect of intensity (P<0.001) and time (P<0.001) on SV was found (Table 4.3). A significant time-by-intensity interaction effect was also found (P<0.01). The interaction effect was only significant when intensities above 198 watts were included in the analysis. Compared to pre-training, post-training SV was 12, 11 and 9% greater at rest, 265 watts and peak power output, respectively (Figure 4.3). The increase in SV at 66, 132 and 198 watts was not statistically significant.

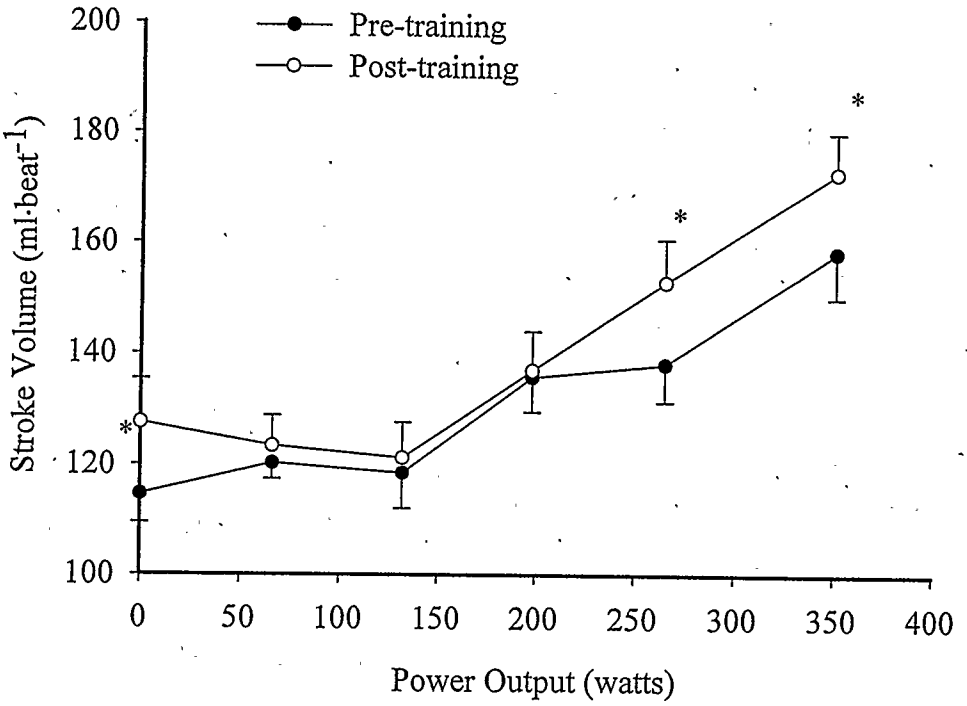

Figure 4.3. The stroke volume response to incremental exercise before and after 7 days of training. Symbol * represents a significant difference post-training when compared to pre-training. Bars represent ± SE (N = 10).

There was a significant main effect of intensity (P<0.001) but not time (P=0.694) on the calculated arteriovenous oxygen difference (Table 4.3). A significant time-by-intensity interaction effect was found (P<0.01). Compared to pre-training, there was a trend for higher post-training $(a-\bar{v})O_2$ at 66, 132 and 198 watts.

Table 4.3. Cardiac output, heart rate and stroke volume before and after 7 days of training.

Power (watts)	Pre-training $\dot{Q}$ ($l \cdot min^{-1}$)	Pre-training HR ($b \cdot min^{-1}$)	Pre-training SV ($ml \cdot b^{-1}$)	Post-training $\dot{Q}$ ($l \cdot min^{-1}$)	Post-training HR ($b \cdot min^{-1}$)	Post-training SV ($ml \cdot b^{-1}$)
NE	8.95	78.4	114.6	9.15	71.1*	127.6*
	(0.4)	(2)	(5)	(0.7)	(2)	(8)
66	12.8^{+}	105.7^{+}	120.3	12.5^{+}	102.3^{+}	123.4
	(0.3)	(3)	(3)	(0.4)	(3)	(5)
132	14.8^{+}	126.4^{+}	118.5	14.5^{+}	121.0^{+}*	121.3
	(0.5)	(5)	(6)	(0.5)	(3)	(6)
198	19.7^{+}	146.4^{+}	135.8^{+}	19.0^{+}	139.7^{+}*	137.0^{+}
	(0.6)	(5)	(6)	(0.6)	(4)	(7)
265	23.2^{+}	169.2^{+}	138.2	24.3^{+}	160.1^{+}*	152.9^{+}*
	(0.9)	(5)	(7)	(1)	(4)	(8)
351^{Δ}	29.2^{+}	186.2^{+}	158.4^{+}	30.5^{+}	177.9^{+}*	172.8^{+}*
	(1)	(4)	(8)	(0.7)	(4)	(7)

Values represent mean ± SE ($N = 10$). Symbol $^{+}$ represents a significant difference ($P<0.05$) when compared to prior workload. Symbol * represents a significant difference ($P<0.05$) when compared to pre-training values. NE, non-exercising; 351^{Δ}, mean of peak power outputs at peak cardiac output determination.

Table 4.4. Calculated arteriovenous oxygen difference before and after 7 days of training.

Power (watts)	Pre-training ($ml \cdot dl^{-1}$)	Post-training ($ml \cdot dl^{-1}$)
NE	4.9	5
	-0.2	-0.3
66	10.9^{+}	11.1^{+}
	-0.5	-0.5
132	13.8^{+}	14.3^{+}
	-0.3	-0.4
198	14	14.8
	-0.3	-0.4
265	14.9	14.5
	-0.4	-0.6
351^{Δ}	14.4	13.7
	-0.4	-0.4

Values represent mean ± SE ($N = 10$). Symbol $^{+}$ represents a significant difference ($P<0.05$) when compared to prior workload. NE, non-exercising; 351^{Δ}, mean of peak power outputs at peak cardiac output determination.

4.4 Cardiac Output: Relationship with Oxygen Consumption

A linear relationship between $\dot{Q}$ and $\dot{V}O_2$ was found before and after training (Figure 4.4). These relationships were not significantly different from each other.

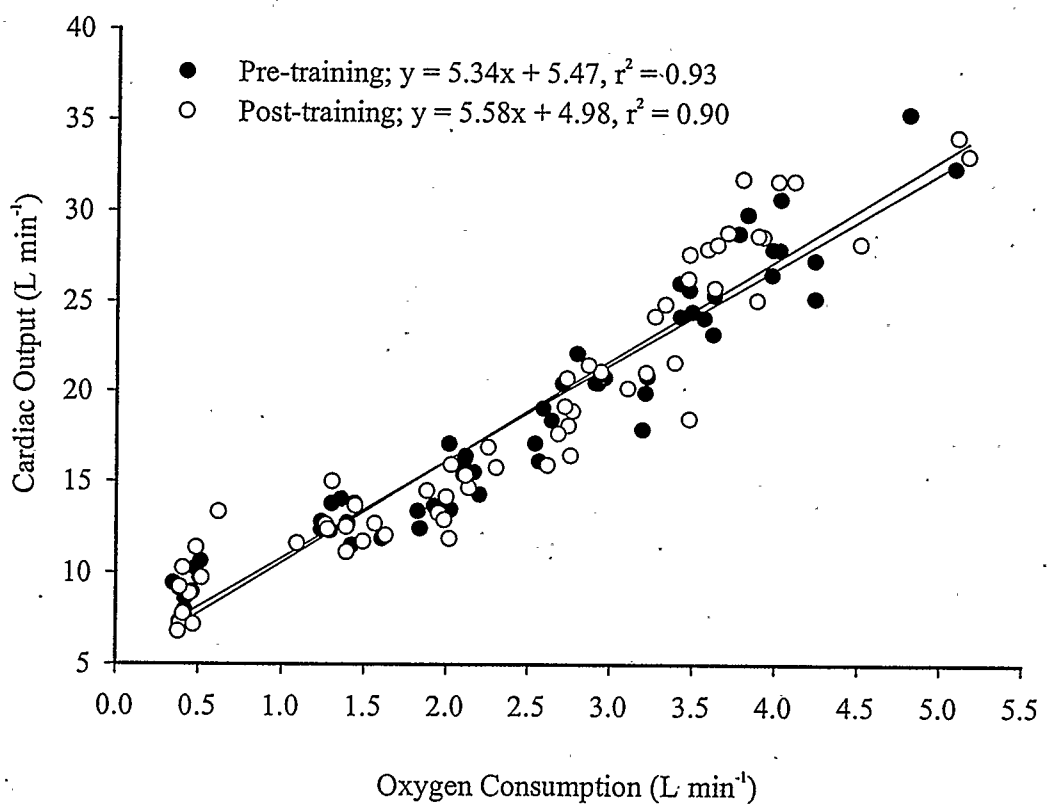

Figure 4.4. The relationship between cardiac output and oxygen consumption before and after 7 days of training. Values represent individual data points at fixed levels of power output.

4.5 The Relationship Between Cardiac Factors

A linear relationship was found between $\dot{Q}$ and HR (Figure 4.5a). While there was a trend for the slope of the relationship to increase post-training, due to the large within group variance, this failed to reach significance. The mean relationship between $\dot{Q}$ and HR is shown in Figure 4.5b.

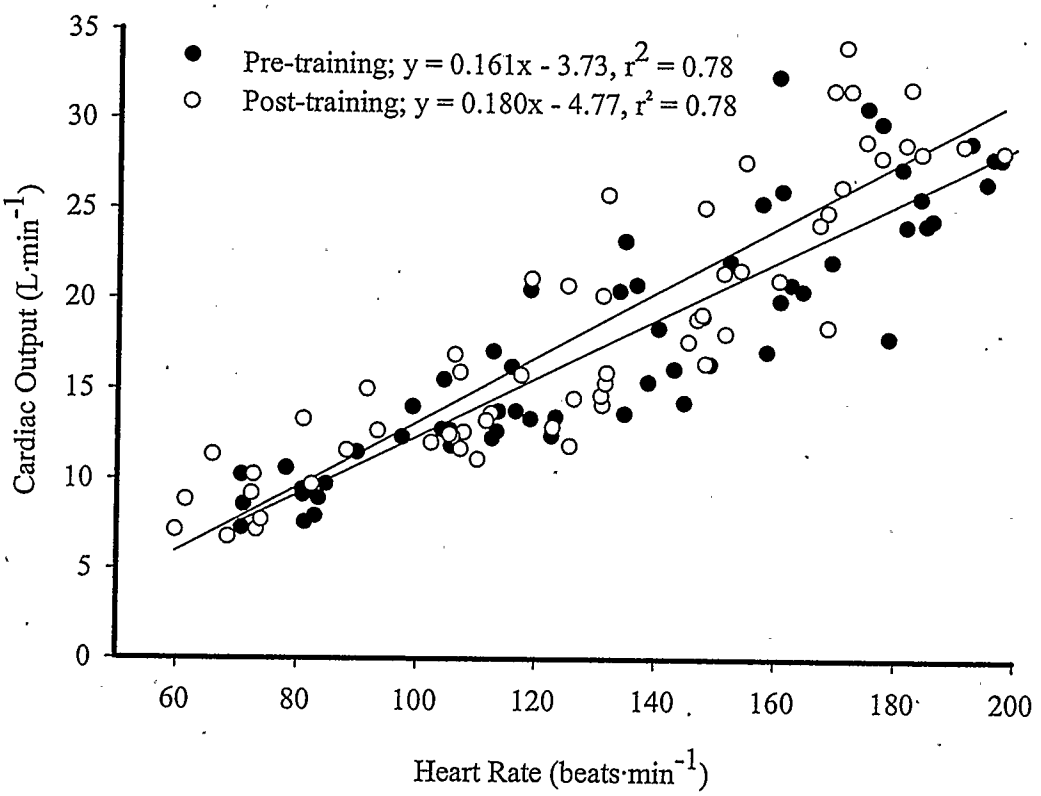

Figure 4.5a. The relationship between cardiac output and heart rate before and after 7 days of training. Values represent individual data points.

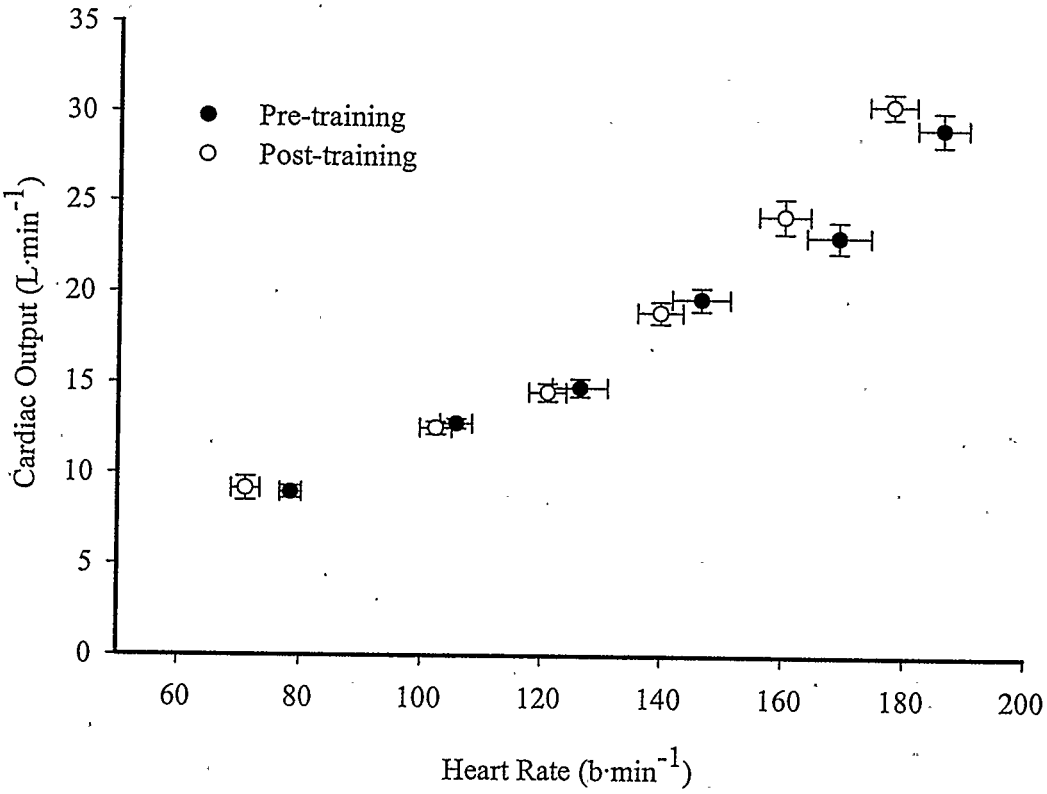

Figure 4.5b. The relationship between cardiac output and heart rate before and after 7 days of training. Bars represent ± SE. ($N = 10$). Each pair of data points (pre and post-training) represents the mean response at fixed workloads.

The relationship between SV and HR is shown in Figure 4.6. A trend for SV to increase at any given HR was noted.

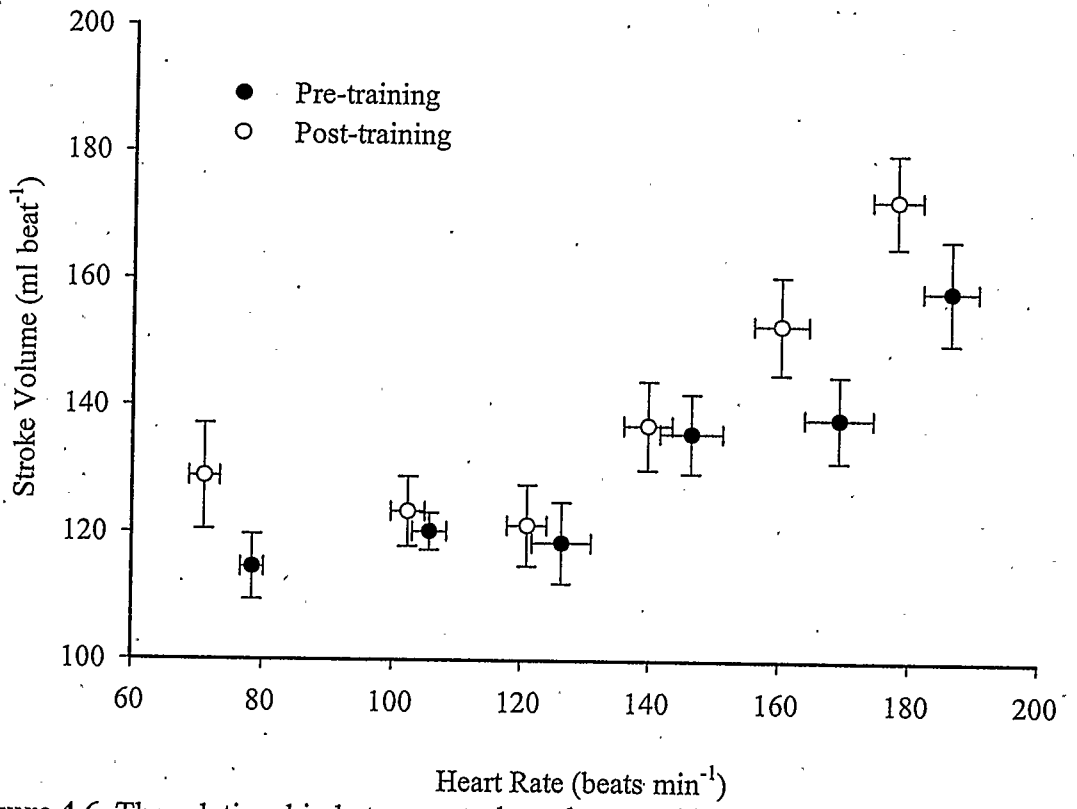

Figure 4.6. The relationship between stroke volume and heart rate before and after 7 days of training. Bars represent ± SE. ($N = 10$). Each pair of data points (pre- and post-training) represents the mean response at fixed workloads.

To test the hypothesis that training increased SV at a given $\dot{Q}$, regression models were fit to the individual SV versus $\dot{Q}$ data. A quadratic regression model was used when it accounted for significantly more variability than the linear model. Quadratic or linear regression parameters were then used to interpolate SV's at $\dot{Q}$'s of 10, 15, 20, 25 and 30 L·min^{-1}. Stroke volume was significantly higher ($P<0.01$) when compared to pre-training at $\dot{Q}$s of 10, 25 and 30 L·min^{-1} (Figure 4.7).

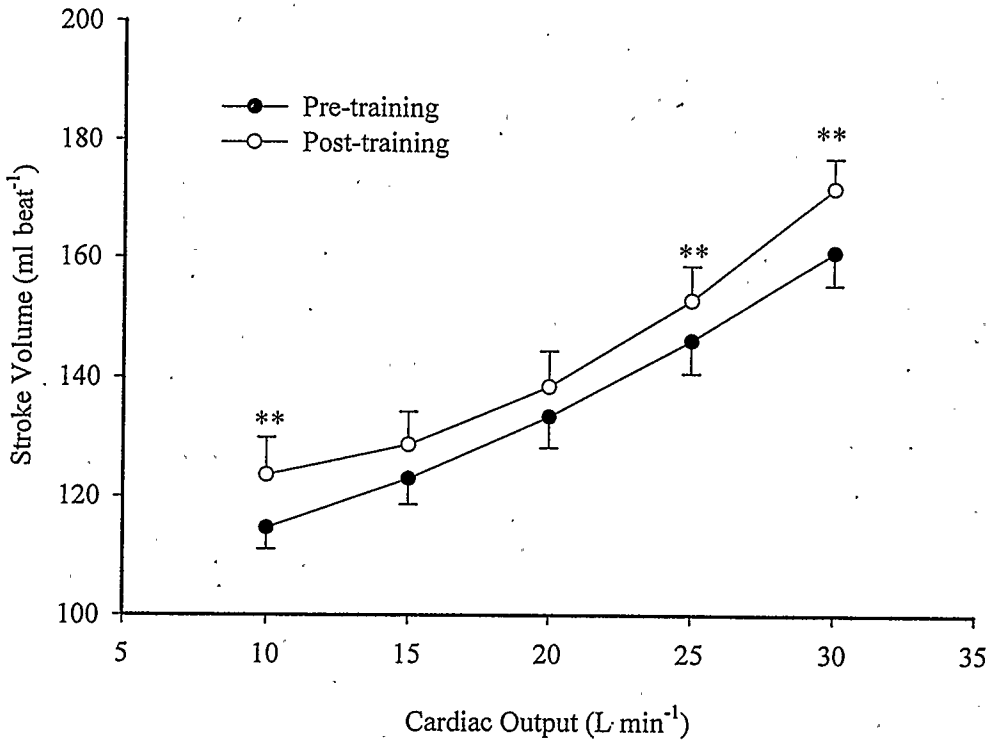

Figure 4.7. Interpolated stroke volume at discrete cardiac outputs before and after 7 days of training. Symbol ** represents a significant difference ($P < 0.01$) when compared to pre-training. Error bars represent ± 1SE. ($N = 10$).

4.6 Blood Parameters

The responses of various blood parameters to exercise training are shown in Table 4.5. A significant increase ($P<0.05$) in PV (6.9%) was found following training. A significant decrease ($P<0.05$) in Hb (3.7%) and Hct (4.2%) was also observed. The increase in Ga concentration approached significance ($P=0.055$), as did the increase in the Gm/Ga ratio ($P=0.066$). No significant differences were found in Gm of α_1-AT levels. When Hb and Hct values were used to predict changes in PV, a 7.3% increase in PV was found post-training ($P<0.05$, Table 4.6). No significant change in PV was found during the training period.

Table 4.5. Plasma volume, hemoglobin, hematocrit, glutamine, glutamate, glutamine/glutamate and alpha-1-anitrypsin before and after 7 days of training.

Parameter	Pre	Post
PV (L)	3.327 (0.34)	3.555 (0.44)*
PV ($ml \cdot kg^{-1}$)	45.16 (5.15)	48.19 (5.73)*
Hb ($g \cdot L^{-1}$)	144.5 (6.64)	139.2 (6.09)*
Hct (%)	42.5 (2.27)	40.7 (1.83)*
Gm (μM)	469.1 (42.0)	473.2 (53.0)
Ga (μM)	113 (18.9)	123.6 (22.8)
Gm/Ga	4.26 (0.89)	3.91 (0.61)
α_1-AT ($g \cdot L^{-1}$)	1.11 (0.14)	1.14 (0.14)

Values represent mean ± SD ($N = 10$). PV, plasma volume; Hb, hemoglobin; Hct, hematocrit; Gm, glutamine; Ga, glutamate; α_1-AT , alpha-1-antitrypsin. Symbol * indicates a significant differences ($P<0.05$) from pre-training.

Table 4.6. Estimation of the change in plasma volume using hemoglobin concentration and hematocrit proportions.

Day	Hb ($g \cdot L^{-1}$)	Hct (%)	ΔPV (%)
PRE	144.5 (6.64)	42.5 (2.27)	--------
T2	144.8 (6.01)	42.1 (1.52)	0.586 (4.15)
T3	141.9 (5.22)	41.1 (1.52)	4.48 (6.03)
T4	144.4 (4.27)	42.1 (1.29)	0.878 (5.14)
T5	142.1 (6.85)	41.3 (2.26)	4.10 (8.01)
T6	145.1 (6.74)	41.9 (1.85)	0.862 (6.92)
T7	142.5 (6.60)	41.5 (2.01)	3.40 (7.08)
POST	139.2 (6.09)	40.7 (1.83)	7.31 (7.34)*

Values represent mean ± SD ($N = 10$). The estimated percent change in plasma volume (ΔPV) for each training day (T2-T7) and post-training (POST) is presented relative to pre-training values (PRE). Blood samples were not taken on the first day of training. Symbol * indicates a significant difference ($P<0.05$) from pre-training.

Chapter 5: Discussion

The main findings of the present study were: 1) training did not alter the $\dot{Q}$ response to exercise; 2) training resulted in a significant increase in SV at rest and during the two highest exercise intensities (265 and 351 watts); 3) training resulted in a significant decrease in the slope of the HR versus power output relationship; 4) training resulted in a significant increase in plasma volume. These findings, taken together with evidence from the literature, have led to four main conclusions: 1) short-term high-intensity training can increase exercising SV in well-trained cyclists 2) the increase in exercising SV appears to occur on different timelines than the increase in plasma volume 3) an increase in peak SV can occur independently of increases in peak $\dot{Q}$ or aerobic performance, and 4) the HR response to cycling exercise is a strong predictor of improvements in SV. The following discussion details the assumptions and evidence that underlie these conclusions.

5.0 Cardiac Output Response to Exercise: The main purpose of this study was to investigate the effect of one week of high-intensity training on the $\dot{Q}$ response to exercise. Training did not significantly alter $\dot{Q}$ at any exercise intensity. It was postulated that training may induce changes in the metabolic demand of cycling, peripheral adaptations that allow for increased extraction of oxygen, or altered arterial oxygen content. Based on components of the Fick equation, any one of these adaptations would result in an altered $\dot{Q}$ at a given power output. Training did not alter $\dot{V}O_2$ at any power output (Table 4.2). In addition, training did not alter the oxygen extraction ability as estimated from $\dot{V}O_2$ / $\dot{Q}$

(Table 4.4). Since $\dot{V}O_2$ was not different at any workload following training, the metabolic demand and mechanical efficiency of cycling can be considered unaltered.

It has been suggested that an increase in $\dot{Q}$ may be necessary to compensate for the reduced arterial oxygen content induced through hemodilution (Kanstrup and Ekblom, 1982; Warburton et al., 1999c). In the present study a 6.9% increase in plasma volume caused a 3.7% decrease in the Hb concentration ($P<0.05$) following training that, under normal oxygen saturation, would equate to a 4% decrease in arterial oxygen content. Several authors (Mier et al., 1996; Warburton et al., 1999c) have shown an increase in $\dot{Q}$ following acute plasma expansion. Warburton et al. (1999c) found an increase in $\dot{Q}$ during submaximal and maximal exercise intensities following an 8% plasma volume expansion with a 6% dextran solution. In contrast to the Warburton et al. (1999c) study, the data from the present study showed no change in submaximal $\dot{Q}$ despite a comparable (6.9%) increase in plasma volume. Since similar measurement techniques were used in the present study, these discrepancies may be due to differences in the $\dot{Q}$ response following acute plasma expansion and training induced plasma expansion. For example, Mier et al (1996) found a significant increase in $\dot{Q}$ at 50% peak $\dot{V}O_2$ when plasma volume was artificially expanded by approximately 10%, but no increase in $\dot{Q}$ following a training-induced increase of plasma volume (~ 10%). Wilmore et al. (2001) found a significant decrease in $\dot{Q}$ at 50% $\dot{V}O_2$max following one year of exercise training.

It is interesting to note that there was a significant time-by-intensity interaction effect on $\dot{Q}$ and $(a-\bar{v})O_2$. This interaction may indicate that the changes in $\dot{Q}$ (Table 4.3) and $(a-\bar{v})O_2$ (Table 4.4) following training were intensity-dependent. Whilst speculative, one potential mechanism to explain this change in $\dot{Q}$ and $(a-\bar{v})O_2$ is that the hemodilution resulted in a circulatory challenge only when exercise intensities reached near maximum levels, a point where muscle oxygen extraction is relatively high and venous oxygen content relatively low. Under this condition an increase in $\dot{Q}$ may be necessary to provide the same rate of oxygen delivery. If venous oxygen content remained the same as that seen pre-training, a decrease in maximum $(a-\bar{v})O_2$ would result.

5.1 Stroke Volume Response to Exercise: Although $\dot{Q}$ was unchanged following seven days of high-intensity training, the same absolute $\dot{Q}$ was achieved with a higher SV and lower HR (Figure 4.7). Convertino et al. (1991) found 10 weeks of exercise training increased resting SV by 17%. A comparable increase in resting SV was found in the present study (11%). Convertino et al. (1991) credited this increase in resting SV to a 19% increase in central venous pressure. Since the ratio between central venous pressure and blood volume was unchanged following training, the authors attributed the increase in central venous pressure to the 8% increase in blood volume (Convertino et al., 1991). Theoretically, using the linear regression parameters given by Convertino et al. (1991) to predict changes in central venous pressure from changes in blood volume ($y = 3.76x - 12.2$), the 3.5% increase in blood volume in the present study equates to a 1% increase in central venous pressure. Although it is not possible to make direct conclusions due to

potential differences in the respective subject pools, it seems unlikely that the modest increase in total blood volume measured in the present study would cause increases in central venous pressure sufficient to increase SV by 9-12%. In addition, an increase in central venous pressure would be expected at all exercise intensities. However, no significant increase in SV was found between rest and 265 watts. Consequently, it can be concluded that the small increase in blood volume measured in the present study contributed minimally to the increase in SV. This conclusion is supported by the data of Mier et al. (1997) where no significant correlation was found between changes in blood volume and increases in left ventricular end-diastolic dimension.

Considerable research has examined the increase in maximum SV in sedentary subjects in response to exercise training (Ekblom et al., 1968; Martin et al., 1987; Mier et al., 1997). Mier et al. (1997) found a 15% increase in maximum SV following 10 days of high-intensity cycle training, whereas Martin et al. (1987) found a 10% increase in upright SV following 12 weeks of intense swim training. Ekblom et al. (1968) reported similar findings, where maximum SV increased by 13% following 16 weeks of training. The present study was unique in that 7 days of intense training resulted in a comparable increase (9%) in maximum SV in well-trained rather than sedentary subjects. It has been suggested that an increase in SV may occur as a result of increased filling time through training-induced bradycardia (Convertino, 1987) However, Figure 4.6 illustrates that SV tended to be higher post-training at any given HR compared to pre-training, suggesting ventricular filling time was not the source of this change. In a cross-sectional study by Zhou et al. (2001), the authors found elite runners and untrained subjects had similar SV's

at submaximal exercise HR's. The main difference between the elite athletes and untrained subjects was the elite athletes were able to increase SV at HR's above 120 b·min^{-1}. Figure 5.0a illustrates the data of Zhou et al. (2001) and demonstrates how SV in the elite subjects increased up to maximum HR, a trend similar to that found in the present study after 7 days of intense training (Figure 5.0b).

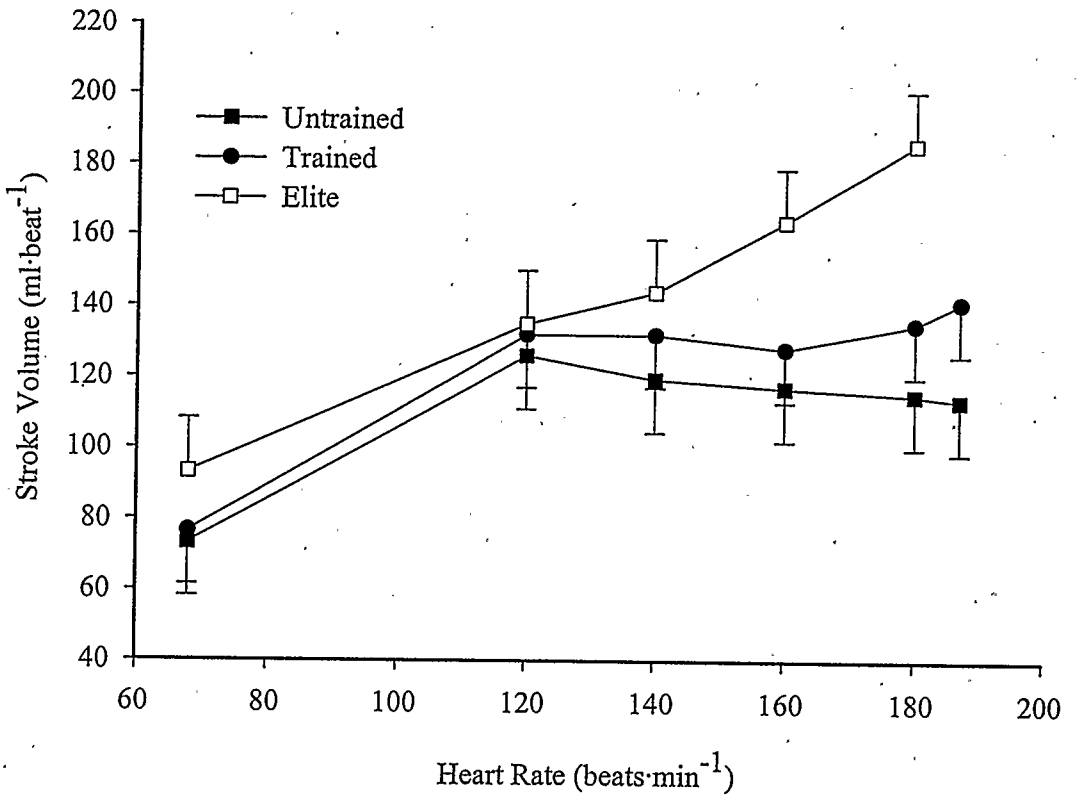

Figure 5.0a. The relationship between stroke volume and heart rate in untrained, trained and elite endurance runners. Maximum oxygen consumption for the untrained (N = 10), trained (N = 10) and elite (N = 5) subjects was 3.76, 4.81 and 5.35 L·min^{-1}, respectively. Data from Zhou et al. (2001). Error bars represent ± SE.

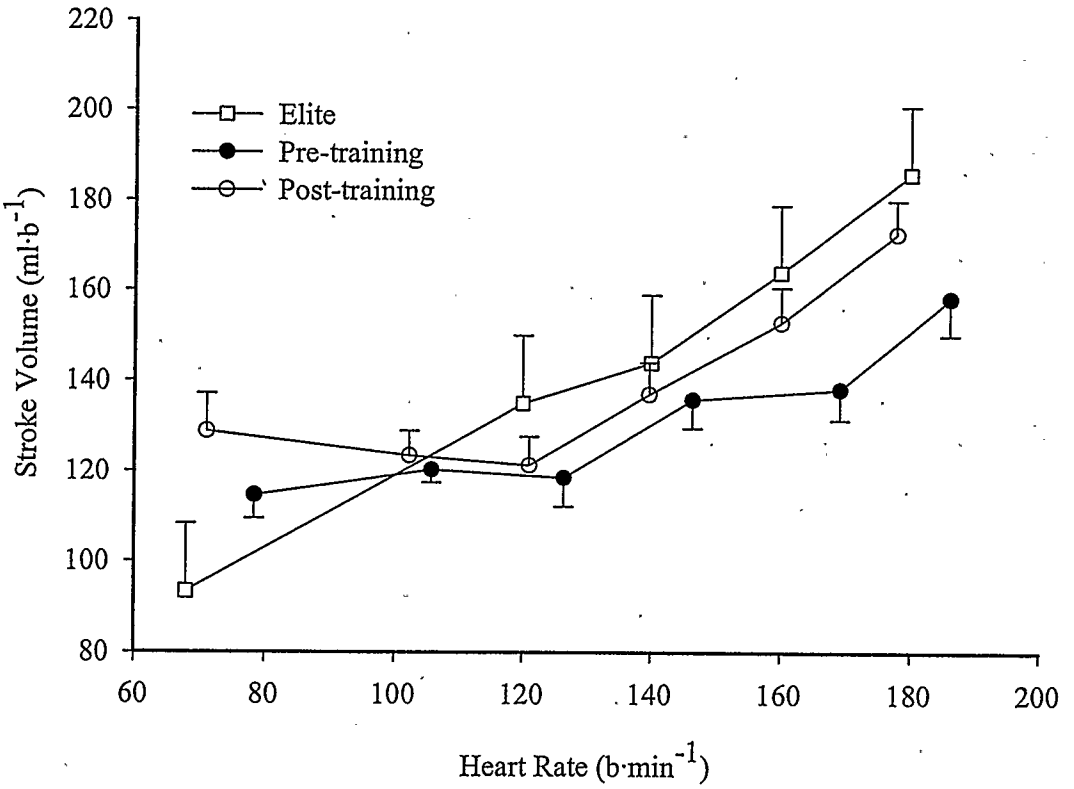

Figure 5.0b. The relationship between stroke volume and heart rate in elite endurance runners (*N=5*) and subjects in the present study (*N=10*). Elite endurance runner data from Zhou et al. (2001). Error bars represent ± SE.

The trend for SV to increase at high exercise intensities in well-trained athletes suggests differences in mechanisms that affect ventricular performance during maximum intensities. These may include differences in ventricular relaxation rates, changes in heart structure that allow for greater end-diastolic volume (pericardium or ventricular restructuring), intensity mediated shifts of the blood volume to the central circulation, improved contractility or altered afterload that results in decreased end-systolic volume.

Gledhill et al. (1994) found well-trained endurance athletes were able to increase SV beyond HR's of 120 $b \cdot min^{-1}$, and attributed this to improved diastolic function in endurance-trained athletes. The authors defined improved diastolic function through measurement of the rate of ventricular filling. It is known that the rate of ventricular filling is dependent on filling pressure (Ishida et al., 1986) and end-systolic volume (Gilbert and Glantz, 1989). Therefore, using the rate of ventricular filling to describe diastolic function may be misleading, and the findings of Gledhill et al. (1994) do not conclusively demonstrate improved diastolic function in elite athletes. However, Woodiwiss and Norton (1995) found an increase in ventricular compliance secondary to reduced left ventricular end-diastolic stiffness in rats after 16 weeks of endurance training. An increase in myocardial compliance may provide the mechanism for increased diastolic function following exercise training (Woodiwiss and Norton, 1995). These authors found that exercise training resulted in a greater end-diastolic volume for any filling pressure. Figure 5.1 shows the data of Woodiwiss and Norton (1995), and illustrates augmented myocardial compliance at higher filling pressures. If exercise training increased myocardial compliance in human subjects after training, an increase in myocardial compliance could provide a mechanism for improved diastolic filling, particularly at higher exercise intensities and corresponding filling pressures. It can be speculated therefore that the subjects in the present study experienced increased ventricular compliance, allowing for a greater end-diastolic volume at equal filling pressures.

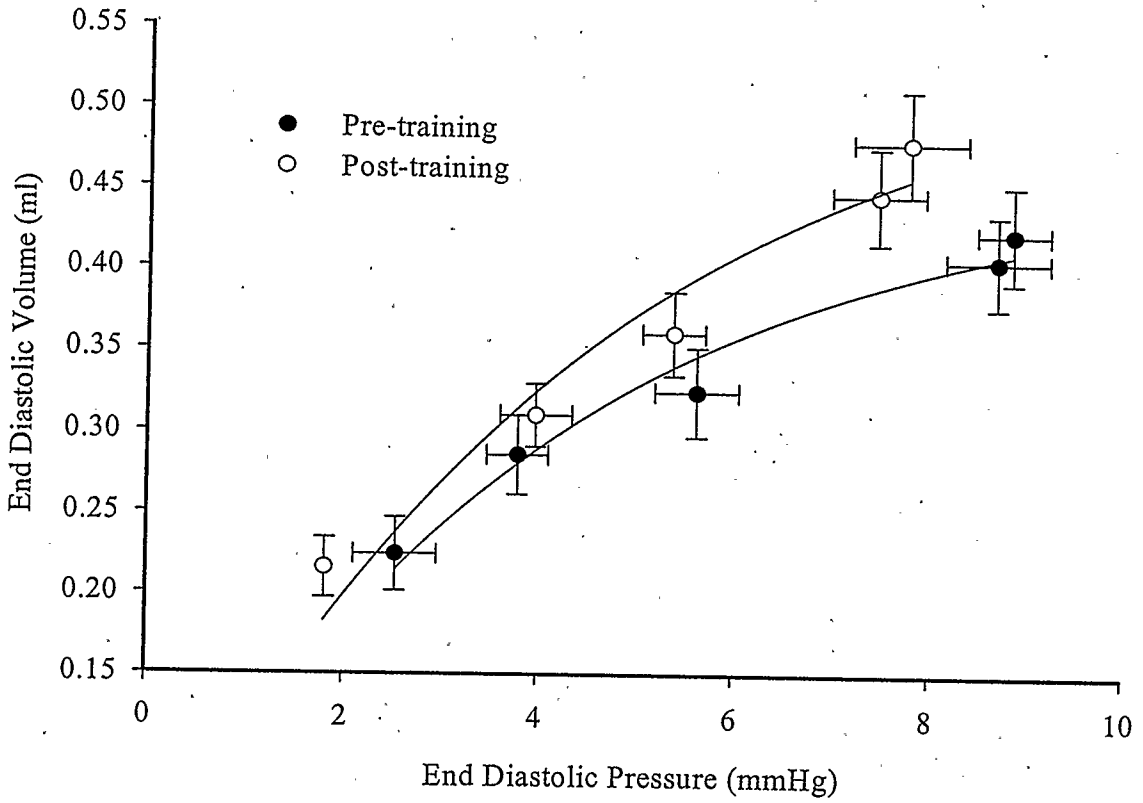

Figure 5.1. The relationship between end-diastolic volume and pressure following 16 weeks of endurance training in rats (pericardium removed). Data from Woodiwiss and Norton (1995) ($N = 11$). Error bars represent ± SE

One obvious shortcoming of the study by Woodiwiss and Norton (1995) lies in that the pericardium was not intact. During periods of acute cardiac dilation, the pericardium may act to constrain the ventricle and limit the extent of end-diastolic volume (Gilbert and Glantz, 1989). Under these conditions the extent of ventricular relaxation may be the primary factor limiting SV at filling pressures associated with maximum exercise. Using the canine model, Stray-Gundersen et al. (1986) evaluated the effect of removing the pericardium on maximum SV (Figure 5.2). The authors found no change in submaximal

SV's, but a 17% increase in maximum SV. It can be seen that the data in Figure 5.2 closely resembles the differences found between elite and trained athletes in the data of Zhou et al. (2001) (Figure 5.0a). Similar trends can be found when evaluating the data from the present study, when SV is plotted against HR for each workload (Figure 4.6). Consequently, pericardium restructuring may provide an alternative or additional mechanism for the increase in peak SV's in the present study. Whether pericardium restructuring can occur following 7 days of training is difficult to speculate and no research to date has detailed if pericardium restructuring can occur following such brief periods of exercise training.

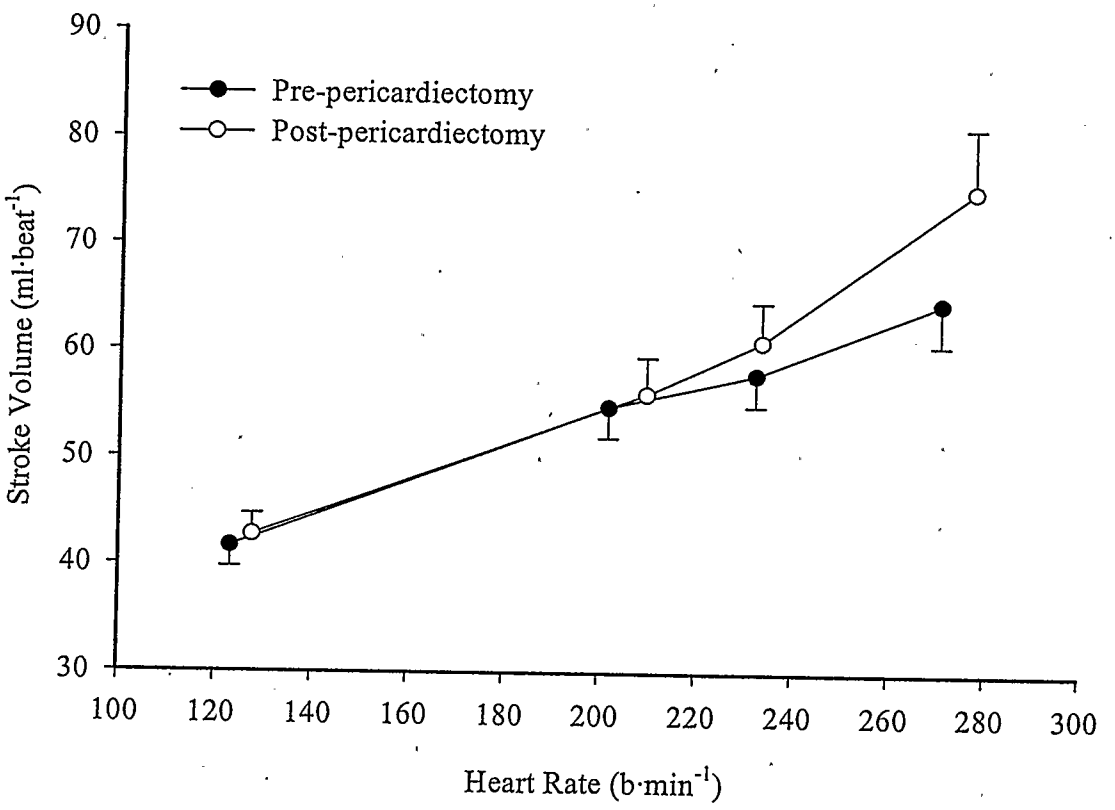

Figure 5.2. The relationship between stroke volume and heart rate pre- and post-pericardiectomy. Data from Stray-Gundersen et al. (1986). Error bars represent ± SE.

Alterations in the redistribution of blood volume from the veins and viscera to the heart and lungs may be another mechanism for explaining the increase in post-training SV's in the present study. Using radionuclide techniques, Flamm et al. (1990) found increases in ventricular end-diastolic volume occurred in concert with decreases in leg blood volume as exercise intensity increased up to 50% $\dot{V}O_2max$. No further increases in end-diastolic volume were found at 75 and 100% $\dot{V}O_2max$, although pulmonary blood volume continued to increase. While the authors suggested the skeletal muscle pump was responsible for the redistribution of blood volume from the legs to the pulmonary circulation, catecholamine-mediated venoconstriction may also induce redistribution of the blood from the veins to the cardiopulmonary circulation. Kjaer et al. (1985) found athletes had higher norepinephrine concentrations at the point of exhaustion when compared to untrained subjects. Following 10 days of high-intensity training, Mier et al. (1997) found a 37% increase ($P<0.06$) in plasma norepinephrine during peak cycle exercise and a 15% increase in peak exercise SV. Although the authors did not report a correlation between the increase in SV and norepinephrine concentration, it seems plausible that the increased norepinephrine concentration may have increased venoconstriction, resulting in greater redistribution of the blood volume to the central circulation. It is interesting to note that the authors did not find a significant correlation between the increase in blood volume (6.3%) and the increase in peak SV (15%). Further research is needed to determine if changes in venous capacitance following training provides a more valid mechanism for increased SV compared to changes in blood volume.

The rapid increase in SV in the present study may also be due to altered ventricular contractility. Several studies have shown an increase in contractility in response to endurance training (Krzeminski et al., 1989; Wisloff et al., 2001) and resistance training (Fisman et al., 2002). Using the HR response to exercise during the training cycle to predict changes in SV (Table 4.1); it can be speculated that the increase in maximum SV occurred by the third day of training as suggested by a reduced maximal HR and unchanged maximum power output. In addition, a significant decrease in the slope of the HR versus power output relationship was found on training day 3. As suggested by Sunagawa et al. (1985), a decrease in the slope of the relationship between HR and $\dot{V}O_2$ may be indicative of increased contractility. Fisman et al. (2002) found increased ventricular contractility in endurance- and resistance-trained athletes when compared to sedentary controls. The increase in SV in the present study may have resulted from an increase in ventricular contractility mediated through combined endurance and resistance training.

It is interesting to note that the increase in resting SV (12%) was nearly identical to the increase in peak SV (9%). Although alterations in ventricular filling pressure and ventricular distension are frequently used to explain acute increases in resting SV, the significant increase in resting SV with the assumed minimal increase in central venous pressure suggests the increase in SV was due to acute alteration of ventricular contractility. Although intensity dependent alterations in venous capacitance have been suggested as a mechanism for improved SV, it seems unlikely that such changes provided a mechanism for increasing SV at rest.

5.2 Heart Rate Response to Exercise: Resting HR was significantly lower when compared to pre-training values, suggesting an alteration in vagal tone. Yamamoto et al. (2001) found a decrease in resting HR in moderately active subjects after 4 weeks of endurance training, which coincided with markers of increased parasympathetic activity. However, no change in resting HR was found after 14 days of endurance training (Yamamoto et al., 2001). Similar findings were reported by Ehsani et al. (1978), where 7 days of intensive swimming in competitive swimmers did not alter resting HR. Given these findings it is difficult to definitively explain the considerable decrease in resting HR in the present study. However, it seems plausible that the training stimulus in the present study was sufficiently intense to induce changes in autonomic control seen by Yamamoto et al. (2001). An additional explanation for the decreased resting HR in the present study lies in the mechanisms of ventricular adaptation which may have allowed for an increased resting SV. For example, if changes in ventricular or pericardial compliance post-training acted as mechanisms to increase the extent of ventricular filling, the same $\dot{Q}$ could be achieved with a lower HR.

It is generally thought that SV limits maximum $\dot{Q}$ in athletes, since maximum HR is generally unaffected by training (Saltin et al., 1968). However, in the present study a significant decrease in maximum HR was found following training, and although maximum SV increased significantly, no increase in maximum $\dot{Q}$ resulted. Costill et al. (1988) found a 6 $b \cdot min^{-1}$ decrease in maximum HR in swimmers after completing 10 days of training at twice the normal training volume. Similar to the present study, Costill et al.

(1988) found no change in $\dot{V}O_2max$ or maximum swimming velocity following the training cycle. Spina et al. (1992) reported a significant decrease in maximum HR in sedentary subjects after 12 weeks of endurance training. However, the increase in SV was sufficient to increase $\dot{Q}$ and $\dot{V}O_2max$. Several mechanisms have been reported that may cause a rapid decrease in maximum HR following intense training. Douglas et al. (1998) found decreased chronotropic responsiveness of beta-adrenergic receptors in triathletes following completion of an ironman triathlon. Hammond et al. (1987) reported a decrease in maximum HR and beta-adrenergic receptor number in pigs after 10 weeks of endurance training. Taking the data collectively, a decrease in beta-receptor responsiveness or density could be one mechanism to explain the decreased maximum HR's found in the present study. Through repeated elevation of circulating catecholamines, the high-intensity training stimulus in the present study may augment such an adaptation.

5.3 Blood profile response to exercise training: The calculated total blood volume (pre-training, 78.3 $ml \cdot kg^{-1}$; post-training, 81.1 $ml \cdot kg^{-1}$) in the present study agrees with that found by others. Gledhill et al. (1994) reported blood volumes of 77.3 $ml \cdot kg^{-1}$ in well-trained endurance athletes ($\dot{V}O_2 max = 4.4\ l \cdot min^{-1}$). Kanstrup and Ekblom (1982) reported blood volumes of 75.2 $ml \cdot kg^{-1}$ in similarly trained athletes. The increase in blood volume in the present study occurred primarily through increased plasma volume (Table 4.5), although this change in plasma volume was less than that reported by other authors. For example, Green et al. (1990) found a 20% increase in plasma volume after 3 days of prolonged duration training, while Green et al. (1984) found a 12% increase in plasma

volume following 3 days of intermittent training. The comparatively small increase in plasma volume in the present study may be due to the high training status of the subjects. For example, Richardson et al. (1996) found a 4.4% increase in plasma volume in well-trained swimmers following 4 days of high-intensity training. It is possible that well-trained athletes experience minimal net changes in plasma volume in response to training due to the already high blood volumes. Thus, the relatively small increase in plasma volume in the present study may be attributed to the relatively high pre-training blood volume of the subjects.

It is interesting to note the cyclic pattern of plasma volume expansion (estimated from Hb and Hct) throughout the training cycle (Table 4.6). The estimated changes in plasma volume were greatest on the training days following the resistance training session. McCarthy et al. (1997) found a 2.8% increase in blood volume following 12 weeks of resistance training. Although the resistance-training load employed by McCarthy et al. (1997) was slightly different than the present study, it seems possible that resistance-training similar to that employed in the present study may provide an important stimulus for inducing blood volume expansion in well-trained athletes with high pre-training blood volumes.

Although no significant change was found in Gm, Ga or α_1-AT concentrations post-training when compared to pre-training, there was a trend for increased Ga and a resultant decrease in the Gm-Ga ratio. Smith and Norris (2000) reported an increased Ga concentration in elite athletes undergoing very high-intensity training cycles. These authors also suggested

that increased Ga could result from insufficient recovery following high-intensity training. However, the lack of change in the Gm concentration in the present study suggests that subject's capacity to tolerate the training stimulus was not exceeded (Smith and Norris, 2000). These findings are supported by the unchanged maximum power output during the daily training tests (Table 4.1).

Evaluation of individual changes in markers of training stress (Appendix F) provides more insight into differences between subjects in their ability to tolerate the training stress. Specifically, subjects 5, 6, 7 and 8 experienced noticeable decreases in plasma Gm concentrations after 7 days of training, suggesting the training stress exceeded the athlete's ability to adapt (Smith and Norris, 2000). Evaluation of the SV data (Appendix F) and maximum power output data suggests adaptation did occur and maintenance of performance was possible. However, given the acute timelines of the study it is difficult to speculate the long-term effects of the training stress on these individuals. Further examination of the HR versus power output relationship (Table 4.1) suggests each of these individuals experienced a reduction in the slope of the relationship after the first day of exercise training. It can be speculated that a shorter duration training cycle would have resulted in equivocal training adaptations without additional training stress. If the training stress was prolonged it seems likely that the subjects may have experienced a decrease in performance. Specifically, subjects 7 and 8 experienced an increase in the intercept of the HR versus power output relationship near the end of the training cycle, secondary to increased submaximal HR's and possible conversion to sympathetic nervous system predominance (Iellamo et al., 2002).

5.4 Critique of methods: The measures of resting $\dot{Q}$ (8.95 and 9.15 $l \cdot min^{-1}$, pre- post-training respectively) in the present study were higher than those reported in previous research. Barker et al. (1999) reported resting $\dot{Q}$ values of 6.4 $l \cdot min^{-1}$ using the same technique as that used in the present study, and 7.0 $l \cdot min^{-1}$ using the direct Fick technique. One of the major differences in the calculation of $\dot{Q}$ in the study by Barker et al. (1999) was that the authors measured the C_2H_2 blood-gas partition coefficient (λ) for each subject, whereas the present study used the mean λ for males reported by Barker et al. (1999). Since the primary focus of this study was changes in $\dot{Q}$, and Barker et al. (1999) reported no change in λ between 7 days of training, the decision to use the mean λ was felt to be justified. However, due to possible differences in the subject pools, it is possible that the C_2H_2 solubility of the subjects in the present study was greater than that reported by Barker et al. (1999). Since the calculated value for $\dot{Q}$ is inversely related to the value of λ, $\dot{Q}$ may have been overestimated.

Simultaneous measurements of $\dot{V}O_2$ and $\dot{Q}$ provided the necessary data for the estimation of $(a-\bar{v})O_2$ based on the modified Fick equation. However, when $(a-\bar{v})O_2$ is calculated in this way, error terms from both $\dot{V}O_2$ and $\dot{Q}$ are included in the estimate. For example, the intensity-by-time interaction found in $\dot{Q}$ was identical to that found for the $(a-\bar{v})O_2$. While it is possible that this may reflect a real change, caution should be exercised when interpreting changes in $(a-\bar{v})O_2$ when it is calculated in this way.

The short plasma half-life of Indocyanine Green (Haller et al., 1993) presents unique challenges to the researcher since it requires precise timing and repeated blood sampling to ensure the decay curve is accurately defined. It has been suggested that different clearance rates of Indocyanine Green may lead to errors in the back-extrapolation of the concentration versus time curve (Schroder et al. 1999). However, the changes in plasma volume in the present study were similar to those reported by other authors. In addition, the calculated change in plasma volume using Hb and Hct (Dill and Costill, 1974) predicted similar increases in plasma volume (7.3%) when compared to the dye-dilution technique (6.9%).

5.5 Limitations of the study: Using data from previous research several mechanisms have been proposed to explain changes in the present data. However, without specific measurement of these mechanisms, no conclusive statements can be made. The greatest limitation in the present study was that left ventricular dimensions and filling pressure were not measured. Consequently, while the proposed mechanisms for increased maximum SV revolved around conditions that increased end-diastolic volume of the heart, no measurements of these variables were made. In addition, it has been suggested that elite endurance athletes demonstrate improved systolic function when compared to untrained subjects (Gledhill et al., 1994; Fisman et al., 2003). Unfortunately no measures of systolic function, end-systolic volume or arterial pressure were performed in this study.

5.6 Conclusions: The present study was undertaken to evaluate changes in the $\dot{Q}$ response to exercise training, and how these changes would be manifested in the HR versus power output relationship. There is a strong trend in the exercise literature to explain increases in maximum SV through changes in the quantity of blood in the system. From the present research and findings of others, it appears that this approach may oversimplify a complex relationship between $\dot{Q}$ and venous capacitance (Tyberg, 2002). The present study demonstrated that increases in SV can be achieved within 7 days of high-intensity training in well-trained cyclists with minimal changes in total blood volume. Furthermore, increases in SV occurred without concomitant increases in maximum $\dot{Q}$ or maximal aerobic capacity. The results showed that changes in maximum SV can be predicted based on changes in the HR versus power output relationship; however the ability to predict maximum $\dot{Q}$ is limited due to potential changes in maximum HR induced by the acute training stimulus. These findings likely reflect the balance between adaptive processes that are considered beneficial for performance (i.e. increased SV) and those considered to hinder performance (i.e. decreased Hb concentration, decreased maximum HR). A thorough understanding of the different adaptive timelines is necessary for achieving optimal performance of an integrated system.

5.7 Future Research Directions

Several potential research directions have developed from completion of this study:

1) Extend the duration of the training stimulus, measuring $\dot{Q}$, arterial pressure and left ventricular dimensions (echocardiography) at day 3, 7, 14, 21.

2) Perform exercise under conditions that increase ventricular preload (i.e. swimming) during high $\dot{Q}$'s.

3) Use direct measurements of $\dot{Q}$, end-diastolic and end-systolic pressures, arterial and venous pressures.

4) Use an animal model to test the hypothesis that short-term high-intensity training causes ventricular and pericardial remodelling.

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Appendix A

Consent Form

Human Performance Laboratory Consent Form

Project Title: An investigation of the effects of seven days of physical training on cardiac output and the subsequent heart rate versus power output relationship

Investigators: Stephen R. Norris, Ph.D., Matthew J. Black, M.Sc. candidate

Sponsor: Sport Science Association of Alberta

This consent form, a copy of which has been given to you, is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your participation will involve. If you would like more detail about something mentioned here, or information not included here, you should feel free to ask. Please take the time to read this carefully and to understand any accompanying information.

The purpose of this research is to evaluate changes in cardiac output during exercise in response to seven days of intensive training. In addition, the specific timelines of cardiac adaptation will be evaluated, with an emphasis on implications for aerobic performance. Blood volume, cardiac dimensions, heart rate and stroke volume will be measured to define the source of changes in cardiac output during exercise. You have been chosen for participation in this study because of your high level of aerobic fitness and your experience with intensive training and competition.

EXPLANATION OF YOUR INVOLVEMENT:

As a participant in this study you are required to undergo the following procedures. Please note that all procedures will be thoroughly explained to you several times before having to perform them.

1. One incremental maximal aerobic power test ($\dot{V}O_2$ max) on a cycle ergometer to determine your cardiorespiratory fitness level and your heart rate response to increasing power outputs.

2. Two incremental workload tests during which cardiac output ($\dot{Q}$) will be determined at rest and during five different workloads by breathing a harmless gas containing acetylene, helium, oxygen and nitrogen.

3. Two measurements of blood volume (BV) by injection of Indocyanine Green dye and withdrawal of venous blood.

4. Seven days of training of approximately two hours daily. Each training session will begin at 07:30 hours. At this time you will be required to report to the human performance laboratory in a rested state. You will perform one incremental test to volitional fatigue. A fingertip blood sample will be obtained after 3 minutes of cycling at 50 watts. Following blood sampling, you will perform one repetition of three minutes duration at each of 100%, 95%, 90%, 85% and 80% of maximal aerobic power. Three minutes rest will be given between each repetition. Following this, five repetitions at 150% maximal aerobic power with one minute and forty seconds rest between repetitions will be performed. This will be followed by 20 minutes of cycling at the first ventilatory threshold. On the afternoon of three training days, you will perform a weight circuit of 11 exercises three times.

5. Provide 2 resting blood samples for determination of glutamine, glutamate and alpha-1-antitrypsin.

6. Your total time commitment is estimated to be approximately 22 hours over the course of 17 days.

Period 1		**Period 2**							**Period 3**
Day #									
1	7	8	9	10	11	12	13	14	15
$\dot{V}O_2$ max	PV Hb/Hct α_1-AT Gm/Ga		Hb/Hct	Hb/Hct	Hb/Hct	Hb/Hct	Hb/Hct	Hb/Hct	PV Hb/Hct α_1-AT Gm/Ga
	$\dot{V}O_2$ max	Cycle (2 hr)	Cycle (2 hr)	Cycle (2 hr)	Cycle (2 hr)	Cycle (2 hr)	Cycle (2 hr)	Cycle (2 hr)	$\dot{V}O_2$ max
	$\dot{Q}$		Weights (45 min)		Weights (45 min)		Weights (45 min)		$\dot{Q}$

Figure 1. Schematic of timelines and the corresponding physiological tests.

Legend:

$\dot{V}O_2$ max; Incremental exercise test with with gas collection

$\dot{Q}$; Measurements of cardiac output during the $\dot{V}O_2$ max test via acetylene breathing

PV, Hb/Hct, α_1-AT, Gm/Ga; Blood sampling for determination of plasma volume, hemoglobin, hematocrit, alpha-1-antirypsin, glutamine and glutamate

Hb/Hct; Blood sample for analysis of hemoglobin and hematocrit

Cycle; Training on a cycle ergomoter at set loads

Weights; Weight circuit for three circuits at 12-15 repetition maximum

EXACT PROCEDURES ARE OUTLINED AS FOLLOWS:

Period 1; Baseline measures of $\dot{V}O_2$ max, blood volume, cardiac dimensions, cardiac output, performance trial and blood parameters.

The initial step will involve determination of $\dot{V}O_2$ max via an incremental test to exhaustion on an electrically braked cycle ergometer. This test will provide maximal aerobic power and the heart rate response to increasing workloads. A minimum requirement for participation in this study is a $\dot{V}O_2$ max of 60-ml·kg^{-1}·min^{-1}. If your $\dot{V}O_2$ max is less than 60-ml·kg^{-1}·min^{-1}, an interpretation of the data and it's relevance to your training tactics will be provided to you free of charge. Beyond this, you will not be permitted to participate in the study. If your $\dot{V}O_2$ is within the required range, blood volume will be determined 7 days later (07:30 hours) followed by an incremental test where cardiac output will be measured by having you breathe a gas mixture containing room air with acetylene and helium added. On the following 7 days you will perform a dynamic postural change test upon waking using a Polar heart rate monitor which will be leant to you. On each of these days you will report to the laboratory at 0730hrs where training will take place for approximately 2 hours. The details of each procedure are listed below;

$\dot{V}O_2$ max Evaluation: This will be evaluated from a cycle ergometer test to exhaustion during which you will be fitted with a 2-way non-rebreathing valve (similar to a snorkel mouthpiece) for gas collection purposes. Heart rate will be monitored with a Polar chest-mounted heart rate monitor. Resistance will be increased every 2 minutes until the second ventilatory threshold, after which the resistance will be increased every minute until you cannot continue or $\dot{V}O_2$ max criteria have been observed by the researchers, whichever comes first.

PV Evaluation: Plasma volume will be determined at 07:30 on the day prior to training by injection of Indocyanine Green dye, a harmless dye that has been used extensively for over 30 years in human research. On the morning prior to cardiac output determination, you will be required to report to the laboratory in a fasted state where you will lie for 30 minutes after a trained technician inserts a catheter in your arm. After 30 minutes, a 20-ml sample of blood will be withdrawn from the catheter. A small needle will then be inserted into your opposite arm and a small amount of Indocyanine Green dye (5 ml) will be injected. The withdrawn blood sample will be used for analysis of blood parameters specific to training fatigue. Twelve blood samples (2.5-ml) will be withdrawn from the cubital vein of your left arm at 30 second intervals between 4 and 10 minutes after injection. You will be permitted to leave the laboratory when you feel recovered. There may be some tenderness at the point of needle insertion.

Cardiac Output Evaluation: Cardiac output will be evaluated during rest and 5 exercise intensities. During the final 30 to 180 seconds of each workload, the intake valve of a 3-

way valve assembly will be switched to a bag containing a harmless gas mixture (0.7% acetylene, 5% helium, 21% oxygen and 73.3% nitrogen). No rebreathing procedure is involved in this maneuver, and blood oxygen and carbon dioxide remain at normal levels. Following breathing the gas mixture, the intake valve will be switched back to room air and the power output will be increased.

Period 2; Training intervention, blood parameters

The purpose of the training intervention is to provide a training stress of sufficient magnitude to induce a transient decrease in aerobic performance capacity. The dynamic postural change test will be completed daily. Following each dynamic postural change test, you will cycle for approximately 2 hours on a cycle ergometer. Part way through each training session, one lactate sample will be obtained through a fingertip blood sample. This training will result in considerable fatigue in your legs. Training outside of this protocol will be discouraged. An example of the training session is as follows:

1. Incremental test to volitional fatigue. Heart rate will be continually recorded.
2. Immediately following this test and after 3 minutes of cycling at 50 watts, a fingertip blood sample will be obtained for analysis of blood lactate concentration. The sample will be obtained by puncturing the skin with a sterile pin-like device.
3. Following lactate sample, you will complete a repetition of 3 minutes duration at each of 100, 95, 90, 85 and 80% of the maximal aerobic power achieved during the first $\dot{V}O_2$max test. Recovery between repetitions will be 3 minutes cycling at 50 watts.
4. 5 repetitions at 150% maximal aerobic power workload of approximately 20 seconds duration, with 1 minute and 40 seconds rest between repetitions.
5. 20 minute at the workload corresponding to the first ventilatory threshold (approximately 70% of maximal heart rate).

In addition to the above training, you will be required to complete a weight circuit (11 exercises, 12 repetition maximum, 3 circuits) on days 2, 4 and 6 of the training intervention. This will take approximately 45 minutes.

Prior to training on days 2 to 7, a venipuncture blood sample will be drawn for analysis of hemoglobin and hematocrit.

Period 3: Post-training and recovery measures of blood volume, cardiac dimensions, cardiac output, performance trial and blood parameters.

The protocol for all post-testing will be identical to that of the pre-tests. On the day immediately following the training intervention, you will be required to report to the laboratory in a 12-hour fasted state for blood volume determination. On the afternoon of the same day, you will perform another incremental test with simultaneous determination of cardiac output. Two and

BENEFITS

This study will assist the investigators in understanding changes that occur in cardiac dynamics during exercise during periods of rest, acute fatigue and recover. The combined analysis of the heart rate response to exercise may provide groundwork for the development of non-invasive, inexpensive field tests used to quantify cardiac adaptations. For you as a participant your cardiovascular performance will be assessed, including determination of left ventricle dimensions and stroke volume that cannot be assessed at most laboratories or testing centers. Upon completion of this study you will receive a detailed analysis of your personal results that may be helpful to you in identifying specific training fatigue and the time course of adaptations important in developing an optimal training plan.

POTENTIAL RISKS AND DISCOMFORTS

Incremental exercise tests. As with all maximal effort testing, you may experience some degree of short duration/transient nausea, dizziness, muscle soreness or discomfort. However, if any of these adverse reactions occur, they should be short-lived.

Blood volume and blood removal. As with injection of many substances, a small percentage of subjects demonstrate an allergic reaction to Indocyanine Green dye. Choosing subjects that do not demonstrate strong allergic reactions has minimized this risk. However, to ensure your safety, a physician will be present during the first determination of blood volume. The dye is naturally cleared from the blood within 24 hours after injection. The process of dye injection and blood removal may present some discomfort, particularly in subjects nervous about needles or blood. Although all blood removal and dye injection procedures have an inherent risk of disease transmission, standard precautions for preventing transmission of blood borne diseases will be practiced. In addition, a trained technician will perform all blood procedures. Some tenderness can be expected from needle insertion, which should not persist for more than 2 or 3 days.

Cardiac output test. The gas inhaled during the determination of cardiac output does not present any negative side effects. While the acetylene in the mixture does diffuse into the blood stream, it is not metabolized by the body and is rapidly expired after approximately 1-minute breathing room air. Since helium does not move beyond the level of the lung, it is rapidly expired within a few normal breaths of room air. The remaining contents in the gas mixture are identical to that of room air.

Training intervention. Side effects from the training intervention will be similar to those experienced during maximal exercise testing. It is likely that nausea will be experienced as a result of the high training intensity. In addition, the repetitive nature of the training

stimulus is likely to result in considerable muscle fatigue and may result in sleep disturbance, irritability and whole body fatigue.

Confidentiality

All information will be kept in strict confidence and your name will not appear on any project documents since a code will be assigned to you upon entry into the study. Data will be kept for a period of 3 years and then destroyed. In the event that you suffer an injury as a result of participating in this research, no compensation will be provided for you by the Sports Science Association of Alberta, the University of Calgary, the Calgary Regional Health Authority or the research group. Nothing said about treatment or compensation in any way alters your rights to recover damages. You still have all your legal rights.

Your signature on this form indicates that you have understood to your satisfaction the information regarding participation in the research project and agree to participate as a subject. In no way does this waive your legal rights nor release the investigators, sponsors, or involved institutions from their legal and professional responsibilities. You are free to withdraw from the study at any time. Your continued participation should be as informed as your initial consent, so you should feel free to ask for clarification or new information throughout your participation. If you have further questions concerning matters related to this research, please contact:

Matthew Black at 220-3432 or Dr. Stephen Norris (supervisor) at 220-7005.

If you have any questions concerning your rights as a possible participant in this research, please contact Pat Evans, Associate Director, Internal Awards, Research Services, University of Calgary, at 220-3782.

_____

Participant's Signature

Date

_____

Investigator and/or Delegate's Signature

Date

_____

Witness' Signature

Date

A copy of this consent form has been given to you to keep for your records

Appendix B

Ethics Approval

UNIVERSITY OF CALGARY

FACULTY OF MEDICINE

Office of Medical Bioethics
Heritage Medical Research Building/Rm 93
Telephone: (403) 220-7990
Fax: (403) 283-8524

2002-04-04

Dr. S.R. Norris
Faculty of Kinesiology
University of Calgary
KN B211
Calgary, Alberta.

Dear Dr. Norris:

Re: An Investigation of the Effects of Seven Days of Physical Training on Cardiac Output and the Subsequent Heart Rate Versus Power Output Relationship
Student: Mr. Matthew J. Black Degree: MSc

GRANT ID: 16448

The above-noted thesis proposal and the consent form have been submitted for Committee review and found to be ethically acceptable. Please note that this approval is subject to the following conditions:

(1) a copy of the informed consent form must have been given to each research subject, if required for this study;
(2) a Progress Report must be submitted by 2003-04-04, containing the following information:
  (i) the number of subjects recruited;
  (ii) a description of any protocol modification;
  (iii) any unusual and/or severe complications, adverse events or unanticipated problems involving risks to subjects or others, withdrawal of subjects from the research, or complaints about the research;
  (iv) a summary of any recent literature, finding, or other relevant information, especially information about risks associated with the research;
  (v) a copy of the current informed consent form;
  (vi) the expected date of termination of this project;
(3) a Final Report must be submitted at the termination of the project.

Please note that you have been named as a principal collaborator on this study because students are not permitted to serve as principal investigators. Please accept the Board's best wishes for success in your research.

Yours sincerely,

Christopher J. Doig, MD, MSc, FRCPC
Chair, Conjoint Health Research Ethics Board

cc: Dr. W. Herzog (information)
Mr. Matthew J. Black

Appendix C

Determination of Plasma Volume Using ICG

Materials

25 mg ICG dye
100 ml Polyethylene glycol solution (120 g/L)
1 20-gauge catheter
1 Butterfly needle
4 5-ml EDTA vacutainers
1 3-ml EDTA vacutainer (CBC)
12 2.5-ml EDTA vacutainers
1 20-ml syringe
4 5-ml syringes
12 3-ml syringes

Subject Preparation

1. Shorten the length of a 20-gauge catheter sampling line to a volume of exactly 2.5 ml when the 3-way stopcock is attached.
2. Insert the catheter into the antecubital vein of the left arm, and attach catheter sampling line.
3. Place subject in the supine position for 30 minutes.
4. Wrap the subjects left arm with a heating pad for the first 25 minutes of rest.

Material Preparation

The following procedures can be done while the subject rests.

1. Fill a small cooler with ice for storing blood samples.
2. Label four 5-ml EDTA vacutainers for the standard curve, one 3-ml vacutainer for CBC, and 12 2.5-ml EDTA vacutainers for mixed blood samples.
3. Fill two 5-ml syringes with sterile dilutent and weigh syringes together in triplicate.
4. Add the dilutent to the vial of ICG, mixing thoroughly. Following mixing, place the dye solution out of direct light.
5. Weigh the empty 5-ml syringes in triplicate.

6. 15 minutes before injection draw 5-ml of the ICG solution into a 5-ml syringe.
7. Remove the butterfly needle from its package and remove the vacutainer adaptor.
8. Weigh the ICG syringe and butterfly needle together in triplicate, without attaching the butterfly needle to the syringe or allowing the butterfly connection to contact any surface.
9. Place the ICG syringe out of direct light and return the butterfly needle to its package.

Dye Injection and Blood Sampling

1. After 30 minutes of rest, draw a 20-ml blood sample from the catheter.
2. Separate the 20-ml sample into the standard curve and CBC vacutainers. Immediately put samples on ice.
3. Insert a butterfly needle into the antecubital vein of the right arm, using a forceps to clamp the line when blood flow begins.
4. Prior to attaching the ICG syringe, release the forceps briefly to allow blood to fill the line, ensuring the needle is in the vein. Connect the syringe to the needle.
5. Inject the ICG solution over 5 seconds, ensuring the subject feels no discomfort.
6. Start two timers at the completion of the dye injection.
7. Remove the butterfly needle with the syringe attached and set aside for weighing. Ensure no dye is lost from the butterfly needle by drawing air into the syringe after removal.
8. Raise and abduct the right arm to 45 degrees for 1.5 minutes. Do not allow the subject to actively raise the arm.
9. Attach a 5-ml syringe to the catheter stopcock and draw 2.5 ml to clear saline from the line.
10. Four minutes after injection draw another 2.5 ml into the 5-ml syringe and discard the 5-ml syringe.
11. Take 2.5-ml blood samples every 30 seconds from 4.5 to 10 minutes post-injection. Sampling should take place as quickly as possible (<5 sec). At the start and finish of

each withdrawal, have an aide note the time. Immediately place each sample in the appropriately marked vacutainer, and place on ice out of direct light.

12. After the final sample remove the catheter and ensure the subject does not feel light-headed before leaving the lab.
13. Weigh the dye syringe/needle complex in triplicate.

Sample Preparation

1. Place all samples (except for the CBC vacutainer) in the centrifuge, and spin at 3000 RPM for 10 minutes.
2. After centrifuging is complete, set the standard curve vacutainers aside.
3. From the remaining vacutainers pipette 900 µl of plasma into appropriately marked test tubes.
4. Pipette 900 µl of the polyethylene glycol solution into each test-tube, cover with parafilm and mix.
5. Centrifuge all test-tubes at 3000 RPM for 10 minutes.
6. After centrifuging, allow the samples to sit for 10 minutes to allow any precipitate to separate from the solution.
7. Pipette the samples through a paper filter into appropriately marked cuvets, ensuring precipitate is not pipetted from the bottom of the solution.
8. Set the wavelength of the Beckman Instruments spectrophotometer to a wavelength of 805 nm, and blank using a cuvet filled with distilled water.
9. Measure the absorbance of each sample at 805 nm.
10. Blank the spectrophotometer and repeat.
11. Set the spectrophotometer to a wavelength of 900 nm, blank and measure the absorbance of each sample.
12. Blank the spectrophotometer and repeat.

Creating the Standard Curve

1. Create a working solution (A) by adding 20 µl of dye to 5.0 ml of centrifuged plasma to achieve an approximate ICG concentration of 10.0 mg/L.

2. Add 900 µl of A to a test tube marked 10 mg/L.
3. Mix 900 µl of A with 900 µl of plasma in a test tube marked 5.0 mg/L (B).
4. Remove 900 µl of B and mix with 900 µl of plasma in a test tube marked 2.5 mg/L (C).
5. Remove 900 µl of C and mix with 900 µl of plasma in a test tube marked 1.25 mg/L (D).
6. Remove 900 µl of D and mix with 900 µl of plasma in a test tube marked 0.625 mg/L (E).
7. To test tubes A, B, C, D and E mix 900 µl of a 120 g/L polyethylene glycol solution (Molecular weight; 3350).
8. Centrifuge the solutions at 3000 RPM for 10 minutes, allow to stand for 10 minutes, then pipette the solution through filter paper into appropriately marked cuvets.
9. Set the wavelength of the spectrophotometer to 805 nm, blank with water and measure the absorbencies as with previous samples.
10. After taking two readings at 805 nm, repeat the procedure using a wavelength of 900 nm.

Determination of Plasma Volume

1. Using the absorbencies of the samples, subtract the mean of the absorbance at 900 nm from the mean of the absorbance at 805 nm to obtain the corrected absorbance for each sample.
2. Calculate the time of sampling for each sample (s) by taking the mean of the start and stop time of blood sampling.
3. Plot the corrected plasma absorbance vs. mean sampling time of each sample.
4. Obtain the theoretical absorption at injection time by mono-exponential back-extrapolation to time zero.
5. Convert the absorbance at injection time to a concentration ($C_{t=0}$) by using the slope and y-intercept from the standard curve.
6. Calculate plasma volume; $PV=D/C_{t=0}$

   Were;

D = injected dose of dye

$C_{t=0}$ = theoretical dye concentration at time of injection.

Example Calculation:

1. Determine concentration of ICG injected [ICG];

   $$[ICG] = \frac{\text{mass of dye (mg)}}{\text{mass of dilutent (g)}}$$

   $$[ICG] = \frac{25 \text{ mg}}{\text{g}}$$

   Assume 1 g of dilutent = 1 ml

   [ICG] = 2.53 mg/ml

2. Determine mass of dye injected (M_{ICG});

   M_{ICG} = volume of dye solution injected (ml) * [ICG]

   M_{ICG} = 4.66 ml * 2.53 mg/ml

   M_{ICG} = 11.8 mg

3. Determine slope (m) and y-intercept (b) from the standard curve of corrected plasma absorbance vs. time.

   m = 7.86

   b = -0.0753

4. Determine ICG absorbance at time of injection (x);

   x = Back-extrapolation of absorbance vs. time plot

   x = 0.459

5. Calculate concentration of plasma ICG at time of injection ($C_{t=0}$);

   $C_{t=0} = m * x + b$

   $C_{t=0}$ = 7.86 * 0.459 -0.0753

   $C_{t=0}$ = 3.53 mg / L

6. Calculate plasma volume (PV);

   $$PV = \frac{M_{ICG} \text{ (mg)}}{C_{t=0} \text{ (mg / L)}}$$

   $$PV = \frac{11.8 \text{ mg}}{3.53 \text{ mg / L}}$$

   PV = 3.34 L

7. Calculate blood volume;

$$BV = \frac{PV}{1 - Hct}$$

$$BV = \frac{3.34}{1 - 0.41}$$

$$BV = 5.66\ L$$

Appendix D

Statistical Analysis: Determination of Sample Size

Sample size determination for continuous data with repeated measures.

$$n = \frac{\sigma^2(z_{1-\beta} + z_{1-\alpha})^2}{(\mu_0 - \mu_1)^2}$$

where:
σ = standard deviation of the measure
β = power (0.80)
α = significance level (0.05)
μ_0 = mean of test 1
μ_1 = mean of test 2

Based on research by Warburton et al. (1999c) the following data were used in the sample size calculation for the variable peak cardiac output.

$\sigma = 1.20$ L
$\mu_0 = 31.0$ L
$\mu_1 = 32.0$ L

Using this data the sample size was estimated to be 9.

Appendix E

Statistical Analysis: Two-Way Analysis of Variance Tests

Table 6.0. Statistical parameters for the analysis of the effect of intensity and time on oxygen consumption.

Source	DF Error	MS Effect	DF Error	MS Error	F	P
Intensity	5	37.79	45	0.0656	575.94	0.0000
Time	1	0.02	9	0.0314	0.66	0.4375
Intensity-by-time	5	0.00	45	0.0049	0.54	0.7434

Table 6.1. Statistical parameters for the analysis of the effect of intensity and time on cardiac output.

Source	DF Error	MS Effect	DF Error	MS Error	F	P
Intensity	5	1179.03	45	4.3815	269.09	0.0000
Time	1	1.61	9	1.3140	1.22	0.2971
Intensity-by-time	5	3.35	45	0.8095	4.14	0.0035

Table 6.2. Statistical parameters for the analysis of the effect of intensity and time on heart rate.

Source	DF Error	MS Effect	DF Error	MS Error	F	P
Intensity	5	31296.02	45	104.6869	298.95	0.0000
Time	1	1342.98	9	74.7194	17.97	0.0022
Intensity-by-time	5	21.02	45	6.7498	3.11	0.0169

Table 6.3. Statistical parameters for the analysis of the effect of intensity and time on stroke volume.

Source	DF Error	MS Effect	DF Error	MS Error	F	P
Intensity	5	6567.28	45	260.9124	25.17	0.0000
Time	1	2020.47	9	72.1107	28.02	0.0005
Intensity-by-time	5	208.15	45	42.2472	4.93	0.0011

Table 6.4. Statistical parameters for the analysis of the effect of intensity and time on calculated arteriovenous oxygen difference.

Source	DF Error	MS Effect	DF Error	MS Error	F	P
Intensity	5	288.96	45	1.9462	148.48	0.0000
Time	1	0.21	9	1.3006	0.16	0.6944
Intensity-by-time	5	1.66	45	0.4244	3.91	0.0050

Appendix F

Raw Data

Table 7.0. Physical characteristics of the subjects.

Subject	Age (yr)	Height (cm)	Weight (kg)
1	30	168.0	64.4
2	27	199.8	91.8
3	27	175.5	70.0
4	25	178.2	75.4
5	23	170.0	64.0
6	20	178.0	73.2
7	20	175.8	74.4
8	25	178.2	74.6
9	25	181.2	77.0
10	27	173.0	73.7

Table 7.1. Details of preliminary maximum oxygen consumption test.

Subject	$\dot{V}O_2$max ($L \cdot min^{-1}$)	VT2 ($L \cdot min^{-1}$)	MAP (watts)	HRmax ($beats \cdot min^{-1}$)
1	4.42	3.39	331	204
2	5.63	4.17	441	165
3	4.45	3.38	397	185
4	4.42	3.36	353	200
5	4.30	3.35	385	208
6	4.94	4.41	420	189
7	4.63	3.80	375	212
8	4.47	3.46	331	196
9	4.62	2.89	375	188
10	4.26	3.37	385	199

Table 7.2. Individual slopes of the regression equation obtained from the daily heart rate versus power output test.

Subject	Training Day						
	T1	T2	T3	T4	T5	T6	T7
1	0.303	0.327	0.324	0.317	0.313	0.302	0.309
2	0.185	0.180	0.176	0.174	0.180	0.177	0.164
3	0.309	0.289	0.289	0.292	0.313	0.309	0.292
4	0.301	0.273	0.269	0.281	0.293	0.306	0.293
5	0.296	0.279	0.263	0.278	0.268	0.262	0.281
6	0.224	0.214	0.205	0.209	0.221	0.213	0.228
7	0.349	0.329	0.320	0.316	0.284	0.281	0.290
8	0.330	0.269	0.290	0.266	0.295	0.253	0.253
9	0.301	0.276	0.280	0.254	0.267	0.298	0.300
10	0.307	0.315	0.279	0.294	0.307	0.296	0.295

Table 7.3. Individual intercepts of regression equation obtained from the daily heart rate versus power output test.

Subject	Training Day						
	T1	T2	T3	T4	T5	T6	T7
1	91.6	85.4	82.3	80.0	81.3	87.4	83.5
2	85.4	80.3	80.9	80.7	79.8	81.3	82.9
3	71.4	74.0	76.3	73.8	71.6	71.4	75.2
4	73.4	76.9	79.6	75.2	74.6	72.1	74.9
5	92.9	97.1	100.3	97.1	97.9	99.4	86.2
6	85.8	85.6	86.4	86.9	82.3	83.4	76.4
7	77.4	83.4	85.4	85.3	90.8	89.9	91.8
8	84.4	91.9	96.1	102.8	93.9	94.6	99.9
9	77.7	79.7	78.4	86.8	81.8	81.7	67.7
10	74.7	70.1	81.8	78.2	76.3	77.4	80.4

Table 7.4. Individual heart rate maximums achieved during the daily heart rate versus power output test.

Subject	Training Day						
	T1	T2	T3	T4	T5	T6	T7
1	187	191	188	180	193	190	192
2	163	153	152	150	158	160	152
3	178	173	171	171	173	176	175
4	199	188	186	186	183	186	179
5	196	196	192	192	190	192	189
6	185	179	174	177	174	175	175
7	203	201	197	198	191	192	192
8	187	185	183	183	183	182	176
9	186	182	182	183	181	187	182
10	183	181	180	182	185	182	184

Table 7.5. Individual maximum power outputs achieved during the daily heart rate versus power output test.

Subject	Training Day						
	T1	T2	T3	T4	T5	T6	T7
1	353	353	353	353	397	397	397
2	441	441	441	441	441	441	441
3	397	397	351	351	351	351	351
4	351	351	351	351	351	351	351
5	397	351	397	397	397	397	397
6	486	486	441	441	441	486	441
7	397	397	397	397	397	397	351
8	309	351	309	309	309	351	309
9	397	397	397	397	397	397	397
10	351	351	351	351	351	351	351

Table 7.6. Individual blood lactate values measured 3 minutes after the completion of the daily heart rate versus power output test.

Subject	Training Day						
	T1	T2	T3	T4	T5	T6	T7
1	8.9	8.2	8.1	8.3	10.9	9.9	10.6
2	13	10.9		14.3	14.1	12.4	10.7
3	12.7	10.2	11.1	11.3	12.6	12.0	12.1
4	15.2	13.2		12.9	14.2	14.6	13.3
5	12.6	12.0		11.6	12.0	10.9	11.1
6	13.1	15.4	15.4	15.1	15.2	15.7	15.7
7	13.7	13.6	11.8	13.2	10.7	11.2	10.6
8	15.2	15.7	15.0	16.3	16.0	16.4	15.2
9	11.3	10.4	9.8	11.1	12	12.6	13.7
10	9.4	9.6	9.9	11.8	12.9	12.0	11.4

Table 7.7. Individual pre-training oxygen consumption at rest and 5 exercise intensities.

Subject	Power (watts)					
	0	66	132	198	265	351^{Δ}
1	0.42	1.24	1.84	2.59	3.56	3.98
2	0.51	1.42	2.16	2.90	3.62	5.08
3	0.48	1.36	2.01	2.71	3.42	4.02
4	0.46	1.44	2.20	2.92	3.49	3.97
5	0.39	1.30	2.10	2.80	3.47	4.02
6	0.51	1.60	2.11	2.96	3.63	4.81
7	0.35	1.29	1.92	2.54	3.19	4.24
8	0.38	1.39	2.11	2.80	3.42	3.77
9	0.42	1.24	1.82	2.56	3.22	4.23
10	0.42	1.39	2.02	2.64	3.21	3.83

351^{Δ}, mean of peak power outputs at peak cardiac output

Table 7.8. Individual post-training oxygen consumption at rest and 5 exercise intensities.

Subject	Power (watts)					
	0	66	132	198	265	351^{Δ}
1	0.39	1.27	1.88	2.77	3.58	3.92
2	0.62	1.56	2.25	2.94	3.63	5.17
3	0.48	1.30	2.03	2.73	3.47	4.11
4	0.40	1.28	2.00	2.74	3.33	3.64
5	0.45	1.44	2.13	2.72	3.27	3.80
6	0.52	1.63	2.30	3.10	3.88	5.10
7	0.40	1.39	2.02	2.76	3.48	4.51
8	0.47	1.49	2.11	2.87	3.47	3.89
9	0.38	1.09	1.95	2.62	3.39	4.01
10	0.39	1.39	1.98	2.68	3.22	3.70

351^{Δ}, mean of peak power outputs at peak cardiac output

Table 7.9. Individual pre-training cardiac output data at rest and 5 exercise intensities.

Subject	Power (watts)					
	0	66	132	198	265	351^{Δ}
1	7.6	12.8	12.4	19.0	24.1	27.9
2	10.6	11.5	15.5	20.5	23.2	32.4
3	10.2	14.0	17.1	20.4	26.0	30.7
4	8.9	13.8	14.3	20.5	24.5	26.5
5	9.1	13.8	15.4	22.1	25.7	27.9
6	9.7	11.9	16.2	20.8	25.4	35.4
7	9.4	12.3	13.7	17.1	17.9	25.2
8	7.3	12.7	16.4	22.1	24.2	28.8
9	7.9	12.3	13.4	16.1	20.8	27.3
10	8.6	12.7	13.5	18.4	19.9	29.8

351^{Δ}, mean of peak power outputs at peak cardiac output

Table 7.10. Individual post-training cardiac output data at rest and 5 exercise intensities.

Subject	Power (watts)					
	0	66	132	198	265	351^{Δ}
1	7.2	12.6	14.5	18.9	28.0	28.6
2	13.3	12.7	16.9	21.1	25.8	33.1
3	11.4	15.0	15.9	20.7	27.7	31.7
4	7.7	12.4	14.1	18.1	24.9	28.2
5	8.8	13.7	14.7	19.2	24.2	31.8
6	9.7	12.0	15.8	20.2	25.1	34.1
7	10.2	11.1	11.9	16.4	18.5	28.2
8	7.2	11.7	15.3	21.5	26.3	28.7
9	6.8	11.6	13.3	15.9	21.6	31.7
10	9.2	12.5	12.9	17.6	21.1	28.8

351^{Δ}, mean of peak power outputs at peak cardiac output

Table 7.11. Individual pre-training heart rate during the determination of cardiac output at rest and 5 exercise intensities.

Subject	Power (watts)					
	0	66	132	198	265	351$^{\Delta}$
1	81	104	122	148	182	196
2	78	90	104	119	135	160
3	71	99	113	134	161	175
4	83	116	145	164	186	195
5	81	113	139	152	184	197
6	85	106	116	137	158	182
7	81	112	135	158	179	206
8	71	113	149	169	185	192
9	83	97	119	143	162	181
10	71	105	123	140	161	177

351$^{\Delta}$, mean of peak power outputs at peak cardiac output

Table 7.12. Individual post-training heart rate during the determination of cardiac output at rest and 5 exercise intensities.

Subject	Power (watts)					
	0	66	132	198	265	351$^{\Delta}$
1	73	108	126	147	177	191
2	81	93	106	119	132	155
3	66	91	107	125	155	169
4	74	106	131	151	168	184
5	61	112	131	148	167	182
6	82	102	117	131	148	171
7	73	110	126	148	169	198
8	60	107	131	151	171	182
9	68	88	111	132	154	172
10	72	105	123	145	160	175

351$^{\Delta}$, mean of peak power outputs at peak cardiac output

Table 7.13. Individual pre-training stroke volume at rest and 5 exercise intensities.

Subject	Power (watts)					
	0	66	132	198	265	351^{Δ}
1	93.7	122.9	101.4	128.9	132.7	142.4
2	135.8	117.4	148.7	172.5	172.4	202.4
3	144.9	141.5	151.7	152.7	161.9	175.4
4	107.1	118.4	98.8	124.5	131.5	136.1
5	112.8	121.4	111.0	145.1	139.6	141.3
6	115.1	112.5	140.2	152.1	160.9	194.4
7	116.6	109.3	101.4	107.9	100.0	122.6
8	103.1	111.9	110.2	130.7	130.7	149.7
9	95.9	126.8	112.4	112.8	128.1	151.1
10	120.9	120.7	109.3	131.0	124.0	168.3

351^{Δ}, mean of peak power outputs at peak cardiac output

Table 7.14. Individual post-training stroke volume at rest and 5 exercise intensities.

Subject	Power (watts)					
	0	66	132	198	265	351^{Δ}
1	97.9	117.2	114.7	128.8	157.6	149.8
2	152.5	135.9	159.2	177.4	195.7	214.3
3	172.5	163.9	148.8	165.6	178.7	187.0
4	104.5	116.9	108.0	119.5	147.6	153.1
5	144.0	121.7	112.1	129.8	144.8	174.4
6	117.9	117.8	134.5	154.0	169.6	199.1
7	140.9	101.1	94.5	111.0	109.6	142.8
8	119.8	109.3	116.6	142.0	154.0	158.0
9	99.0	131.6	119.0	120.8	140.4	183.9
10	127.0	118.7	105.1	121.4	131.2	165.0

351^{Δ}, mean of peak power outputs at peak cardiac output

Table 7.15. Individual pre-training arteriovenous oxygen difference at rest and 5 exercise intensities.

Subject	Power (watts)					
	0	66	132	198	265	351^{Δ}
1	5.5	9.7	14.8	13.6	14.8	14.2
2	4.8	13.5	13.9	14.2	15.6	15.7
3	4.7	9.7	11.8	13.3	13.1	13.1
4	5.2	10.4	15.4	14.3	14.3	15.0
5	4.2	9.4	13.6	12.7	13.5	14.4
6	5.2	13.5	13.0	14.3	14.3	13.6
7	3.7	10.5	14.1	14.8	17.9	16.8
8	5.2	11.0	12.9	12.6	14.1	13.1
9	5.2	10.0	13.7	15.9	15.5	15.5
10	5.2	11.0	15.0	14.4	16.1	12.8

351^{Δ}, mean of peak power outputs at peak cardiac output

Table 7.16. Individual post-training arteriovenous oxygen difference at rest and 5 exercise intensities.

Subject	Power (watts)					
	0	66	132	198	265	351^{Δ}
1	5.4	10.0	13.0	14.6	12.8	13.7
2	4.3	12.3	13.3	13.9	14.1	15.6
3	4.3	8.7	12.7	13.2	12.6	13.0
4	5.2	10.3	14.1	15.2	13.4	12.9
5	5.0	10.6	14.6	14.2	13.5	11.9
6	5.3	13.5	14.6	15.4	15.5	14.9
7	3.9	12.5	17.0	16.8	18.8	16.0
8	6.6	12.7	13.8	13.3	13.2	13.6
9	5.6	9.4	14.7	16.4	15.7	12.7
10	4.2	11.1	15.4	15.2	15.3	12.8

351^{Δ}, mean of peak power outputs at peak cardiac output

Table 7.17. Individual pre-training interpolated stroke volume at cardiac outputs of 10, 15, 20, 25 and 30 $L \cdot min^{-1}$.

Subject	Cardiac Output ($L \cdot min^{-1}$)				
	10	15	20	25	30
1	105.4	117.2	129.1	141.0	152.9
2	127.4	144.9	162.4	179.9	197.4
3	139.7	147.4	155.1	162.8	170.5
4	104.7	113.8	122.9	132.0	141.0
5	112.1	121.3	130.4	139.5	148.6
6	114.3	130.3	146.2	162.2	178.1
7	114.3	103.4	105.9	121.7	150.9
8	104.7	115.2	125.7	136.2	146.7
9	105.7	118.0	130.2	142.4	154.7
10	118.1	118.7	127.5	144.4	169.4

Table 7.18. Individual post-training interpolated stroke volume at cardiac outputs of 10, 15, 20, 25 and 30 $L \cdot min^{-1}$.

Subject	Cardiac Output ($L \cdot min^{-1}$)				
	10	15	20	25	30
1	106.3	119.2	132.1	145.0	157.9
2	139.6	156.3	172.9	189.6	206.2
3	171.6	161.8	160.4	167.5	182.9
4	105.8	118.5	131.1	143.7	156.3
5	133.5	124.0	126.2	140.1	165.8
6	115.5	133.1	150.6	168.2	185.7
7	118.5	106.2	108.5	125.3	156.5
8	114.2	125.5	136.8	148.1	159.4
9	111.2	126.8	142.4	158.0	173.6
10	120.3	116.4	124.2	143.7	174.8

Table 7.19. Individual hemoglobin response to 7 days of exercise training.

Subject	Day							
	Pre	T2	T3	T4	T5	T6	T7	Post
1	150	150	148	149	150	150	148	143
2	148	151	140	144	135	139	138	137
3	136	140	136	138	135	141	136	132
4	151	150	143	151	148	151	143	140
5	142	135	134	138	134	135	136	136
6	146	144	139	145	142	142	139	138
7	154	153	151	148	152	156	158	153
8	139	140	143	143	148	144	141	132
9	145	145	145	145	138	152	144	139
10	134	140	140	143	139	141	142	142

Table 7.20. Individual hematocrit response to 7 days of exercise training.

Subject	Day							
	Pre	T2	T3	T4	T5	T6	T7	Post
1	0.45	0.43	0.43	0.44	0.45	0.44	0.43	0.42
2	0.43	0.43	0.40	0.42	0.39	0.40	0.40	0.40
3	0.40	0.41	0.40	0.40	0.40	0.42	0.39	0.39
4	0.44	0.43	0.42	0.44	0.43	0.44	0.43	0.41
5	0.41	0.40	0.39	0.41	0.39	0.39	0.41	0.39
6	0.44	0.44	0.41	0.42	0.41	0.41	0.40	0.41
7	0.45	0.44	0.44	0.43	0.44	0.44	0.46	0.45
8	0.42	0.41	0.41	0.42	0.43	0.42	0.41	0.39
9	0.43	0.42	0.41	0.42	0.39	0.43	0.41	0.40
10	0.38	0.40	0.40	0.41	0.40	0.40	0.41	0.41

Table 7.21. Individual pre-training plasma volume (PV), glutamate (Ga), glutamine (Gm) and alpha-1-antitrypsin (α_1-AT).

Subject	PV (L)	Ga (μM)	Gm (μM)	α_1-AT ($g \cdot L^{-1}$)
1	3.48	97	440	1.06
2	3.90	132	494	1.18
3	2.68	116	408	1.19
4	3.07	88	434	0.90
5	3.29	135	497	1.12
6	3.26	113	476	1.21
7	3.15	81	524	0.87
8	3.40	114	450	1.28
9	3.31	133	533	1.20
10	3.73	121	435	1.10

Table 7.22. Individual post-training plasma volume (PV), glutamate (Ga), glutamine (Gm) and alpha-1-antitrypsin (α_1-AT).

Subject	PV (L)	Ga (μM)	Gm (μM)	α_1-AT ($g \cdot L^{-1}$)
1	3.68	101	440	1.06
2	4.48	135	545	1.18
3	2.77	118	416	1.21
4	3.55	103	505	0.93
5	3.68	121	419	1.07
6	3.38	121	422	1.34
7	3.44	91	446	0.99
8	3.63	155	551	1.31
9	3.76	162	522	1.21
10	3.19	129	466	1.13

Appendix G

Regression Analysis for Interpolation of Stroke Volume at Discrete Cardiac Outputs

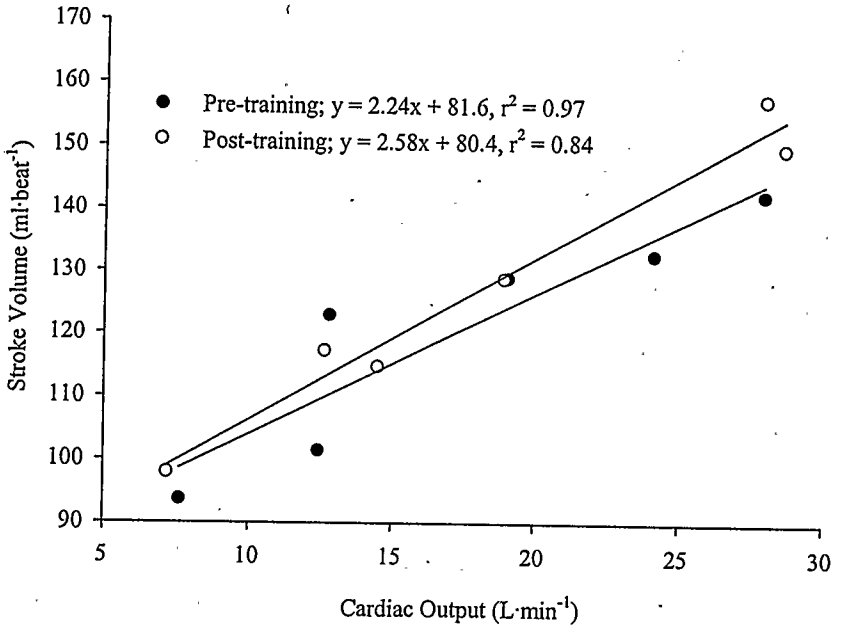

Figure 8.0. The relationship between stroke volume and cardiac output for subject 1 before and after 7 days of training. The regression equations pre- and post-training were used to interpolate the stroke volume at cardiac outputs of 10, 15, 20, 25 and 30 $L \cdot min^{-1}$.

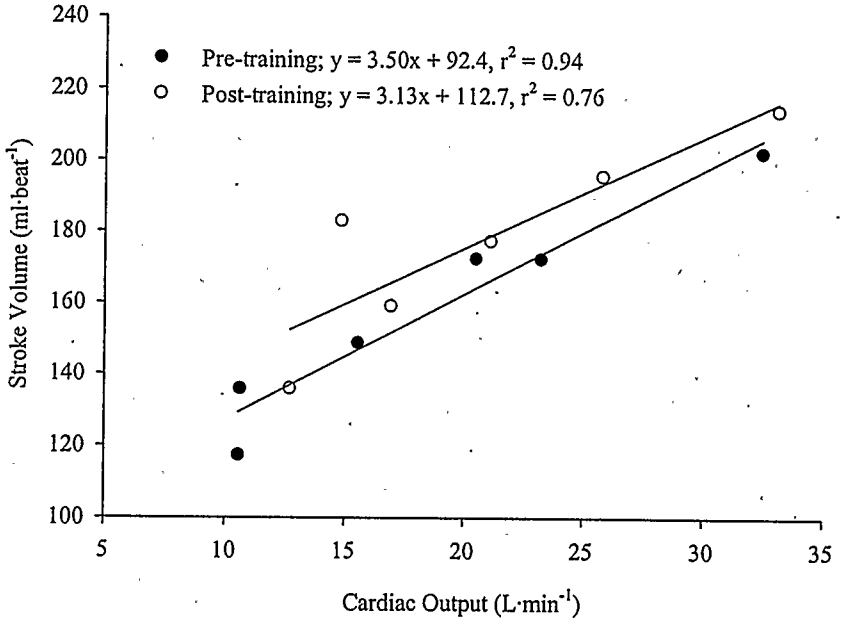

Figure 8.1. The relationship between stroke volume and cardiac output for subject 2 before and after 7 days of training. The regression equations pre- and post-training were used to interpolate the stroke volume at cardiac outputs of 10, 15, 20, 25 and 30 L·min^{-1}.

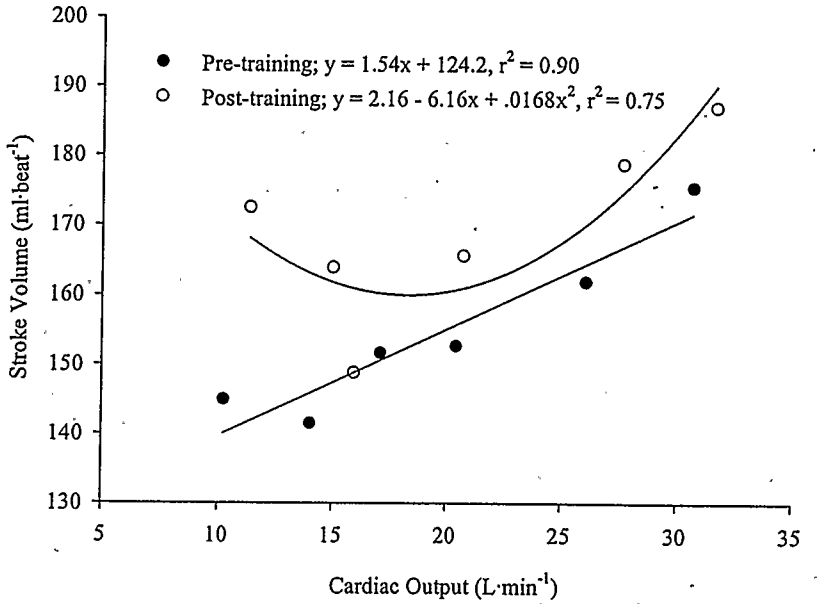

Figure 8.2. The relationship between stroke volume and cardiac output for subject 3 before and after 7 days of training. The regression equations pre- and post-training were used to interpolate the stroke volume at cardiac outputs of 10, 15, 20, 25 and 30 L·min^{-1}.

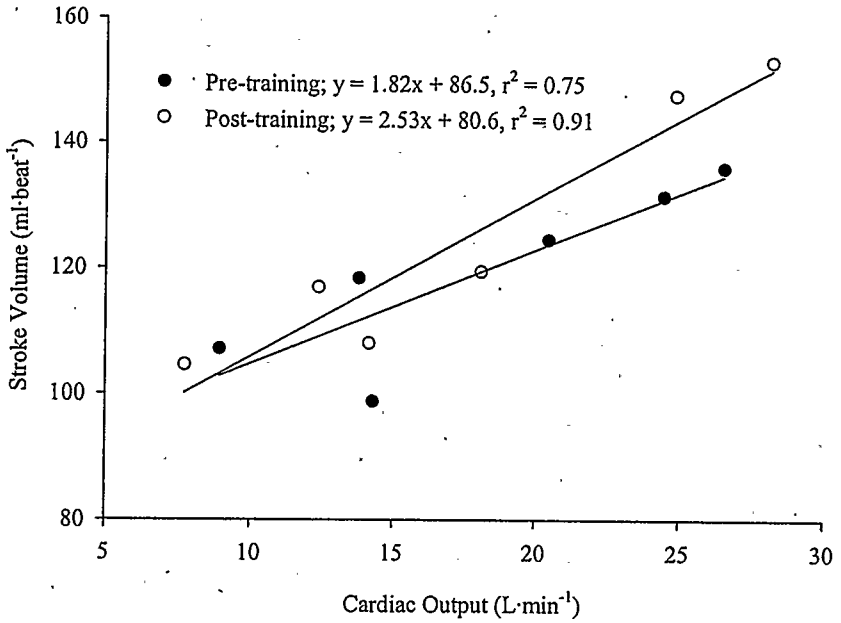

Figure 8.3. The relationship between stroke volume and cardiac output for subject 4 before and after 7 days of training. The regression equations pre- and post-training were used to interpolate the stroke volume at cardiac outputs of 10, 15, 20, 25 and 30 L·min^{-1}.

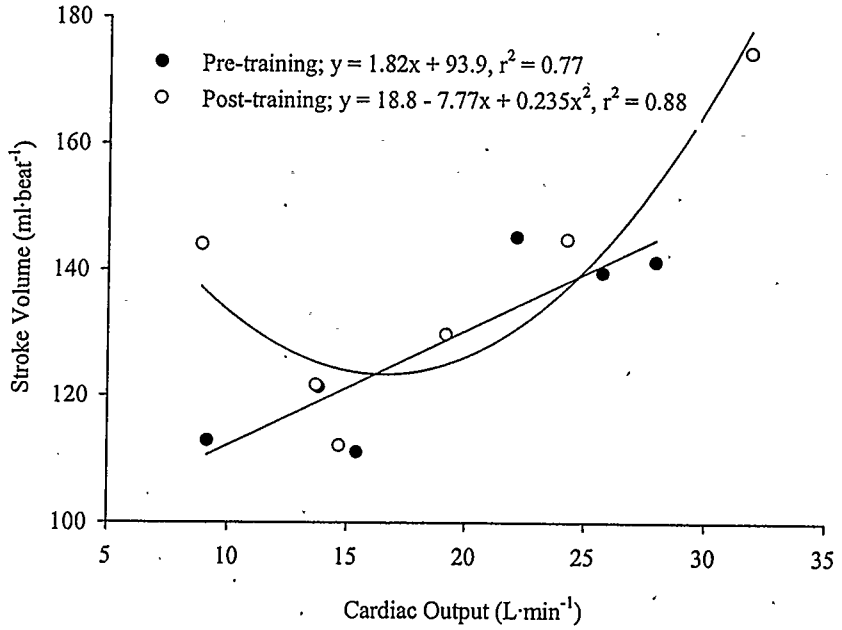

Figure 8.4. The relationship between stroke volume and cardiac output for subject 5 before and after 7 days of training. The regression equations pre- and post-training were used to interpolate the stroke volume at cardiac outputs of 10, 15, 20, 25 and 30 L·min^{-1}.

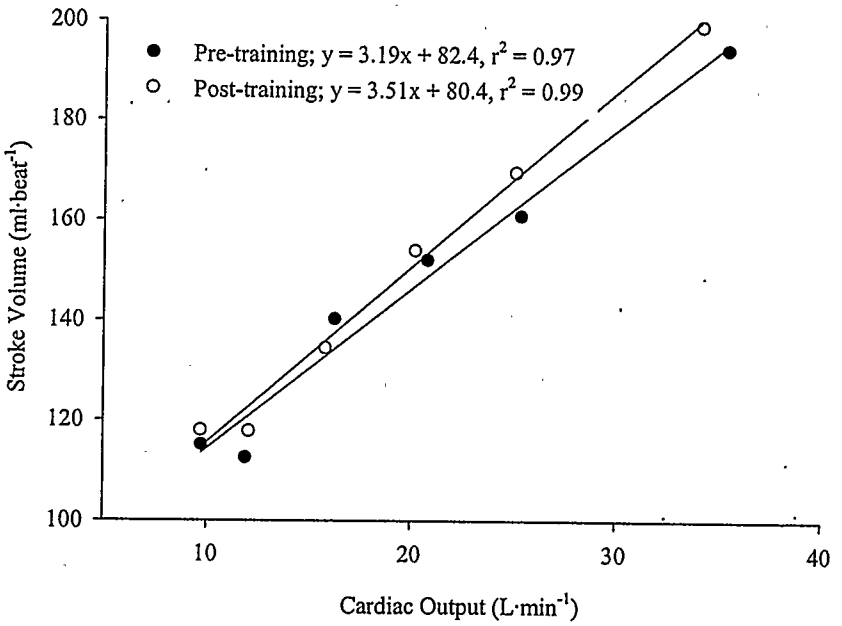

Figure 8.5. The relationship between stroke volume and cardiac output for subject 6 before and after 7 days of training. The regression equations pre- and post-training were used to interpolate the stroke volume at cardiac outputs of 10, 15, 20, 25 and 30 $L \cdot min^{-1}$.

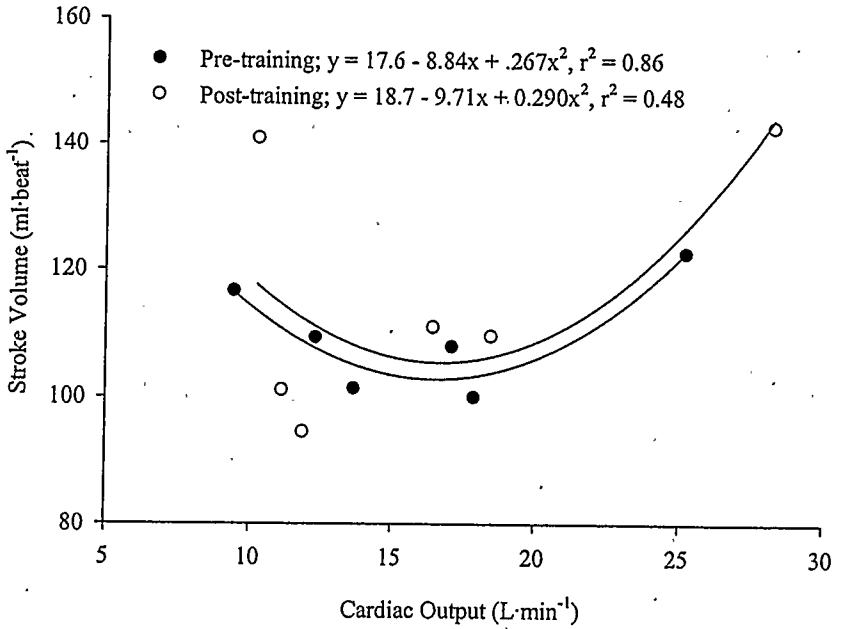

Figure 8.6. The relationship between stroke volume and cardiac output for subject 7 before and after 7 days of training. The regression equations pre- and post-training were used to interpolate the stroke volume at cardiac outputs of 10, 15, 20, 25 and 30 $L \cdot min^{-1}$.

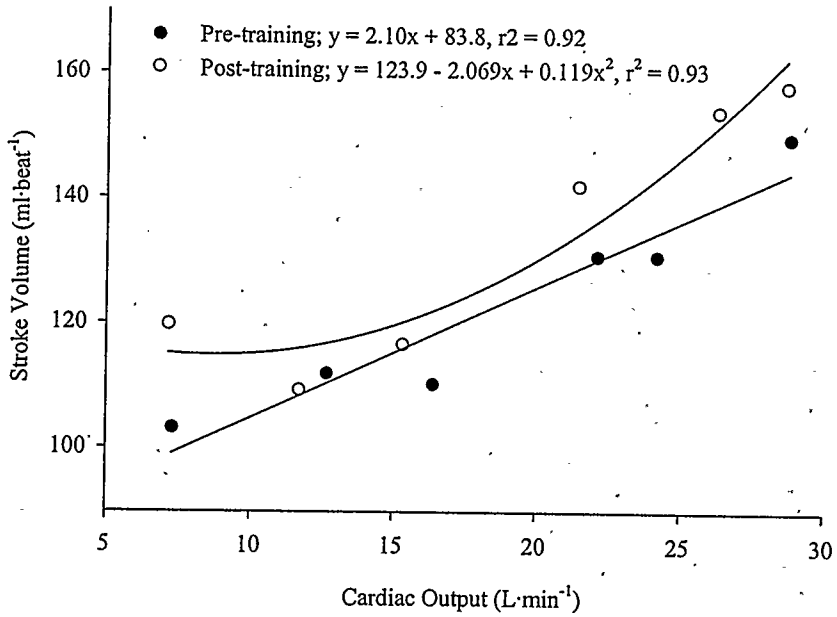

Figure 8.7. The relationship between stroke volume and cardiac output for subject 8 before and after 7 days of training. The regression equations pre- and post-training were used to interpolate the stroke volume at cardiac outputs of 10, 15, 20, 25 and 30 $L \cdot min^{-1}$.

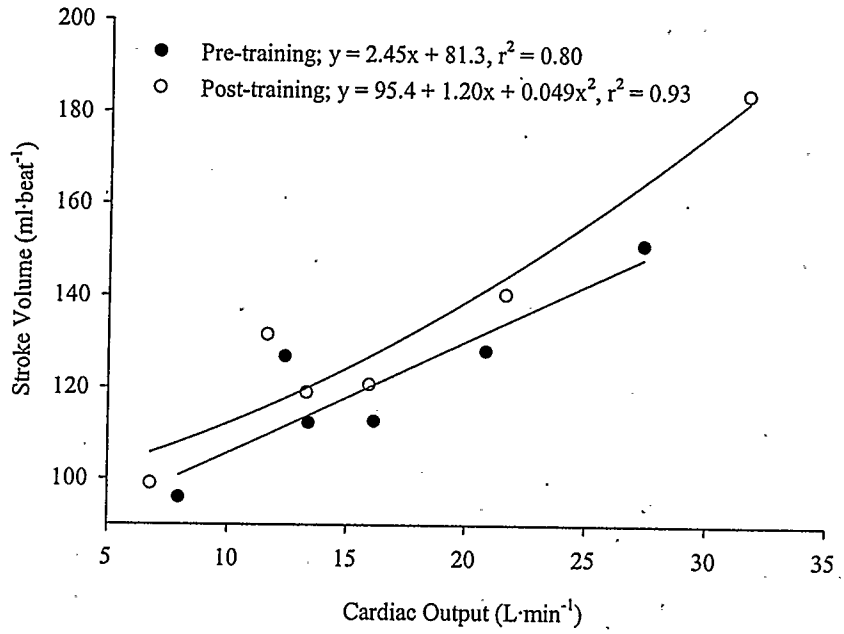

Figure 8.8. The relationship between stroke volume and cardiac output for subject 9 before and after 7 days of training. The regression equations pre- and post-training were used to interpolate the stroke volume at cardiac outputs of 10, 15, 20, 25 and 30 $L \cdot min^{-1}$.

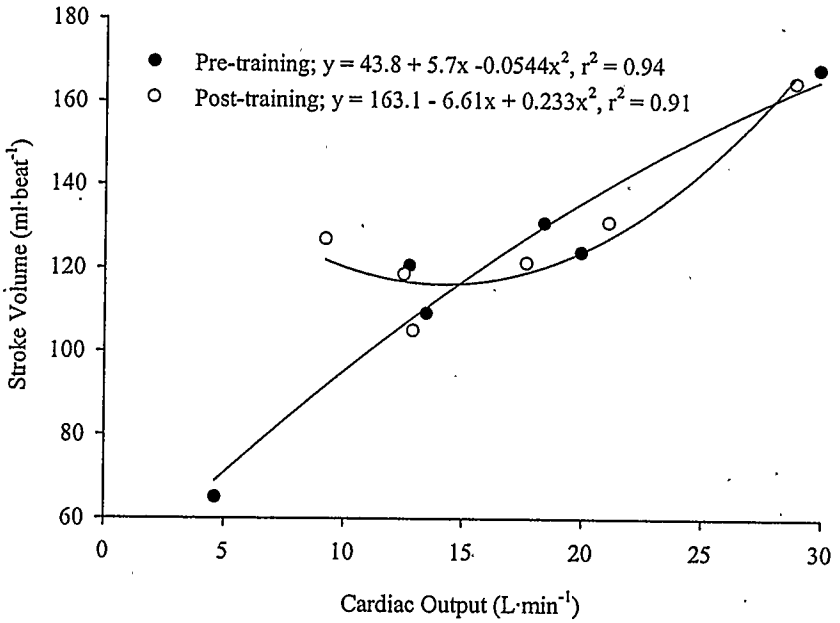

Figure 8.9. The relationship between stroke volume and cardiac output for subject 10 before and after 7 days of training. The regression equations pre- and post-training were used to interpolate the stroke volume at cardiac outputs of 10, 15, 20, 25 and 30 $L \cdot min^{-1}$.