



2009-12-10

Influence of Cardiac Output on Oxygen Uptake Kinetics

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Influence of Cardiac Output on Oxygen Uptake Kinetics

Crystelle K. Grant

A thesis submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of
Master of Science

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April 2010

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ABSTRACT

Influence of Cardiac Output on Oxygen Uptake Kinetics

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Master of Science

The purpose of this study was to evaluate increased cardiac output (\dot{Q}) on oxygen kinetics at exercise intensities above and below the lactate threshold (LT). We hypothesized the increase in \dot{Q} using head-out water immersion (HOI) while treadmill running would reduce the rate constant of the fast component and reduce the amplitude of the slow component of oxygen kinetics compared with land treadmill running. Subjects ($n=10$) performed two 6 min exercise bouts at a $\dot{V}O_2$ 15% below and above the LT on a land and underwater treadmill following rest. A single exponential equation [$\dot{V}O_2(t) = \dot{V}O_2(b) + A_1 \cdot (1 - e^{-t/TC_1})$] was used to evaluate $\dot{V}O_2$. The slow component at the end of exercise was estimated by subtracting ($\dot{V}O_2(b) + A_1$) from the $\dot{V}O_2$ plateau. The mean LT for HOI running $1.80 \pm .09 \text{ L} \cdot \text{min}^{-1}$ was significantly lower ($p < 0.05$) than $2.15 \pm 1.03 \text{ L} \cdot \text{min}^{-1}$ while running on the land. The \dot{Q} during HOI exercise below and above the LT ($16.5 \pm 0.6 \text{ L} \cdot \text{min}^{-1}$, $18.0 \pm 1.2 \text{ L} \cdot \text{min}^{-1}$) was significantly higher ($p < 0.05$) than the \dot{Q} during exercise below and above the LT on land ($11.5 \pm 0.8 \text{ L} \cdot \text{min}^{-1}$, $13.0 \pm 0.7 \text{ L} \cdot \text{min}^{-1}$). During HOI exercise below LT time to reach steady-state $\dot{V}O_2$ was delayed ($8 \pm 2 \text{ s}$). Exercise above LT showed similar phase one time constants for all exercise trials. The amplitude of the slow component was not influenced by HOI. As such, the increase in \dot{Q} during HOI exercise did not hastening $\dot{V}O_2$ uptake kinetics.

Keywords: oxygen uptake kinetics, head-out water immersion, hemodynamics

ACKNOWLEDGEMENTS

I would like to express my appreciation to Dr. Allen C. Parcell and Dr. Pat R. Vehrs for their help and participation as my committee. I would like to acknowledge my peer and dear friend Stephanie J. Zobell for all the push she gave me to keep moving forward as well as the memorable experiences we shared together in the process. I'm especially grateful to Dr. Gary W. Mack, my committee chair, for his continual patience, help, and support.

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Influence of Cardiac Output on Oxygen Uptake Kinetics

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ABSTRACT

The purpose of this study was to evaluate increased cardiac output (\dot{Q}) on oxygen kinetics at exercise intensities above and below the lactate threshold (LT). We hypothesized the increase in \dot{Q} using head-out water immersion (HOI) while treadmill running would reduce the rate constant of the fast component and reduce the amplitude of the slow component of oxygen kinetics compared with land treadmill running. Subjects ($n=10$) performed two 6 min exercise bouts at a $\dot{V}O_2$ 15% below and above the LT on a land and underwater treadmill following rest. A single exponential equation [$\dot{V}O_2(t) = \dot{V}O_2(b) + A_1 \cdot (1 - e^{-t/TC_1})$] was used to evaluate $\dot{V}O_2$. The slow component at the end of exercise was estimated by subtracting ($\dot{V}O_2(b) + A_1$) from the $\dot{V}O_2$ plateau. The mean LT for HOI running $1.80 \pm .09 \text{ L} \cdot \text{min}^{-1}$ was significantly lower ($p < 0.05$) than $2.15 \pm 1.03 \text{ L} \cdot \text{min}^{-1}$ while running on the land. The \dot{Q} during HOI exercise below and above the LT ($16.5 \pm 0.6 \text{ L} \cdot \text{min}^{-1}$, $18.0 \pm 1.2 \text{ L} \cdot \text{min}^{-1}$) was significantly higher ($p < 0.05$) than the \dot{Q} during exercise below and above the LT on land ($11.5 \pm 0.8 \text{ L} \cdot \text{min}^{-1}$, $13.0 \pm 0.7 \text{ L} \cdot \text{min}^{-1}$). During HOI exercise below LT time to reach steady-state $\dot{V}O_2$ was delayed ($8 \pm 2 \text{ s}$). Exercise above LT showed similar phase one time constants for all exercise trials. The amplitude of the slow component was not influenced by HOI. As such, the increase in \dot{Q} during HOI exercise did not hastening $\dot{V}O_2$ uptake kinetics.

Keywords: oxygen uptake kinetics, head-out water immersion, hemodynamics

INTRODUCTION

Oxygen uptake kinetics describes the time course in which oxygen uptake ($\dot{V}O_2$) increases when transitioning from one steady-state to another. At the onset of light- to moderate-intensity exercise, $\dot{V}O_2$ rapidly increases from its resting value to a higher steady-state value which matches the increased oxygen demands of working muscle. It has been well established that there is a linear relationship between $\dot{V}O_2$ and power output (14). Thus, at any given power output, within the range of moderate- or low-intensity exercise, a steady-state $\dot{V}O_2$ can be predicted. However, the dynamics of the relationship between $\dot{V}O_2$ and power output changes at high intensity exercise.

At high intensity exercise, defined as exercise intensities above the lactate threshold (LT), $\dot{V}O_2$ is no longer predictable by power output in the same way that it is for moderate intensity exercise. The initial rapid rise in $\dot{V}O_2$ at the onset of exercise is followed by a subsequent slow continued rise in $\dot{V}O_2$ rather than achieving steady-state. As such, the $\dot{V}O_2$ during the time period when steady-state would normally occur exceeds the values predicted from the power output (1, 14). The initial rapid rise in $\dot{V}O_2$ is termed the fast component of oxygen uptake kinetics, while the subsequent slow rise above steady-state values during high intensity exercise is called the slow component of oxygen uptake. The rate at which $\dot{V}O_2$ increases during the fast component of oxygen uptake, is described quantitatively by a rate constant usually measured in seconds. Tolerance to exercise at intensities above the LT is limited, in part, by the slow component of oxygen kinetics. The cause for this additional oxygen cost has not yet been identified but several factors are postulated as contributors.

Poole et al. (12) categorized potential contributing factors to the slow component of oxygen uptake kinetics into peripheral factors (within the exercising limbs) and central factors (rest of the body). Possible peripheral factors include such things as lactate and H^+ accumulation, muscle blood flow, recruitment of lower-efficiency fast-twitch fibers, muscle temperature, and muscle mass recruited. Potential central factors may include the increased oxygen cost associated with intensified respiratory muscle activity, cardiac, and accessory muscle work, increased body core temperature, and liver metabolism.

To determine the relative contributions of peripheral and central factors Poole et al. (12) made simultaneous measurements of pulmonary and muscle $\dot{V}O_2$ from minute 3 to fatigue during severe exercise. Due to the high correlation of the two measurements, he concluded that leg $\dot{V}O_2$ accounted for 86% of the rise in pulmonary $\dot{V}O_2$. A subsequent and similar study by Grassi et al. (5) measuring leg and pulmonary $\dot{V}O_2$ in the early phase of transition from rest to exercise (first 10 - 15 s) found no significant differences in oxygen kinetics for either leg or pulmonary $\dot{V}O_2$. These data indicate that whole body pulmonary oxygen uptake kinetics closely reflect muscle oxygen consumption and therefore most of the increased oxygen cost associated with work above the LT is attributable to peripheral factors within the exercising muscle. However, we suspect that some peripheral factors may be linked with limitations in central factors. For example, below optimal oxygen delivery to skeletal muscle could contribute to lactic acid accumulation and the early onset of fatigue. Therefore, one cannot exclude the role of central factors in mediating the slow component of oxygen uptake kinetics.

Hughson et al. (8) compared the kinetics of $\dot{V}O_2$ in upright, supine, and supine exercise with the application of lower body negative pressure (LBNP). They were able to establish a drop in cardiac output (\dot{Q}) (a central factor) with upright exercise and look at the effects on muscle

blood flow (a peripheral factor). Exercise in the supine posture slowed the $\dot{V}O_2$ kinetic response because of a decrease in skeletal muscle blood flow despite an increase in \dot{Q} . However, supine exercise with the application of LBNP restored the $\dot{V}O_2$ kinetic response seen with upright exercise. Lower body negative pressure counteracts the effects of exercise in a supine posture by increasing muscle blood flow. These data suggest that oxygen transport to skeletal muscle may be a limiting factor in oxygen uptake kinetics during submaximal exercise. One way to further examine the relationship between oxygen delivery and oxygen uptake kinetics is to manipulate central hemodynamics during exercise.

Central hemodynamics can be manipulated through the use of head-out water immersion (HOI). One of the most notable changes observed with water immersion is a significant increase in stroke volume (SV) (11, 15). The increase in SV is related to an increase in left ventricular end diastolic volume (3, 13). With slightly lower or no changes observed in the heart rate response at rest and during moderate intensity exercise (3, 4, 11, 13, 15) when compared with land trials, the increased SV is primarily responsible for the overall increase in \dot{Q} . Yun et al. (15) showed an approximate 50% increase in \dot{Q} with HOI cycling. Park et al. (11) suggested the higher \dot{Q} during water exercise compared to exercising on land at the same workload leads to a hyperfusion of the peripheral tissues at rest and during exercise. This hyperfusion may provide better oxygen delivery to working skeletal muscle and affect the oxygen kinetics associated with treadmill running.

We hypothesized that the increase in \dot{Q} during treadmill running in water would reduce the rate constant of the fast component of oxygen uptake kinetics. In addition, we predicted that the increase in \dot{Q} would also reduce the magnitude of the slow component of oxygen kinetics

associated with exercise above the LT. Therefore the purpose of this study was to evaluate the influence of increased \dot{Q} on oxygen kinetics at exercise intensities above and below the LT during land and HOI treadmill running. Exercise \dot{Q} during land treadmill running was compared to exercise \dot{Q} during HOI treadmill running.

METHODS

Subjects. Ten college-aged, active males with a mean age of 23.8 ± 0.36 years, body mass (BM) of 83.8 ± 3.97 Kg, height of 182.8 ± 1.54 cm, and peak aerobic capacity ($\dot{V}O_{2\text{peak}}$) measured during treadmill running on land of 54.1 ± 2 ml $O_2 \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$ BM participated in this study. This study was approved by the University Institutional Review Board and all subjects provided written informed consent prior to participating in this study.

Experimental Design. Each subject completed five exercise sessions. The first session was used to determine peak aerobic capacity ($\dot{V}O_{2\text{peak}}$), the next two exercise sessions were used to determine the LT during running on land and during HOI. Finally, two exercise sessions were used to evaluate oxygen uptake kinetics during exercise on land or during HOI, using two exercise intensities, 15% below LT and 15% above LT.

$\dot{V}O_{2\text{peak}}$ was determined for each subject using a graded exercise test on a land treadmill with oxygen consumption averaged every 15 s using a ParvoMedics TrueOne (ParVo Medics, Inc., Sandy, UT) metabolic cart. The graded exercise test consisted of a 5-min warm-up at 0% grade during which time the subject self-selected a treadmill speed that approximated their normal running velocity. Then the grade was increased 2.5% every 2 min until the subject

reached volitional fatigue. A minimum of one week was allowed between the determination of $\dot{V}O_{2peak}$ and subsequent testing.

All subsequent exercise tests were spaced a minimum of three days apart. LT determination was performed in a randomized cross-over design. Each subject's LT was determined while running at 0% grade on a treadmill on land and in water. HOI treadmill exercise occurred in an average water temperature of $30.8 \pm .2^{\circ}\text{C}$ with the water level adjusted to the level of the xiphoid process (± 5 cm). For each LT exercise test, an 18-gauge catheter was placed in a large vein of the subject's forearm. The subject was fitted with a heart rate monitor and a headpiece holding a one-way breathing valve to allow measurement of heart rate and the measurement of oxygen consumption, averaged every 15 s, by the metabolic cart, respectively. The subject then stood on the treadmill (in air and during HOI) for 30 min to allow equilibration of body water compartments before a resting blood sample was collected. The LT protocol started by walking at 3.5 mph at 0% grade for 4 min with a blood sample drawn during the last minute of the stage. Subsequent running stages were 3 min long with blood samples drawn during the last minute of each stage. The initial running speed was chosen to elicit oxygen consumption approximately equal to 40% of their previously determined land $\dot{V}O_{2peak}$. Thereafter the treadmill speed was increased by 0.5 mph every 3 min until the subject met or exceeded 90% of their measured land $\dot{V}O_{2peak}$.

Blood samples (5 ml) were immediately placed in pre-cooled EDTA-vacutainers and placed on ice. The plasma was immediately separated from the red cells and analyzed for lactate concentrations using YSI 2300 lactate analyzer (Yellow Springs Instruments Co. Inc., Yellow Springs, OH). During incremental exercise, an abrupt transition occurs in the rate of increase of

blood lactate with increasing $\dot{V}O_2$. The transition point, identified as the LT, was determined using the semi-log plot of plasma lactate and $\dot{V}O_2$ (2).

Oxygen kinetics was also determined in a random crossover design. Subjects were instrumented with a heart rate monitor, a headpiece assembly for monitoring oxygen uptake by the metabolic cart, and cardiac impedance electrodes. The metabolic cart was programmed to collect metabolic and ventilatory parameters on a breath-by-breath basis (described as pseudo-breath-by-breath by the manufacturer). Cardiac impedance tapes were placed around the neck and chest to obtain measures of SV during exercise. Two tapes were placed approximately one inch apart around the circumference of the neck. An additional two tapes were placed around the circumference of the thorax, one superior to the xiphoid process and the other three to four inches inferior to the xiphoid process. Subjects performed two 6-min exercise bouts on the same day on either the land treadmill or the underwater treadmill. For one exercise bout the treadmill speed was set to elicit $\dot{V}O_2$ that was matching 15% below the subject's LT. For the other exercise bout the treadmill speed was set to elicit $\dot{V}O_2$ that was 15% above the LT. Treadmill speed was determined from the subject's previous LT tests on land or during HOI.

Prior to the exercise bout subject warmed up with 5 min of light jogging and then rested in a standing position for 10 min. Each trial began with oxygen uptake and cardiovascular parameters measured during 2 min of standing rest with feet astride the moving treadmill belt and hands holding the treadmill guard rails. At the start of the exercise test, subjects supported their body mass with their hands on the guard rails until their leg speed matched the treadmill belt speed (approximately 2-3 strides) after which they let go of the guard rails and began running. Subjects ran for 6 min and at the end of the 6 min the subject dismounted the treadmill and cardiac output was determined during the first 5-10 s immediately following exercise. The first

3-4 useable cardiac cycles immediately following exercise were used to estimate peak \dot{Q} during exercise. The measurement of cardiac output was followed by a 3-min active recovery and then 1 hour of rest before performing their second exercise bout.

Oxygen kinetics data analysis. For each exercise test, breath-by-breath oxygen uptake data were first filtered to remove spurious data points, interpolated to give values second by second and then time aligned to the start of exercise. Nonlinear regression techniques were used to fit the $\dot{V}O_2$ data during the 6-min exercise bout excluding the first 20 s of data. The sum of squared error was minimized and was used as the criterion for convergence using Prism software (GraphPad Software Inc.). The initial mathematical model consisted of one (moderate exercise) or two (heavy exercise) exponential terms, each representing a specific phase of the response (1). The first exponential term associated with the onset of exercise was excluded because curve fitting began at 20 s

$$\begin{aligned} \dot{V}O_2(t) = \dot{V}O_2(b) + A_1 \cdot (1 - e^{-t/TC_1}) & \quad \text{phase 1 : primary component} \\ + A_2 \cdot (1 - e^{-(t-TD_2)/TC_2}) & \quad \text{phase 2 : slow component} \end{aligned}$$

where t is time and $\dot{V}O_2(t)$ is the $\dot{V}O_2$ value at any given time; $\dot{V}O_2(b)$ is the resting baseline value; A_1 , and A_2 are the asymptotic amplitudes for the two exponential terms: primary, and slow components, respectively; TC_1 , and TC_2 are the time constants of the primary, and slow components, respectively; and TD_2 is the time delay of the slow component. Only 60% of the above LT trials could be curve fit by a double exponential model. Therefore, all exercise sessions were curve fit using a single exponential model and the slow component at the end of exercise was estimated by subtracting A_1 from the plateau in oxygen uptake ($\dot{V}O_2$ plateau) during the last 30 s of data collection.

Corresponding changes in cardiac impedance and EKG measurements of heart rate were used to calculate hemodynamic parameters. These parameters are calculated using the equation

$$SV = \frac{\tilde{n} \cdot L^2 \cdot T \cdot dZ/dt \text{ min}}{Z_0^2}$$

where SV = ventricular stroke volume (ml), ρ (blood resistivity) = 135 ohm cm, L = the mean distance between the two inner pieces of impedance tape, Z_0 = the mean impedance between the two inner electrodes in ohms, (dZ/dt)min = the minimum value of dZ/dt occurring during the cardiac cycle in ohms per second, and T = the ventricular ejection time in seconds as obtained from the dZ/dt waveform. Cardiac output was calculated by multiplying SV by HR.

Statistical Analysis. The experimental design is a simple balanced ANOVA for repeated measures with main effects of treatment (land versus air) and exercise intensity (above and below the LT) as repeated measures. This design allows each subject to act as their own control. Major variables measured and used for analysis include steady-state $\dot{V}O_2$, heart rate, lactate concentration, LT expressed in $\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, SV, \dot{Q} , and rate constants for oxygen uptake kinetics. The statistical analysis was performed using SAS general linear model analysis with significance set at a p value <0.05.

RESULTS

Lactate threshold. The mean LT for HOI running ($1.80 \pm .09 \text{ L} \cdot \text{min}^{-1}$) was significantly lower ($p < 0.05$) than the ($2.15 \pm 1.03 \text{ L} \cdot \text{min}^{-1}$) determined while running on the land treadmill. Figure 1 plots the mean plasma lactate concentration as a function of mean $\dot{V}O_2$ values and illustrates the leftward shift in the LT with running on the underwater treadmill. Due to this

leftward shift in the LT, the steady-state $\dot{V}O_2$ at 15% above the LT was significantly lower ($p < 0.05$) during HOI running ($2.21 \pm .14 \text{ L} \cdot \text{min}^{-1}$) than the $\dot{V}O_2$ at 15% above the LT during land treadmill running ($2.67 \pm .14 \text{ L} \cdot \text{min}^{-1}$). The steady-state $\dot{V}O_2$ values at exercise intensities 15% below the LT were significantly higher ($p < 0.05$) on land ($1.95 \pm 0.14 \text{ L} \cdot \text{min}^{-1}$) than during HOI running ($1.65 \pm 0.11 \text{ L} \cdot \text{min}^{-1}$) as well.

Hemodynamic parameters. HOI running resulted in Z_0 values during rest and exercise that were significantly lower than measurements made during land trials (Fig. 2). SV was elevated ($p < 0.05$) during HOI at rest ($113.7 \text{ ml} \pm 8.0 \text{ ml}$) compared to land ($80.1 \text{ ml} \pm 6.0 \text{ ml}$). SV remained elevated during HOI running at both 15% above and below the LT compared to land trials. Additionally, SV during exercise on land did not differ significantly from the resting value. However, SV during HOI exercise was higher during exercise than at rest ($p < 0.05$, Fig. 2). Heart rate was slightly lower during HOI trials when compared with land.

Cardiac Output. The \dot{Q} during HOI exercise below ($16.5 \pm 0.6 \text{ L} \cdot \text{min}^{-1}$) and above the LT ($18.0 \pm 1.2 \text{ L} \cdot \text{min}^{-1}$) was significantly higher ($p < 0.05$) than the \dot{Q} during exercise below ($11.5 \pm 0.8 \text{ L} \cdot \text{min}^{-1}$) and above the LT on land ($13.0 \pm 0.7 \text{ L} \cdot \text{min}^{-1}$). The steady state $\dot{V}O_2$ values and the corresponding \dot{Q} values for all ten subjects at exercise intensities below and above the LT as well as at rest were pooled and graphed in Figure 3. Cardiac output rose during exercise in a linear fashion with oxygen uptake as shown in Figure 3. However, the rate of increase in \dot{Q} per unit increase in $\dot{V}O_2$ was greater during HOI than during land exercise. Therefore, \dot{Q} increased with HOI at any given $\dot{V}O_2$ compared with \dot{Q} values on land at the same $\dot{V}O_2$.

Oxygen uptake kinetics. Figure 4 shows the mean $\dot{V}O_2$ versus time for the four exercise conditions. During HOI exercise below the LT, time to reach $\dot{V}O_2$ plateau was delayed by 8 s despite the increase in \dot{Q} (Table 1). However, during exercise above LT we noted similar phase-one time constants for land (34 ± 2 s) and HOI (33 ± 3 s) exercise trials. The magnitude of the slow component (A_2) during exercise above LT was not influenced by HOI.

DISCUSSION

The main finding of this study was that HOI running increased \dot{Q} at any given $\dot{V}O_2$ but did not quicken the oxygen uptake kinetics. In fact, at exercise below LT oxygen uptake kinetics were slowed during HOI running, suggesting that the increase in \dot{Q} may not have been directed toward the active skeletal muscle. Additionally, HOI running caused a leftward shift in the LT. This resulted in subjects running at the same percentage of their LT but different $\dot{V}O_2$ values when running on a land treadmill compared to HOI running. Despite running at lower $\dot{V}O_2$ values during HOI, similar or slightly slower $\dot{V}O_2$ kinetics were observed. Furthermore, the difference in LT may suggest altered blood flow distribution or motor unit recruitment with HOI running compared to running on a land treadmill.

A likely explanation for the slowed $\dot{V}O_2$ kinetics below the LT and lack of change in $\dot{V}O_2$ kinetics above the LT with HOI is that the increased \dot{Q} was not directed to active skeletal muscle. We cannot conclude with certainty where the distribution of the increased \dot{Q} went, but it is possible that at least a portion of it was directed to respiratory and cardiac muscles. In a study conducted by Hajduczuk et al. (6) studying regional blood flow responses to HOI in intact and cardiac-denervated dogs, 20 min of HOI resulted in significant increases in blood flow to the

intercostal muscles, diaphragm, cardiac muscle, as well as several abdominal organs. The hydrostatic pressure outside the thorax is thought to increase mechanical loading of the chest wall leading to a higher metabolic requirement of the respiratory muscles (6). This mechanism is thought to explain the hyperemia observed in the respiratory muscles. Similarly, increases in cardiac work due to increased preload and after load are thought to account for the increased blood flow to cardiac muscle (6). More research is needed to determine regional blood flow responses to HOI during exercise.

Changes in regional blood flow distribution during HOI running may stem from changes in the sympathetic nervous system response to HOI. Hayashi and Yoshida (7) compared oxygen uptake kinetics during sitting arm-cranking exercise at 80% of the ventilatory threshold on land and immersed in water. No significant differences in baseline, gain, or steady-state $\dot{V}O_2$ values were found. However Hayashi and Yoshida actually report a greater $\dot{V}O_2$ mean response time (sum of τ and TD) with water immersion than on land. This is consistent with our results showing a larger TC_1 (Table 1) or slower oxygen kinetics with HOI below the LT. Hayashi and Yoshida propose suppressed sympathetic nervous system activity as well as increased oxygen stores induced by HOI to account in part for their observations. They reasoned suppressed sympathetic nervous system activity would consequently depress the amount of vasoconstriction in nonworking muscle thereby reducing blood distribution to working muscle despite the increased \dot{Q} . A study by Connelly et al. (4) supports the notion that water immersion may alter the sympathetic nervous system response. Plasma norepinephrine concentrations were reduced at 80% and 100% peak $\dot{V}O_2$ with HOI during upright leg cycle exercise when compared with land. Epinephrine concentration was also lower at peak $\dot{V}O_2$ with HOI compared with land.

Thus a decreased sympathetic response during HOI may also contribute to a decreased blood flow to working muscle despite an increase in \dot{Q} .

Further support that the increased \dot{Q} was not directed to active skeletal muscle comes from the shift in LT. The leftward shift in LT may be a result of altered blood flow distribution or motor unit recruitment. Although $\dot{V}O_2$ responses are similar on land and in water at a given treadmill speed, studies show different muscle activation patterns when running on land versus water. Kaneda et al. (9) noted a significant decrease in the electromyographic activity of the soleus and gastrocnemius muscles during water walking and deep water running compared with land walking. Greater hip extension with water walking has also been noted (9, 10). These changes could cause a larger recruitment of fast twitch fibers accounting for the faster lactate accumulation with HOI.

Limitations. An unexpected observation during HOI running was the shift in the LT. Subjects ran at fixed percentages of their LT rather than fixed treadmill speeds or $\dot{V}O_2$ values. This resulted in subjects running at different speeds and $\dot{V}O_2$ values on land than in the water. Specifically, subjects ran at a lower $\dot{V}O_2$ during HOI but lactate concentrations were similar to land trials. Yet despite an increase in \dot{Q} and a lower $\dot{V}O_2$, oxygen kinetics were unchanged suggesting the increased \dot{Q} was not shunted to active skeletal muscle. A possible solution to this problem may be to run subjects at a fixed speed and $\dot{V}O_2$ for both land and HOI trials which falls below either LT value. Similarly a speed and $\dot{V}O_2$ could be chosen which falls above both the LT on land and the LT with HOI. However this would result in subjects running at different percentages of their specific HOI and land LT values.

In conclusion HOI running was effective in increasing \dot{Q} at any given $\dot{V}O_2$ but did not hasten oxygen uptake kinetics as described by the magnitude of the slow component or TC_1 . Contrary to our hypothesis, oxygen kinetics were actually slower below the LT with HOI. The combination of altered muscle recruitment patterns, changes in regional blood flow distribution, and decreased sympathetic responses provide possible explanations regarding the oxygen kinetics and LT shift with HOI .

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Table 1. *Oxygen Uptake Kinetics Parameter Estimates*

	BELOW LT		ABOVE LT	
	LAND	WATER	LAND	WATER
$\dot{V}O_2$				
baseline	0.38 ± 0.03	0.37 ± 0.03	0.41 ± 0.06	0.4 ± 0.06
A1	1.49 ± 0.10	1.29 ± 0.11	2.18 ± 0.16	1.81 ± 0.12*
TC1	31 ± 1	39 ± 2*	34 ± 2	33 ± 2
$\dot{V}O_2$ plateau	1.93 ± 0.13	1.66 ± 0.12*	2.67 ± 0.15	2.25 ± 0.13*
A2 est	----	----	0.09 ± 0.03	0.04 ± 0.03

Values represent Mean ± 1 SEM for 10 subjects. $\dot{V}O_2$ baseline, $\dot{V}O_2$ at baseline; A₁, magnitude of rise in oxygen uptake during the initial fast component; TC₁, time constant required to reach A₁; $\dot{V}O_2$ plateau, mean $\dot{V}O_2$ of last 30 s of data; A₂ est, estimated magnitude of the slow rise in oxygen uptake during exercise above lactate threshold. * $p < 0.05$ different from LAND

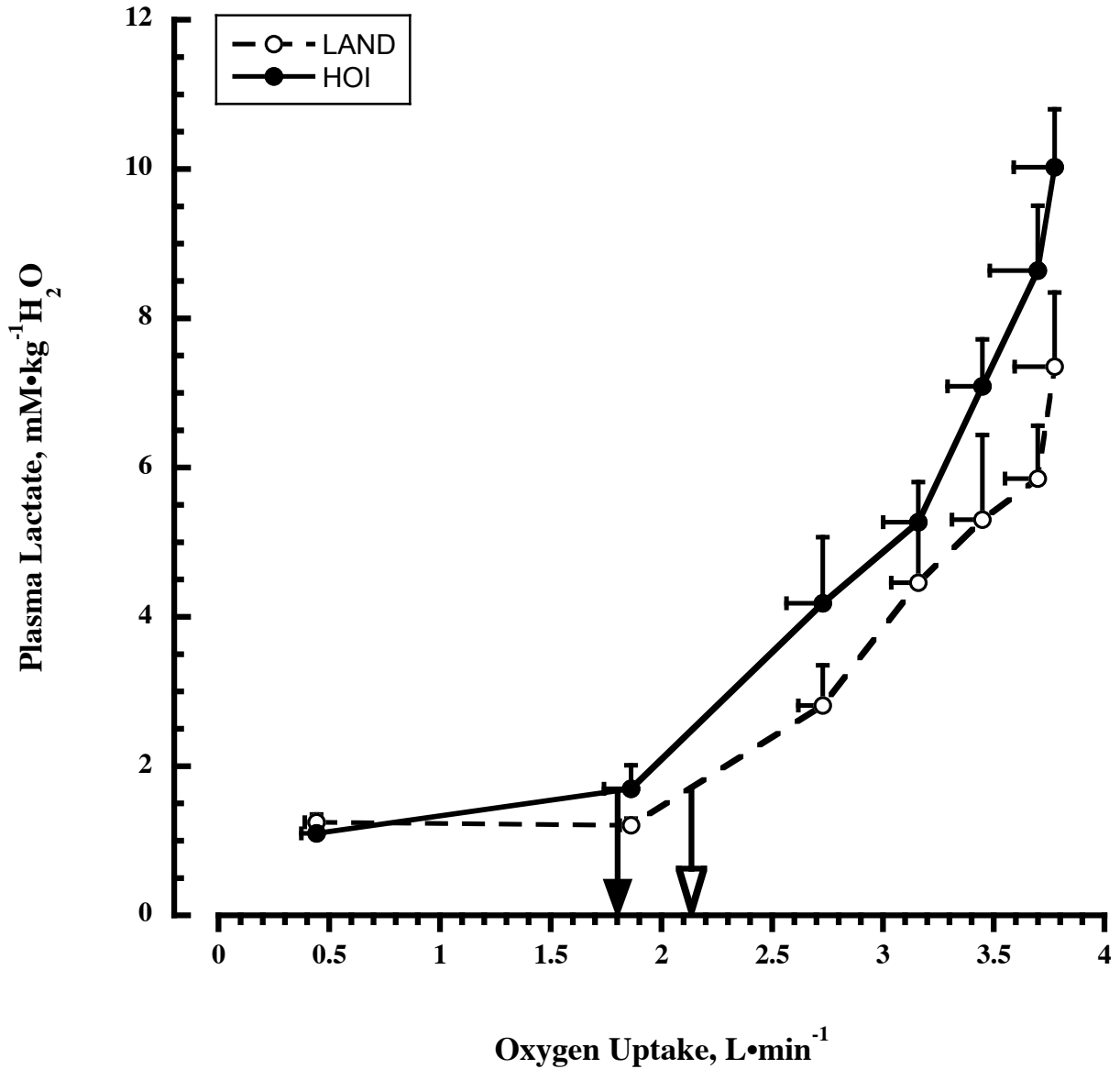


Fig. 1. Mean plasma lactate concentration as a function of average energy cost of walking (3.5 mph) and running on a treadmill on land and underwater. Values represent Mean \pm 1 SEM. $n = 11$ for 0 to 6.0 mph, $n = 10$ for 6.5 mph, $n = 8$ for 7.0 mph, and $n = 7$ for 7.5 mph. Arrows represent average lactate threshold for each treatment group.

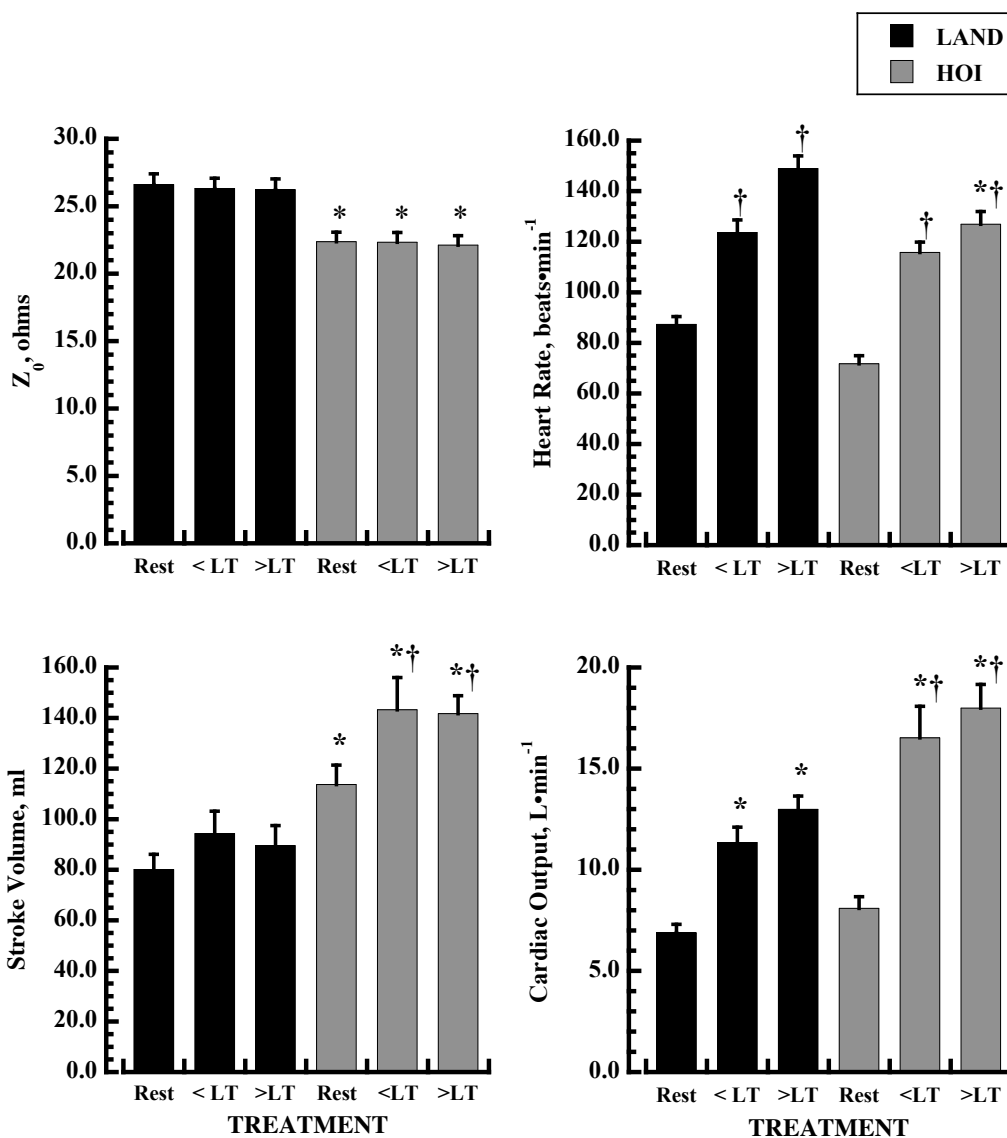


Fig. 2. Mean values of thoracic impedance (Z_0 , upper left), heart rate (HR, upper right), stroke volume (SV, lower left), and cardiac output (Q, lower right) during treadmill running above and below the lactae threshold (LT) on land and with head-out water immersion(HOI). Values represent Mean \pm 1 SEM. $n = 10$ LAND = land at rest, HOI = head-out water immersion at rest, < LT= exercise at 15% below LT, > LT = exercise at 15% above LT. * $p < 0.05$ water different from land. † $p < 0.05$ different from land or HOI at rest.

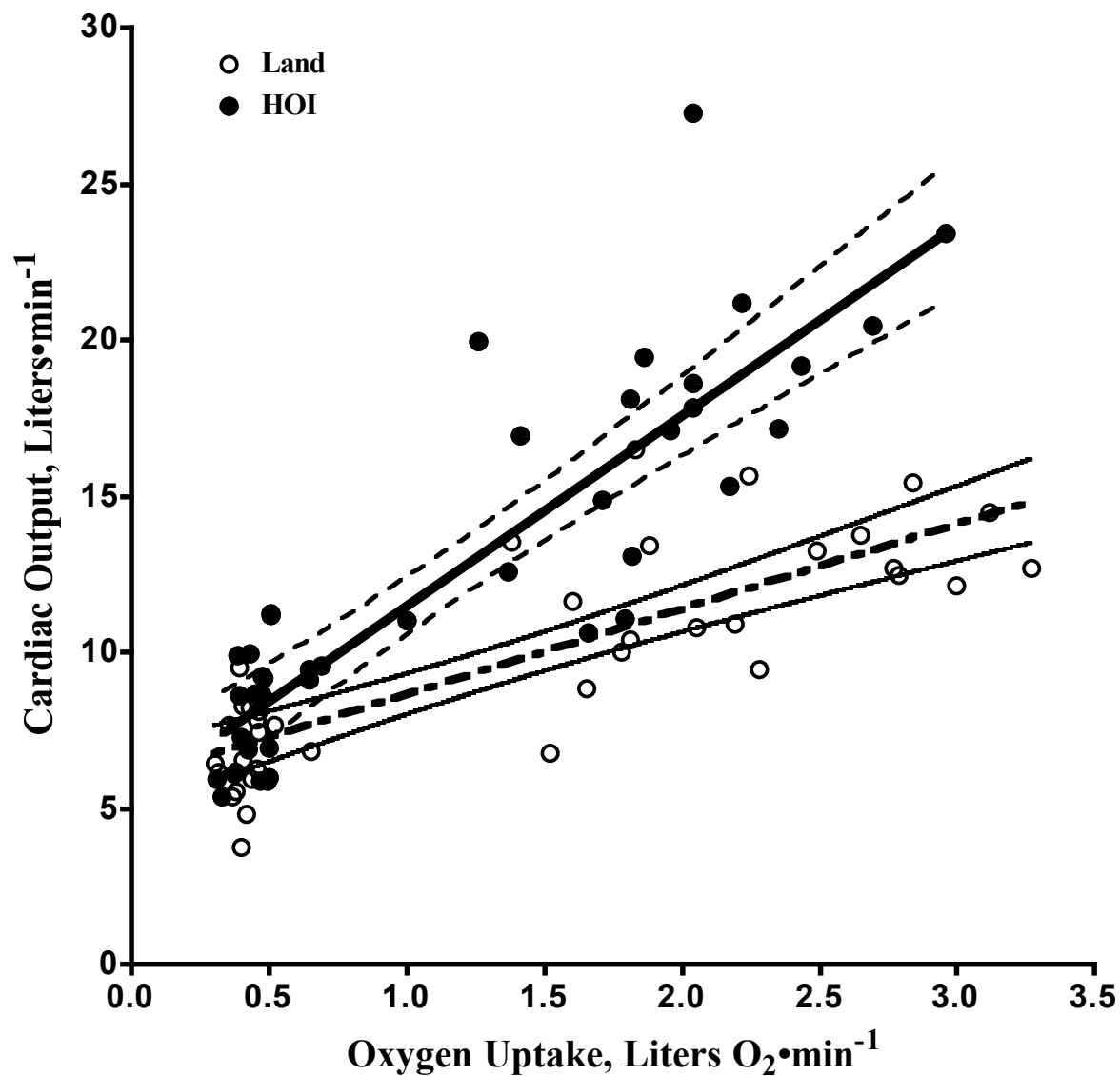


Fig. 3. The relationship between cardiac output ($L \cdot \text{min}^{-1}$) and oxygen uptake ($L \cdot \text{min}^{-1}$) during treadmill running above and below the LT on land and with head-out water immersion. Values represent individual data from each subject \pm 95% confidence intervals.

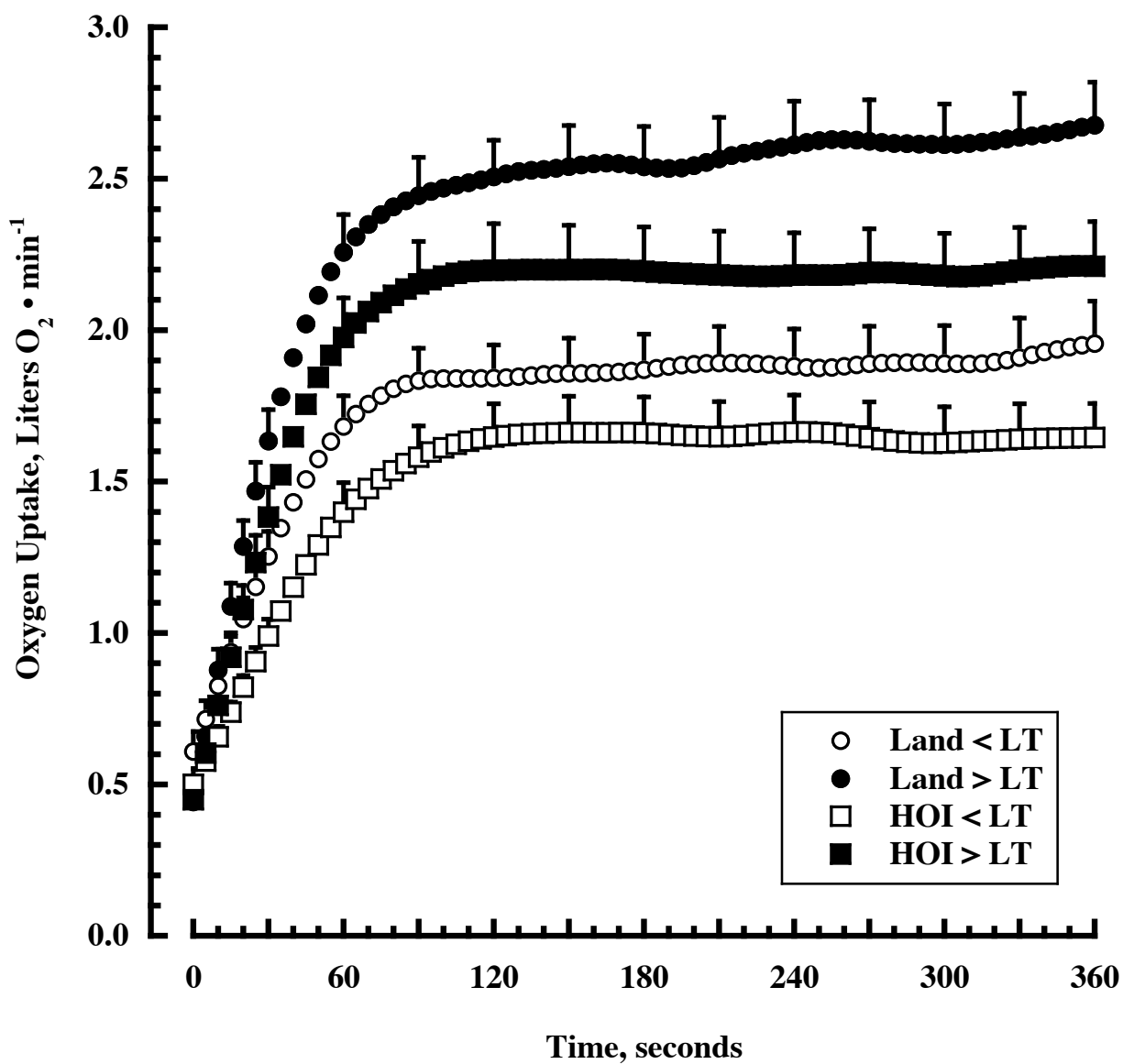


Fig. 4. Mean $\dot{V}O_2$ values as a function of time for the four conditions below and above the lactate threshold (LT) on land and during head-out immersion (HOI). Values represent Mean ± 1 SEM. $n = 10$. Error bars represented in only one direction for clarity of graph.

Appendix A

Prospectus

Chapter 1

Introduction

The metabolic cost of exercise can be estimated from measuring the rate of whole body oxygen consumption ($\dot{V}O_2$) which closely approximates cellular respiration. McCreary et al. (14) tracked changes in intramuscular phosphocreatine (PCr) and phosphate (Pi) using ^{31}P -nuclear magnetic resonance spectroscopy during transients from rest to moderate intensity exercise. The time constant for the on-transient response for PCr averaged 47 seconds while the time constant for oxygen consumption averaged 45 sec. The similarity in the kinetics of PCr and oxygen consumption supports the hypothesis that whole body pulmonary oxygen uptake kinetics accurately reflects muscle adenosine triphosphate (ATP) kinetics and presumably muscle oxygen consumption.

During incremental aerobic exercise, oxygen consumption increases in proportion to the intensity of exercise until a maximal rate of oxygen consumption ($\dot{V}O_{2\text{max}}$) is reached. During exercise at a light- to moderate-intensity, oxygen consumption rapidly increases at the onset of exercise and then plateaus to a steady state, during which time $\dot{V}O_2$ meets the energy demands of working muscle. The initial rise in oxygen consumption is termed the fast component of oxygen kinetics.

Lactate threshold correlates to the intensity of exercise which elicits a marked increase in the accumulation of blood lactate. Accumulation of blood lactate occurs when lactate production exceeds lactate clearance. When exercising at an intensity above the lactate threshold there is an additional oxygen cost above the expected steady-state value, termed the slow component of oxygen kinetics. The cause for this additional oxygen cost has not been identified but is

important to the endurance athlete because it can limit athletic performance. Because exercise intensities above the lactate threshold elicit an increasing oxygen cost, the athlete becomes limited in the time they can sustain the activity. Many studies suggest the increasing oxygen cost or slow component of oxygen kinetics may be attributable to limitations in oxygen delivery to the working muscle. If limited oxygen delivery does contribute to increased oxygen consumption above the lactate threshold, increased blood perfusion to working muscle may counteract these effects. Increased muscle perfusion may be accomplished through an increased cardiac output.

The capacity to utilize oxygen during exercise is dependent on oxygen delivery to the tissues as well as the ability to extract oxygen from the blood. This relationship is described by the Fick Equation:

$$\dot{V}O_2 = \text{Cardiac Output} \times (C_a - C_{\bar{v}})O_2 \text{ diff}$$

Cardiac output (\dot{Q}) is the amount of blood pumped by the left ventricle expressed in $L \cdot \text{min}^{-1}$.

The arteriovenous oxygen difference is the difference in oxygen content between the arteries and veins expressed in milliliters of oxygen per 100ml of blood. Maximal, \dot{Q} , $(C_a - C_{\bar{v}})O_2 \text{ diff}$, and $\dot{V}O_{2\text{max}}$ can be increased with endurance training.

The capacity to perform endurance exercise is related to one's $\dot{V}O_{2\text{max}}$ and lactate threshold. Lactate threshold is an important marker for training and racing because endurance exercise becomes limited with the accumulation of blood lactate. However, lactate threshold can increase with endurance training. A study evaluating the energy cost of cross country skiers when racing found that subjects maintained an average intensity corresponding to the onset of blood lactate (23). Coyle et al. (8) measured time to fatigue during exercise at 88% of $\dot{V}O_{2\text{max}}$ in

competitive cyclists with similar $\dot{V}O_{2\max}$ values. Subjects were divided into two groups, those having a high lactate threshold (mean 81.5% of $\dot{V}O_{2\max}$), and those having a lower lactate threshold (mean 65.8% of $\dot{V}O_{2\max}$). Time to fatigue was twofold longer in the high lactate threshold group. This data shows the importance of $\dot{V}O_{2\max}$ and lactate threshold in endurance performance and that endurance can vary greatly among athletes with similar $\dot{V}O_{2\max}$ values.

One way to increase cardiac output during exercise is through the use of water immersion. Water treadmills are becoming an increasingly popular form of exercise for injured athletes to maintain the cardiovascular benefits of training. While water running has proved a fairly effective alternative to running on a land treadmill, there are notable differences in the cardiovascular response to exercise in the water. One such difference is an increase in the cardiac output during water treadmill running (26). By using water treadmill running as a mode of exercise, the effects of an increased cardiac output on the slow component of oxygen kinetics can be examined. By better understanding the causes of excess oxygen consumption at high intensity exercise we can identify specific metabolic causes of fatigue and thereby design training that might improve athletic performance.

Problem Statement

The purpose of this study is to evaluate the influence of \dot{Q} on oxygen kinetics at exercise intensities above and below the lactate threshold. Exercise \dot{Q} will be manipulated by altering hydrostatic pressure gradients on the lower extremities using head-out water immersion while treadmill running.

Hypothesis

First, the increase in \dot{Q} during treadmill running in water will reduce rate constant of the fast component of oxygen kinetics. Second, the increase in \dot{Q} will reduce the magnitude of the slow component of oxygen kinetics associated with exercise above the lactate threshold.

Null Hypothesis

The increase in \dot{Q} during treadmill running in water will have no effect on the time it takes to reach steady-state rates of oxygen consumption during exercise above the lactate threshold. There will be no change in the magnitude of the slow component.

Assumptions

The relationship between treadmill speed and $\dot{V}O_2$ will be similar for treadmill running in water and treadmill running on land.

Delimitations

The results are only applicable to the subject population: active male college students.

Limitations

Due to treadmill speed limitations of the underwater treadmill, we will not be able to evaluate individuals with a maximal aerobic capacity of $> 60 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ body mass.

Significance of the Study

Because exercise intensities above the lactate threshold elicit an ever increasing oxygen cost, the athlete becomes limited in the time they can sustain the activity as they approach their $\dot{V}O_{2\text{max}}$. By better understanding the causes of the slow component of oxygen uptake kinetics at high intensity exercise we can identify specific metabolic causes of fatigue and thereby design training programs that might improve athletic performance. Furthermore, water treadmill running is becoming a more popular form of rehabilitation for injured athletes. This

study will provide information about the differences in oxygen kinetics between land treadmill running and underwater treadmill running. This information can help injured athletes using underwater treadmill running better maintain their cardiovascular endurance during the time of their rehabilitation.

Chapter 2

Review of Literature

Oxygen uptake kinetics describes the time course in which oxygen uptake increases when transitioning from one steady state to another. Oxygen kinetics is measured as volume of oxygen consumed per unit time. The most familiar measures of $\dot{V}O_2$ are as an absolute rate in liters per minute (L/min) or as a relative rate measured in milliliters of oxygen per kilogram of body weight per minute ($\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). $\dot{V}O_2$ measurements are most commonly made by the use of a metabolic cart that measures the ratios of oxygen and carbon dioxide content in expired air. The $\dot{V}O_2$ represents the total amount of aerobic metabolism occurring in the body.

At the onset of light to moderate intensity exercise, $\dot{V}O_2$ rapidly increases from its resting value to a higher steady-state value which matches the increased oxygen demands of the body. It has been well established that there is a linear relationship between $\dot{V}O_2$ values and power output (24). Thus, at any given power output, within the range of moderate or low intensity exercise, a steady state $\dot{V}O_2$ can be predicted. Moderate intensity exercise has been defined as work at a power output below the threshold for accumulation of blood lactate (i.e. lactate threshold) (2, 5, 18, 25). A steady state $\dot{V}O_2$ is usually reached within 3-5 minutes of the onset of moderate intensity exercise in healthy individuals (24). However, the dynamics of the relationship between $\dot{V}O_2$ and power output changes at higher exercise intensities.

At high intensity exercise, defined as exercise intensities above the lactate threshold, $\dot{V}O_2$ is no longer predictable by power output in the same way that it is for moderate intensity exercise. The initial rapid rise in $\dot{V}O_2$ at the onset of exercise is followed by a subsequent slow continued rise in $\dot{V}O_2$ rather than achieving steady state. As such, the $\dot{V}O_2$ during the time

period when steady state would normally occur exceeds the values predicted from the power output (3, 24). The initial rapid rise in $\dot{V}O_2$ is termed the fast component of oxygen uptake kinetics, while the additional slow rise above steady-state values during high intensity exercise is called the slow component. Tolerance to exercise at intensities above the lactate threshold is limited, in part, by the slow component of oxygen kinetics. The slow component is thought to represent a drop in muscle mechanical efficiency. Thus, the slow component is of great interest to the endurance athlete who attempts to race at exercise intensities close to their lactate threshold.

Several factors are postulated to contribute to the slow component of pulmonary oxygen uptake. David C. Poole (2) organized potential contributing factors to the slow component of oxygen uptake kinetics into two general categories: peripheral factors (within the exercising limbs) and central factors (rest of the body). Possible peripheral factors include such things as lactate and H^+ accumulation, muscle blood flow, recruitment of lower-efficiency fast-twitch fibers, muscle temperature, and muscle mass recruited. Potential central factors may include the increased oxygen cost associated with intensified respiratory muscle activity, cardiac, and accessory muscle work, increased body core temperature, and liver metabolism.

PERIPHERAL FACTORS

Lactate and H^+ Ion Accumulation

Many studies show a significant correlation between the appearance and relative amplitude of the slow component and the net increase in blood lactate (2, 5, 17). This led to suggestions that the catabolism of lactate as an exercise substrate may increase exercise $\dot{V}O_2$. However, when Carter et al. (5) compared the $\dot{V}O_2$ kinetics of treadmill running and cycle ergometry, similar increases in lactate were seen despite a greater rise in the $\dot{V}O_2$ slow

component during cycling compared with running. This study suggests concomitant increases in $\dot{V}O_2$ and lactate may be coincidental. These observations were confirmed by Barstow et al. (2) who evaluated the influences of muscle fiber type on $\dot{V}O_2$ kinetics. Because type I and type II muscle fibers have different oxidative capacities, lactate production would be expected to correlate with fiber type distribution as well as $\dot{V}O_2$ if the catabolism of lactate was indeed causing an increase in the $\dot{V}O_2$ slow component. Barstow et al. (2) found no such correlation between end-exercise lactate levels and the percentage of type I fibers. Furthermore, direct lactate infusion into working dog muscle did not affect the magnitude of the slow component (16) This suggests the magnitude of the slow component, although correlated, is not driven directly by increases in lactate. However, lactate does cause the release of H^+ ions which can lead to metabolic acidosis.

Metabolic acidosis may consequently affect the oxygen hemoglobin dissociation curve. Grassi et al. (11) measured changes in oxygenated hemoglobin and deoxygenated hemoglobin in the vastus lateralis muscle during incremental exercise. Muscle deoxygenation was significantly correlated with the onset of blood lactate accumulation and attributed to a rightward shift of the oxygen hemoglobin dissociation curve determined by the onset of lactic acidosis.

Increased Muscle Blood Flow

Hughson et al. (12) measured the kinetics of $\dot{V}O_2$ in upright, supine, and supine exercise with the application of lower body negative pressure (LBNP). Exercise in the supine posture slows the $\dot{V}O_2$ kinetic response. However supine exercise with the application of LBNP restores the $\dot{V}O_2$ kinetic response seen with upright exercise. Lower body negative pressure counteracts the effects of exercise in a supine posture by increasing muscle blood flow.

Although the effect of LBNP on the slow component of $\dot{V}O_2$ kinetics was not studied, these data support the hypothesis that oxygen transport to skeletal muscle may be a limiting factor in oxygen uptake kinetics at submaximal exercise. Lower body negative pressure in the supine posture will reduce cardiac output, but results in an increase in muscle blood flow. This suggests muscle blood flow may be more important than cardiac output in determining $\dot{V}O_2$ kinetics. However, increasing cardiac output in an upright posture would likely contribute to an increase in muscle blood flow.

Increased Muscle Temperature

Increased muscle temperature has been hypothesized to speed $\dot{V}O_2$ kinetics in at least two ways: 1) it may increase the rate of the limiting reactions associated with oxidative phosphorylation, and/or 2) cause a rightward shift of the oxyhemoglobin dissociation curve. Burnley et al. (4) examined the effects of elevated muscle temperature on the $\dot{V}O_2$ fast and slow components. Subjects underwent 40 min of passive muscle warming in a hot water bath at 42°C before performing 6 min of heavy exercise on a cycle ergometer. Muscle temperature was elevated on average by 2.6°C but no significant differences in the $\dot{V}O_2$ response were observed. Increased muscle temperature does not show any affect on $\dot{V}O_2$.

Recruitment of Lower-efficiency Fast-Twitch Muscle Fibers

Type II (fast twitch) muscle fibers have been shown to be less energetically efficient than type I (slow twitch) muscle fibers. Thus, it has been hypothesized that additional recruitment of lower-efficiency fast-twitch muscle fibers at high intensity exercise contributes to an increasing $\dot{V}O_2$ slow component. Barstow et al. (2) hypothesized the magnitude of the $\dot{V}O_2$ slow component to be positively correlated with the recruitment of type II muscle fibers. Muscle

biopsies of the vastus lateralis were obtained to determine fiber-type distribution. Additionally four exercise transitions at equivalent metabolic work rates were performed at different pedal frequencies (45, 60, 75, and 90 rpm). The assumption being higher recruitment of type II motor units at lower pedaling frequencies would show a greater influence of muscle fiber type on $\dot{V}O_2$ kinetics. As hypothesized it was found that the greater the percentage of type I fibers the smaller the relative size of the $\dot{V}O_2$ slow component. Unexpectedly greater amplitude for the fast component was also seen with greater percentages of type I fibers. Contrary to the hypothesis, pedaling frequencies did not seem to affect the relative contributions of the slow and fast components to the overall $\dot{V}O_2$ kinetics. This study supports the theory fiber-type distribution and recruitment may contribute to the $\dot{V}O_2$ slow component.

Muscle Mass Recruitment

Koga et al. (13) compared oxygen uptake kinetics for one-legged and two-legged cycle ergometer exercise. During heavy exercise when muscle recruitment patterns were normalized, based upon EMG recordings, the slow-component of oxygen uptake kinetics was similar for one or two legged exercise. Thus, they concluded that the $\dot{V}O_2$ kinetics for moderate to heavy exercise was independent of the muscle mass recruited.

CENTRAL FACTORS

Intensified Respiratory Muscle Activity

The increase in pulmonary ventilation which occurs above the lactate threshold could contribute to the increased oxygen cost associated with the slow component of $\dot{V}O_2$ kinetics. Aaron et al. (1) measured the O_2 cost of hyperpnea as well as the time to respiratory muscle fatigue. At maximum exercise, the O_2 cost of ventilation averaged $10 \pm 0.7\%$ of the $\dot{V}O_{2max}$.

Subjects were able to voluntarily mimic the work of breathing at maximum $\dot{V}O_2$ uptake for 3-10 times longer than the duration of the maximum exercise. It was concluded that intensified respiratory activity contributes to the total $\dot{V}O_{2max}$, but overall is non-fatiguing and sustainable.

To determine the relative contributions of peripheral and central factors Poole et al. (17) made simultaneous measurements of pulmonary and muscle $\dot{V}O_2$ from minute 3 to fatigue during severe exercise. Due to the high correlation of the two measurements, he concluded that leg $\dot{V}O_2$ accounted for 86% of the rise in pulmonary $\dot{V}O_2$. A subsequent and similar study by Grassi et al.(10) measuring leg and pulmonary $\dot{V}O_2$ in the early phase of transition to exercise (first 10 s-15 s) found no significant differences in oxygen kinetics. Thus, while central factors may contribute to the increased oxygen cost associated with work above the lactate threshold, a much larger percentage is likely attributable to peripheral factors within the exercising limb. However, some peripheral factors may be derived from limited central factors. For example, below optimal oxygen delivery to skeletal muscle could contribute to lactic acid accumulation and the early onset of fatigue. Therefore, one cannot exclude the role of central factors in mediating the slow component of oxygen uptake kinetics. One way to examine this problem is to manipulate central hemodynamics during exercise and monitor its effects on oxygen uptake kinetics.

WATER IMMERSION

Head-out water immersion affects a number of cardiovascular responses at rest and during dynamic exercise. Water immersion introduces hydrostatic pressure forces on the body which decrease venous capacitance and increase intrathoracic pressure. This leads to a central shift in blood volume observed with water immersion. The cephalad redistribution of blood

volume elicits changes in several cardiovascular and metabolic parameters (i.e., heart rate, blood lactate, $\dot{V}O_2$, and cardiac output) at rest and during exercise.

Although resting heart rate and heart rate response to moderate intensity exercise are only slightly decreased or unchanged with water immersion, heart rate at maximal exercise is lower (10-15 bpm) (6, 7, 9, 21, 22). The cause for a lower maximal heart rate with water immersion is unclear. Altered baroreceptor activity and a reduction in sympathetic neural outflow are possible suggestions accounting for the lower maximal heart rate response (6, 9, 21). Connelly et al. (7) investigated the sympathoadrenal response to graded dynamic exercise with water immersion by measuring plasma norepinephrine and epinephrine concentrations. The reduction in plasma catecholamine concentrations at high intensities suggested that water immersion does reduce the sympathoadrenal response (7). The reasons for the lower plasma catecholamine concentrations only at higher work intensities in water than on land are unknown.

Likewise, Connelly et al. (7) reported lower plasma lactate concentrations during water immersion exercise but only at maximal effort. Town and Bradley (22) also reported that maximal exercise in shallow and deep water elicited lower blood lactate levels when compared to land exercise. On the contrary Svendenhag (21) reported higher blood lactate levels with water immersion expressed relative to $\dot{V}O_2$ and to % $\dot{V}O_2$ at submaximal and maximal exercise intensities. Frangolias and Rhodes (9) further reported no differences in lactate concentrations 30 s. after the onset of exercise and 5 min post exercise. Frangolias and Rhodes (9) attributes the discrepancies of these various studies to the differences in familiarity with water running and training of the subjects.

Maximal measures of $\dot{V}O_2$ are dependent on exercise mode. Frangolias and Rhodes (9), Town and Bradley (22), and Svendenhag and Seger (21) all reported lower $\dot{V}O_{2max}$ values with

water treadmill running. Connelly et al. (7), Christie et al. (6), and Sheldah (20) reported no significant differences in $\dot{V}O_{2\max}$ values between water immersion cycling and land cycling. The differences between cycling- and running-water immersion are attributed to the fact water immersion and land ergometer cycling are more similar with respect to musculature utilized and control of body position. The biomechanics of water immersion running as well as hydrostatic responses and gravitational effects may explain the differences between land and water running $\dot{V}O_{2\max}$.

One of the most notable changes observed with water immersion is a significant increase in stroke volume (15, 26). Increased stroke volume is related to an increase in the left ventricular end diastolic volume (6,20). With slightly lower or no changes observed in the heart-rate response at rest and during moderate intensity exercise (6, 7, 15, 20), when compared with land trials, the increased stroke volume is primarily responsible for the overall increase in cardiac output. Indeed Yun et al. (26) showed an approximate 50% increase in cardiac output with head-out-water immersion cycling. Park et al.(15) suggest the higher cardiac output during water exercise compared to exercising on land at the same workload leads to a hyperfusion of the peripheral tissues at rest and during exercise. This hyperfusion may provide better oxygen delivery to working skeletal muscle and affect the oxygen kinetics associated with treadmill running.

Chapter 3

Methods

Subjects

Ten college-aged (18-33 yrs old) males will be recruited for this study. Subjects will qualify if they meet all of the following requirements:

1. A $\dot{V}O_{2\max}$ between 40 and 60 ml·kg⁻¹·min⁻¹
2. Active, engaging in 30 min of moderate aerobic activity at least 3/week
3. No lower extremity injuries in the last 4 months
4. Not taking any medication
5. Body fat not to exceed 25%

Subjects will be asked not to change their current exercise program during the course of the study.

Method or Procedures

The proposed project consists of five days of testing.

1. **Day 1** (45 min) consists of the determination of $\dot{V}O_{2\max}$ during treadmill running on land.

If the volunteer's $\dot{V}O_{2\max}$ does not fall within 40 to 60 ml·kg⁻¹·min⁻¹ no further test will be administered and the individual will be excluded from the study. The exclusion criteria is dictated by the maximal speed of the underwater treadmill. If the subject's $\dot{V}O_{2\max}$ exceeds this defined criteria it is likely that we will not be able to define the

lactate threshold while running in water. Following determination of $\dot{V}O_{2max}$ the subject will spend 10-15 min becoming familiarized with running on the underwater treadmill.

2. **Days 2 and 3** (30 min each day) consist of determination of lactate threshold while running on a land treadmill and a water treadmill.
3. **Day 4 and 5** (90 min each day) consist of monitoring oxygen uptake kinetics during two steady-state runs at intensities defined as 15% below and 15% above the exercise mode specific lactate threshold.

Upon arrival at the laboratory subjects will read and sign an informed consent form approved by the BYU Institutional Review Board. Subjects will have been instructed to arrive well hydrated. The subjects will void their bladder and a urine sample will be collected to monitor urine specific gravity (USG) to insure adequate hydration. A USG of less than 1.015 will be considered adequately hydrated. Those subjects not meeting this requirement will be asked to ingest an additional 5 ml/kg of water and USG will be reexamined following a 60 min postingestion period. Following verification of proper hydration the subjects' height and weight will be taken and the subjects will be instrumented with a polar heart rate monitor.

Day 1: Maximal aerobic capacity

A $\dot{V}O_{2max}$ test will be initially performed on a land treadmill to determine the aerobic capacity of each subject. The exercise test will consist of a 5 min warm-up at 0% grade during which time the subject will self-select a treadmill speed that approximates their normal running velocity. Treadmill grade will then be increased 2.5% every 2 min until a maximal grade of 15% (limit of treadmill) is achieved. If needed, additional stages will be accomplished by increasing treadmill speed 0.5 mph per stage (see Table 1). We anticipate that the selected speed will range between 6.5 and 8 miles per hour (an expected oxygen cost of 32-40 ml·kg⁻¹·min⁻¹). The subject

will continue exercise until volitional fatigue. The $\dot{V}O_{2\max}$ test will be considered valid if a plateau in $\dot{V}O_2$ is observed despite increases in speed or grade of the treadmill, or if the subject reaches 90% of their age predicted heart rate and has a respiratory exchange ratio of 1.1 or higher. During the exercise test oxygen consumption will be monitored every 15 sec using a ParVo System metabolic cart (Parvomedics Inc. Sandy, UT). Just prior to the initiation of the exercise test the subject will be instrumented with a headpiece holding a one-way breathing valve to allow collection of expired gases. The expired gases will be sampled for composition by a ParVo System metabolic cart. Calibration of the metabolic cart will be performed before each test and verified immediately following the test. Calibration of the flowmeter will be performed using a 3-liter syringe at three different flow rates: slow stroke (peak flow <80L/min), medium stroke (peak flow 200L/min), and fast stroke (peak flow 400L/min). Oxygen and carbon dioxide gas analyzers will be calibrated using room air and a medical grade gas of known concentrations.

Days 2 and 3: Lactate threshold testing

An 18-gauge catheter is placed in the median cubital vein of the forearm of the subject by a well-trained technician. The subject will then stand on the treadmill for 30 min to allow equilibration of body water compartments before a resting blood sample is collected. During this equilibration period, just prior to the initiation of the exercise test the subject will be instrumented with a headpiece holding a one-way breathing valve to allow collection of expired gases and the measurement of oxygen consumption.

The lactate threshold protocol will be performed entirely at 0% grade on the treadmill. The subject will start by walking at 3.5 mph for 5 min as a warm-up (see Table 2). After a 3 ml blood sample is collected during the final minute of Stage 1 the speed will be increased to elicit a

oxygen consumption approximately equal to 30% of their previously determined $\dot{V}O_{2max}$. This selected speed will be maintained for 3 min and a blood sample will be drawn between minute 2 and 3 of this (and every) stage. After each blood sample, treadmill speed will be increased by 0.5 mph per stage. When the subject's oxygen consumption meets or exceeds 90% of their measured $\dot{V}O_{2max}$ the test will be terminated and treadmill speed will be reduced to 3.5 mph to allow the subject to recover.

During the exercise test to measure the lactate threshold, the catheter will be flushed with a sterile saline solution frequently to prevent clotting. Blood samples (3-5 ml) will be immediately placed in cooled EDTA-vacutainers. After the exercise test, the blood sample will be well mixed and a small amount of whole blood will be used to determine hematocrit and hemoglobin concentration. The remainder of the blood will be centrifuged at 1500 xg for 15 min at 4°C. The plasma will be immediately separated from the red blood cells and analyzed for lactate concentrations using a YSI 2300 lactate analyzer. The same protocol will be followed when measuring lactate threshold while running on a treadmill on land and in water. The water depth will be adjusted hit the subject between the sterna notch and the top of the xiphoid process. Because the maximal speed of the water treadmill is limited to 7.5 mph, hydro jets will be used to increase workload past 7.5mph. Each additional stage the jets will be increased by 20% of their maximal flow rate.

Analysis of lactate threshold will be assessed from the blood samples drawn during the study. Lactate increases with increasing oxygen uptake ($\dot{V}O_2$) during incremental exercise. A mathematical model that fits the data to a line of best fit can be used to detect lactate threshold with more precision than visual detection techniques. During incrementally increasing work, an abrupt transition occurs in the rate of increase of blood lactate with increasing $\dot{V}O_2$. The

transition is defined in the log-log model via a mathematical model that can define the location of this transition. Error effects are minimized using this method by using the least squares curve-fitting procedure. The functional relationship can be expressed mathematically as the power law:

$$[La^-] = [La^-]_0 \times \left(\frac{\dot{V}O_2}{\dot{V}O_{2o}} \right)^b$$

where $[La^-]$ is the lactate concentration at any time t , $[La^-]_0$ is the lactate concentration at the threshold, $\dot{V}O_2$ is the oxygen uptake, $\dot{V}O_{2o}$ is the $\dot{V}O_2$ at the threshold, and b is the slope of the regression line (3). Analysis of lactate data will include comparison of $\dot{V}O_2$ to plasma lactate concentration, and % $\dot{V}O_2$ based on the land treadmill speed versus lactate concentration.

Days 4 and 5: Oxygen Uptake Kinetics

Oxygen kinetics will be measured on a subsequent visit to the laboratory. Subject preparation will be identical to previous test days. On these days the subject will be instrumented with a heart rate monitor, a headpiece assembly for monitoring oxygen uptake by the metabolic cart, and cardiac impedance electrodes. The metabolic cart will be programmed to collect metabolic and ventilatory parameters on a breath by breath basis. Cardiac impedance tapes will be placed around the neck and chest to obtain measures of stroke volume during exercise. Two tapes will be placed approximately one inch apart around the circumference of the neck. Two tapes will be placed around the circumference of the thorax, one superior to the xiphoid process and the other three to four inches inferior to the xiphoid process. Subject will perform two 6-min exercise bouts on the same day on either the land treadmill or the underwater treadmill. For one exercise bout the treadmill speed will be set to elicit an oxygen uptake equal to that matching 15% below the subject's lactate threshold. For the other exercise bout the treadmill speed will be set to elicit an oxygen uptake equal to that 15% above the lactate

threshold. Treadmill speed will be determined from the subject's previous lactate threshold tests in which their $\dot{V}O_2$ was measured as speed was incrementally increased. The order of the tests will be randomized. Prior to the exercise bout subject will warm-up with 5 minutes of light jogging and then rest in a standing position for 10 minutes. Subject will begin with 2 min of standing rest with feet astride the moving treadmill belt and hands holding the treadmill guard rails. At the start of the exercise test, subject will support their body mass with their hands on the guard rails until their leg speed matches treadmill belt speed, after which they will let go of the guard rails and begin running. Subject will run for 6 min followed by a 3 min active recovery and then 1 hour of rest to reestablish a baseline before performing their second exercise bout. Subject may sit down during the 1 hour rest period.

For each exercise test breath-by-breath oxygen uptake data will be interpolated to give values second by second and will be time aligned to the start of exercise. Nonlinear regression techniques will be used to fit the $\dot{V}O_2$ data after the onset of exercise with an exponential function. The sum of squared error will be minimized and will be used as the criterion for convergence. The mathematical model will consist of two (moderate exercise) or three (heavy exercise) exponential terms, each representing a specific phase of the response (1). The first exponential term starts with the onset of exercise [*time* (*t*) 0], whereas the other terms begin after independent time delays,

$$\begin{aligned} \dot{V}O_2(t) = \dot{V}O_2(b) + A_c \cdot (1 - e^{-t/\tau_c}) & \quad \text{phase 1 : cardiodynamic component} \\ + A_p \cdot (1 - e^{-(t-TD_p)/\tau_p}) & \quad \text{phase 2 : primary component} \\ + A_s \cdot (1 - e^{-(t-TD_s)/\tau_s}) & \quad \text{phase 1 : slow component} \end{aligned}$$

where $\dot{V}O_2$ (b) is the resting baseline value; A_c , A_p , and A_s are the asymptotic amplitudes for the three exponential terms: cardiodynamic, primary, and slow components, respectively; τ_c , τ_p , and τ_s are the time constants of the cardiodynamic, primary, and slow components, respectively; and TD_p and TD_s are the time delays of the primary and slow components, respectively. The *Phase 1* term will terminate at the start of *Phase 2* (i.e., at TD_p) and be assigned the value for that time (A'_c)

$$A'_c = A_c \cdot (1 - e^{-TD_p/\tau_c})$$

The $\dot{V}O_2$ at the end of *Phase 1* (A'_c) and the amplitude of *Phase 2* (A_p) will be summed to calculate the amplitude at the end of the primary component (A_{c+p}). The slow component at the end of exercise will be calculated and will be used in preference over the asymptotic value, which can lie beyond physiological limits. The gain of the primary component (G_{c+p} ; A_{c+p}/Δ running speed expressed relative to body mass) for the two exercise intensities also will be calculated.

Corresponding changes in cardiac impedance will be combined with EKG measurements to provide hemodynamic parameters. These parameters are calculated using the equation

$$\Delta V = \frac{\rho \cdot L^2 \cdot T \cdot (dZ/dt)_{\min}}{Z_0^2}$$

where ΔV = ventricular stroke volume (ml), ρ (blood resistivity) = 135 ohm cm, L = the mean distance between the two inner pieces of impedance tape, Z_0 = the mean impedance between the two inner electrodes in ohms, $(dZ/dt)_{\min}$ = the minimum value of dZ/dt occurring during the cardiac cycle in ohms per sec, and T = the ventricular ejection time in seconds as obtained from the dZ/dt waveform. The cardiac output (\dot{Q}) will be calculated by multiplying the SV by the HR.

Data Analysis

The experimental design is a simple balanced ANOVA for repeated measures with main effects of treatment (land versus air) and exercise intensity (above and below the lactate threshold) as repeated measures. This design allows each subject to act as their own control. Major variables measured and used for analysis will include $\dot{V}O_2$, heart rate, rate of perceived exertion, lactate concentration, LT expressed in $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, SV, \dot{Q} , and rate constants for oxygen uptake kinetics. The analysis will be performed using SAS general linear model analysis with significance set at a p value of $p<0.05$.

Table 1

Test protocol example with self-selected speed of 7 mph

Stage	Time	MPH	Grade
1	Resting	standing	0
2	0-5 min	3.5 to 7*	0
3	5-7 min	7	2.5
4	7-9 min	7	5.0
5	9-11min	7	7.5
6	11-13min	7	10
7	13-15min	7	12.5
8	15-17min	7	15.0
9	17-19min	7.5	15.0
10	19-21min	8.0	15.0

* self-selected speed during warm-up

Table 2:

Lactate Threshold Test Protocol: Example with selected speed set at 6 mph.

Stage	Time	MPH	Sample#
1	Resting	standing	1
2	1-3 min	3.5	2
3	3-6 min	6	3
4	6-9 min	6.5	4
5	9-12min	7	5
6	12-15min	7.5	6
7	15-18min	8	7
8	18-21min	8.5	8
9	21-24min	9.0	9
10	24-27min	9.5	10
11	27-30min	10.0	11

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