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Simulation of Oxygen Uptake Kinetics in Exercise

Tokuo YANO and Masahiro HORIUCHI

Abstract

The kinetics of oxygen uptake in exercise was simulated with assuming the kinetics of muscle oxygen uptake and considering the circulatory time delay. There were three phases in the simulated kinetics of oxygen uptake. The effects of the differences in time constant of cardiac output and muscle oxygen uptake and in venous blood volume on these phases of oxygen uptake kinetics were examined in the present simulation. Cardiac output had an effect on phase 1, muscle oxygen uptake on phase 2, and venous blood volume on phase 1 and 2. Furthermore the present simulation could become a possible way for estimating muscle oxygen uptake without previously assuming venous blood volume. Accordingly the simulation curve visually fitted for the measured oxygen uptake was obtained when parameters of venous blood volume and time constant of muscle oxygen uptake were controlled at 1.5 l and 30 s, respectively. The estimated time constant of muscle oxygen uptake was slower than the measured time constant of cardiac output. Thus the present result at the onset of step exercise could not suggest evidence supporting the transport limitation hypothesis of oxygen uptake kinetics.

Key words : oxygen uptake, circulatory time delay, simulation, exercise.

After the step increase in work rate (step exercise), oxygen uptake ($\dot{V}O_2$) increases for initial 2–3 min and then remains at the steady state. During the recovery from exercise $\dot{V}O_2$ decreases to resting value. It is questioned what physiological factor adjusts the $\dot{V}O_2$ relating to exercise. HUGHSON and MORRISSEY (1983) have pointed out that two hypotheses for the adjustment factors of $\dot{V}O_2$ have recently been proposed. One is that $\dot{V}O_2$ is controlled by the biochemical process in the working muscle (HENRY, 1951 ; WHIPP and MAHLER, 1980 ; MAHLER, 1985 ; SAHLIN et al., 1988). The other is that the oxygen transported by cardiovascular system limits $\dot{V}O_2$ (BERG, 1947 ; LINNARSSON, 1974 ; HUGHSON and MORRISSEY, 1983 ; MURPHY et al., 1989).

It is well known that steady-state $\dot{V}O_2$ increases in proportion to the rise of cardiac output (ÅSTRAND et al., 1964). Therefore the cardiac output or heart rate at the onset of step exercise has also been compared with $\dot{V}O_2$. Some studies confirmed the oxygen transport limitation hypothesis (HUGHSON and MORRISSEY, 1983 ; MURPHY et al., 1989) while other reports showed contrary results (CERRETELLI et al., 1966 ; YANO, 1985). However

in these studies the effect of body oxygen stores in exercise was not always taken into consideration.

INMAN et al. (1987) estimated the kinetics of muscle oxygen uptake ($m\dot{V}O_2$) with adding the oxygen stores change to $\dot{V}O_2$, and indicated the similar response of $m\dot{V}O_2$ to cardiac output at the onset of step exercise. Thus the oxygen transport may intimately relates to $m\dot{V}O_2$.

WHIPP et al. (1982) have classified the kinetics of $\dot{V}O_2$ at the onset of step exercise into three phases. Accordingly, on phase 1 the increase of $\dot{V}O_2$ is formed by dynamic change of cardiovascular system without appreciable fall of mixed venous oxygen tension. On phase 2, $\dot{V}O_2$ rises exponentially and mixed venous oxygen tension falls. On phase 3, $\dot{V}O_2$ represents steady state. BARSTOW and MÓLE (1987) suggested from their computer simulation of oxygen uptake kinetics that phase 2 related to $m\dot{V}O_2$. Later, BARSTOW et al. (1990) studied the effect of blood flow on $m\dot{V}O_2$ using a computer simulation and suggested that oxygen delivery would not limit $m\dot{V}O_2$ at the onset of step exercise.

However, in BARSTOW's former simulation, the circulatory time delay which corresponded to the time required to deliver the blood in muscle to the lung, was defined in the phase 1 but not clearly in phase 2. In latter simulation, the model can apply to the only step exercise since the empirical result was included. Thus these problems on simulation of oxygen uptake kinetics in exercise are still left.

Therefore the purposes of this study were to improve the former problems in simulation of oxygen uptake kinetics in exercise, and to estimate $m\dot{V}O_2$ using the data of $\dot{V}O_2$ and cardiac output to examine the transport limitation hypothesis.

MODEL

$\dot{V}O_2$ can be determined by the Fick equation following time course(t) in the lung. That is,

$$\dot{V}O_2(t) = \dot{Q}(t) (Cao_2 - C\bar{v}O_2(t)) \quad (1)$$

where $\dot{Q}$; cardiac output, Cao_2 ; arterial oxygen content, $C\bar{v}O_2$; mixed venous oxygen content. Cao_2 is assumed to be constant in exercise (0.2 ml/ml) since the data of Cao_2 indicated less change in exercise (see ÅSTRAND et al., 1964).

As muscle venous oxygen content ($mC\bar{v}O_2$) is transported to the lung, the $mC\bar{v}O_2$ is assumed to be equal to $C\bar{v}O_2$ after a certain delay. That is (see Figure 1),

$$mC\bar{v}O_2(t') = C\bar{v}O_2(t) \quad (2)$$

This circulatory time delay is assumed to correspond to the replacement time of venous blood (VB) by blood flow. That is,

$$\int_0^t \dot{Q}(t) dt = VB \quad (3)$$

As it is assumed that appreciable fall in $C\bar{v}O_2$ starts from the first arrival of $mC\bar{v}O_2$, $C\bar{v}O_2$ at the initial stage is $C\bar{v}O_2$ at rest (Figure 1).

$mC\bar{v}O_2$ in Equation (2) can be determined by the Fick equation following time course in the muscle. This is,

$$mC\bar{v}O_2(t') = Cao_2 - m\dot{V}O_2(t') / \dot{Q}(t') \quad (4)$$

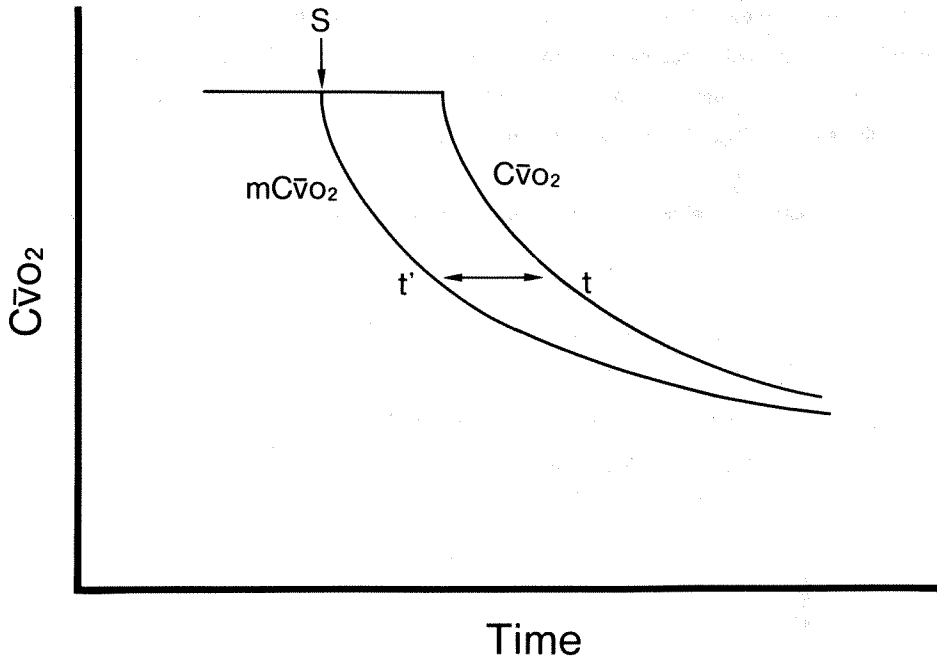


Fig. 1. Schema of changes in $m\bar{C}\bar{V}O_2$ and $C\bar{V}O_2$ at the onset of step exercise. After starting the step exercise(S), $m\bar{C}\bar{V}O_2$ decreases. After transport delay for replacing venous blood, $C\bar{V}O_2$ starts to decrease. The $C\bar{V}O_2$ at the time t is equal to $m\bar{C}\bar{V}O_2$ at the time t' .

Then $m\bar{C}\bar{V}O_2$ is forced to be zero when $m\bar{C}\bar{V}O_2$ is calculated as below zero in Equation (4).

Thus Equation (1) can be solved if V_B and kinetics of $m\dot{V}O_2$ and $\dot{Q}$ in exercise are quantitatively assumed.

ASSUMED ITEMS AND PARAMETERS

Although the present model does not require the fixed equations for $\dot{Q}(t)$ and $m\dot{V}O_2(t)$, it is general practice to assume that they behave as mono-exponential manner to the step exercise. Those are,

$$m\dot{V}O_2(t) = (\dot{V}O_{2ss} - \dot{V}O_{2r}) (1 - e^{-t/a}) + \dot{V}O_{2r} \quad (5)$$

$$\dot{Q}(t) = (\dot{Q}_{ss} - \dot{Q}_r) (1 - e^{-t/b}) + \dot{Q}_r \quad (6)$$

where symbols of ss and r mean steady state and rest values, and a and b are time constants of $m\dot{V}O_2$ and $\dot{Q}$, respectively. Then it is also assumed that oxygen uptake is equal to the value of muscle oxygen uptake at steady state in exercise and at rest. In computer simulation, a, b and V_B were controlled.

USED DATA

The data necessary for Equations (5) and (6) are shown in table 1. The oxygen uptake

was determined in every minute in exercise and for 5 min at rest by the Douglas bag method. The cardiac output was measured by Impedance method. The time constant of $\dot{V}_{O_2}$ and $\dot{Q}$ was determined with approximating to the function with mono-exponent and no time delay nature. Refer to YANO (1985) concerning the detail.

Table 1. Used data for the present simulation

	rest (l/min)	Steady-state (l/min)	time constant (sec)
$\dot{V}_{O_2}$	0.31	1.18	40
$\dot{Q}$	4.9	8.6	14

Time Constant was obtained with no time delay and mono-exponential function(see YANO, 1985). $\dot{V}_{O_2}$: oxygen uptake determined by the Douglas bag method, $\dot{Q}$: cardiac output determined by Impedance method.

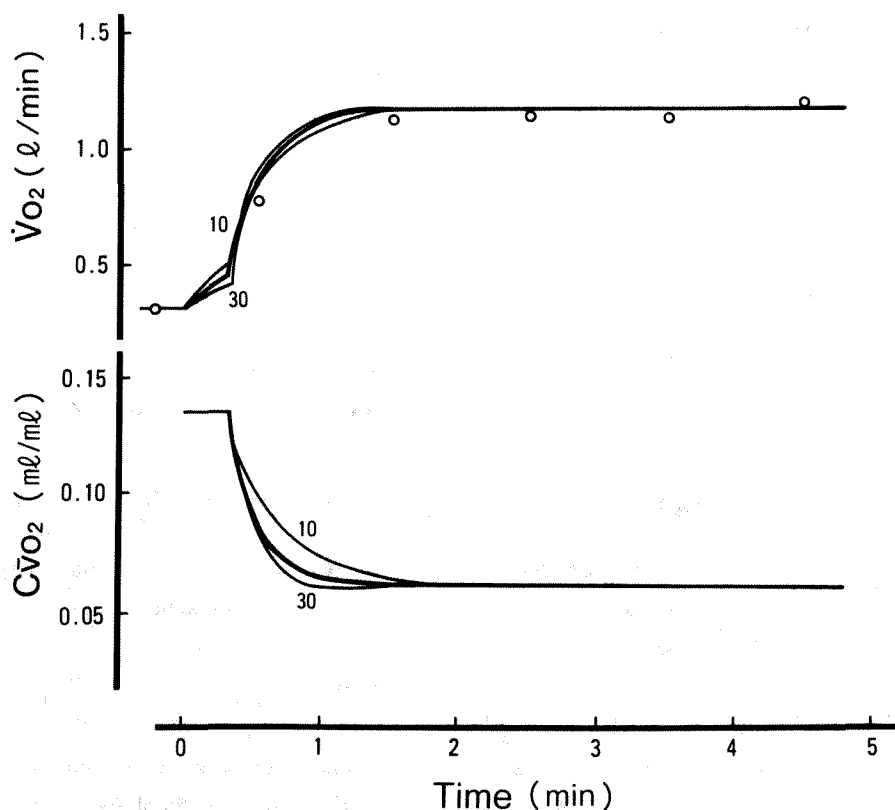


Fig. 2. The effect of simulated time constant of $\dot{Q}$ on $\dot{V}_{O_2}$ (upper panel) and CvO_2 (lower panel). A standard curve (thick line) is figured by the parameters of 2.0 l for V_B , time constants of 20 s for $\dot{Q}$ and of 20 s for $m\dot{V}_{O_2}$. The time constant of $\dot{Q}$ is changed from 10 to 30 s without changing the other parameters. Circles show the measured $\dot{V}_{O_2}$.

RESULTS

All $\bar{C}\dot{V}O_2$ did not become below zero in exercise. When the time constant of $m\dot{V}O_2$ was faster than that of $\dot{Q}$, $\bar{C}\dot{V}O_2$ temporarily decreased below the steady state value of $\bar{C}\dot{V}O_2$ in exercise. A standard curve consisted of parameters of 2.0 l for VB and time constant of 20 s for $\dot{Q}$ and of 20 s for $m\dot{V}O_2$ is shown in Figure 2-4.

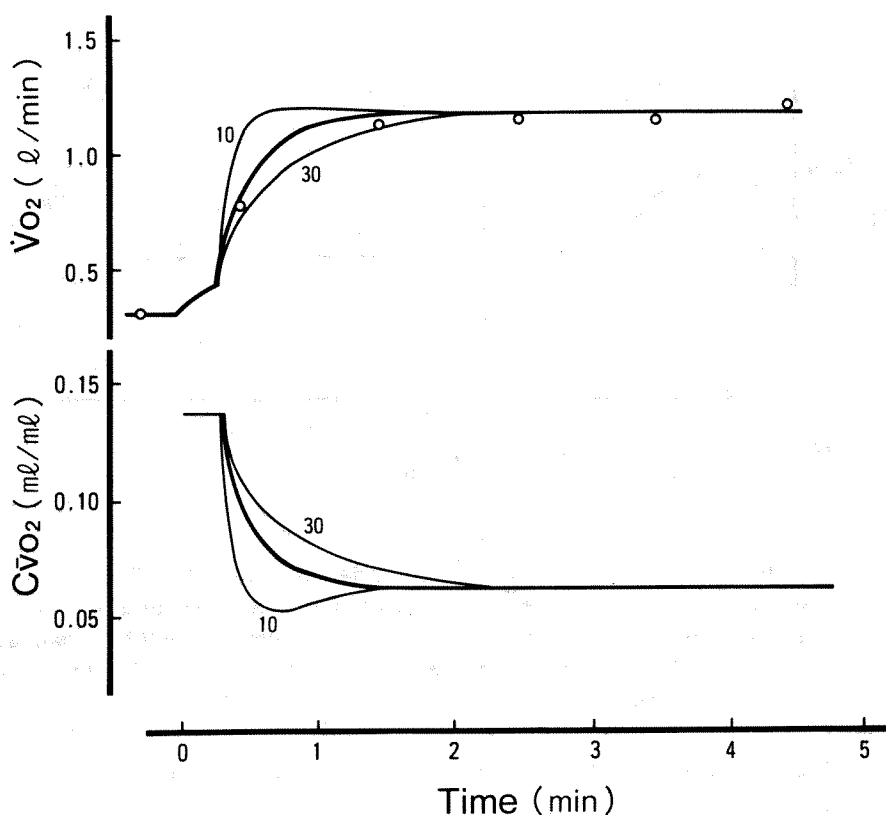


Fig. 3: The effect of simulated time constant of $m\dot{V}O_2$ on $\dot{V}O_2$ (upper panel) and $\bar{C}\dot{V}O_2$ (lower panel). A standard curve (thick line) is figured by the parameters of 2.0 l for VB, time constants of 20 s for $\dot{Q}$ and of 20 s for $m\dot{V}O_2$. The time constant of $m\dot{V}O_2$ is changed from 10 to 30 s without changing the other parameters. Circles show the measured $\dot{V}O_2$.

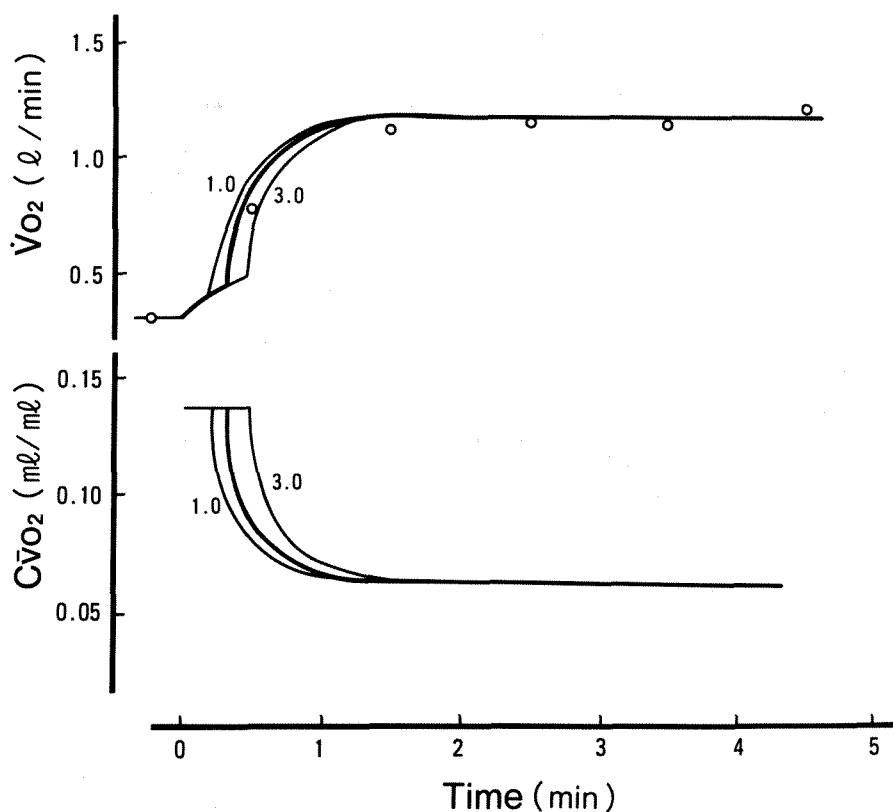


Fig. 4. The effect of simulated VB on $\dot{V}O_2$ (upper panel) and on $C\dot{V}O_2$ (lower panel). A standard curve (thick line) is figured by the parameters of 2.0 l for VB and time constants of 20 s for $\dot{Q}$ and of 20 s for $m\dot{V}O_2$. The VB is changed from 1.0 to 3.0 l without changing the other parameters. Circles show the measured $\dot{V}O_2$.

Figure 2 shows the effect of response rate of cardiac output on $\dot{V}O_2$. Adjustment of $\dot{Q}$ response in simulation was characterized in phase 1, but entirely indicated less effect. The faster $\dot{Q}$ responded, more quickly $\dot{V}O_2$ reacted and vice versa. Within the simulated range, the circulatory time delay in phase 1 did not indicate appreciable difference with changing the response rate of $\dot{Q}$.

Figure 3 shows the effect of response rate of $m\dot{V}O_2$ on $\dot{V}O_2$. Adjustment of $m\dot{V}O_2$ in simulation was characterized in phase 2. The faster $m\dot{V}O_2$ responded, the more quickly $\dot{V}O_2$ reacted and vice versa. A curve with time constant of 10 s for $m\dot{V}O_2$ showed temporarily overshooting $\dot{V}O_{2ss}$.

Figure 4 shows the effect of the difference in VB on $\dot{V}O_2$. Adjustment of VB in simulation was characterized in phase 1 and 2. The larger VB became, the longer the circulatory time delay became in phase 1 and vice versa. The difference in volume of VB slightly altered the $\dot{V}O_2$ in phase 2.

The simulation curve visually fitted for the measured $\dot{V}O_2$ was obtained by the parameters of 1.5 l of VB and time constant of 30 s for $m\dot{V}O_2$ when the measured data of $\dot{Q}$ was used (time constant ; 14 s) (Figures 5). The simulated time constant of $m\dot{V}O_2$ was slower than the measured time constant of $\dot{Q}$, and higher than $\dot{V}O_2$. The area lying between $m\dot{V}O_2$ and $\dot{V}O_2$ indicates oxygen stores changing in exercise.

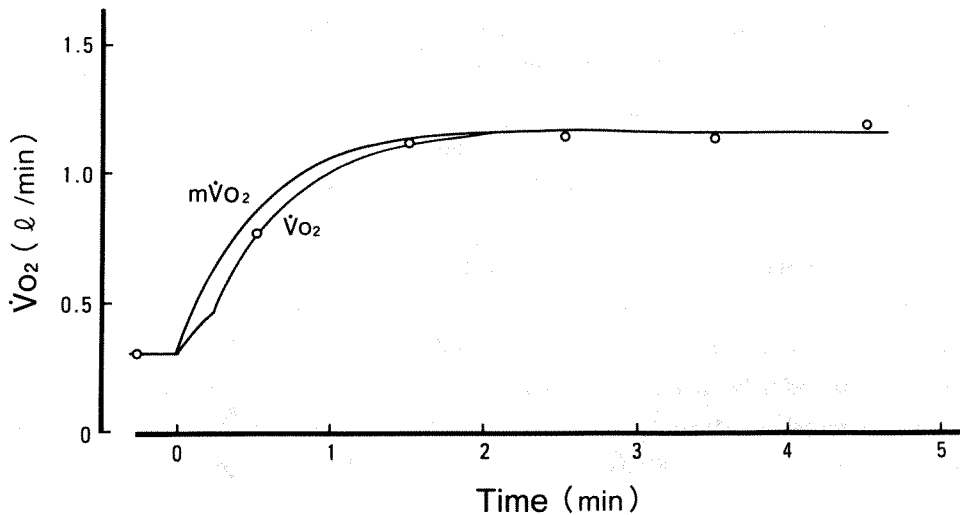


Fig. 5. An optimal simulation curve for the measured $\dot{V}O_2$ (upper panel). Circles show the $\dot{V}O_2$ at the onset of step exercise. The simulation curve for $\dot{V}O_2$ was visually fitted by the parameters of 1.5 l of VB and time constant of 30 s for $m\dot{V}O_2$ when the measured data of $\dot{Q}$ were used (time constant ; 14). The area lying between $m\dot{V}O_2$ (upper curve) and $\dot{V}O_2$ (lower curve) is the change in venous oxygen stores.

DISCUSSION

The oxygen uptake in the muscle begins to increase immediately after exercise. In the muscle $mC\bar{v}O_2$ is determined mainly by $m\dot{V}O_2$ and $\dot{Q}$. Then the muscle venous blood is transported to the lung. Oxygen uptake in the lung is formed by the arterio-venous oxygen difference at rest and the change of $\dot{Q}$ before the transport (phase 1) and by both changes in arterio-venous oxygen difference and $\dot{Q}$ after the transport to the lung (phase 2). These details were simulated in the present study.

In the present simulation, it was assumed that $C\bar{v}O_2$ at phase 1 remained a resting value. However a recent study have indicated that mixed venous oxygen saturation decreases at fairly early phase (CASABURI et al., 1989).

At rest, $C\bar{v}O_2$ is a value in the mixed blood from the muscle and the other organs. Therefore if muscle blood flow increases, the mixing rate tends to muscle site. If oxygen

content from muscle at rest is lower than that from the other organs, the mixed $\bar{C}\dot{V}O_2$ could decrease. This means that three-compartment model which consists of muscle, lung and the other organs sites, may yield more accurate simulation. Nevertheless three-compartment model requires more indefinite parameters than present ones. Therefore the present study avoided employing much more assumptions.

When $m\bar{C}\dot{V}O_2$ was calculated as below zero, the $m\bar{C}\dot{V}O_2$ was forced to be zero in the present simulation. Accordingly $m\dot{V}O_2$ is not equal to $\dot{Q} (CaO_2 - m\bar{C}\dot{V}O_2)$. In this case, it is implicitly assumed that muscle oxygen stores are available. In this meaning, $m\dot{V}O_2$ is not termed as oxygen consumption but oxygen uptake. However, this problem did not take place within the range examined in the present study (see Figures 2-4).

The results obtained in the present simulation indicated that the difference in VB had effects on phase 1 and 2, response rate of $\dot{Q}$ on phase 1, and response rate of $m\dot{V}O_2$ on phase 2.

According to the Fick equation, phase 1 in the kinetics of $\dot{V}O_2$ should be affected by arterio-venous oxygen difference and $\dot{Q}$. However since $\dot{Q}$ could change in early phase of exercise and arterio-venous oxygen difference was assumed to be constant, phase 1 was subjected to the effect of $\dot{Q}$. Furthermore the duration of phase 1 could be determined by the degree of VB since the circulatory time delay related to the replacement time of venous blood by blood flow. Therefore the response rate of phase 1 relates to the change of $\dot{Q}$ and the duration to the degree of VB.

About the effect of VB on phase 2, it becomes easy to understand when an extreme example is introduced. For example, if $\dot{Q}$ has already attained steady state before starting the phase 2 due to the huge VB, the shape of phase 2 would be affected by the only $m\bar{C}\dot{V}O_2$, and if VB is close to zero, the increasing rate of phase 2 would be affected by $m\bar{C}\dot{V}O_2$ as well as $\dot{Q}$ change. Thus the difference in volume of VB can affect phase 2 through the lag between effects by $\dot{Q}$ and $m\bar{C}\dot{V}O_2$. Furthermore, since in both examples the $m\bar{C}\dot{V}O_2$ relates to phase 2, the $m\dot{V}O_2$ change which makes $m\bar{C}\dot{V}O_2$ alter, can also affect phase 2.

The present simulation could become a possible way for estimating $m\dot{V}O_2$ without previously assuming VB. Accordingly the simulation curve visually fitted to the measured $\dot{V}O_2$ was obtained when the parameters of VB and time constant $m\dot{V}O_2$ were controlled at 1.5 l and 30 s, respectively. The estimated time constant of $m\dot{V}O_2$ was slower than the measured time constant of $\dot{Q}$.

INMAN et al. (1987) estimated VB (3.55 l) basically from a subject's and weight to estimate the venous oxygen stores change in exercise and yielded the estimation of $m\dot{V}O_2$. Consequently, the $m\dot{V}O_2$ responded similarly to $\dot{Q}$ change. However the $m\dot{V}O_2$ estimated by INMAN et al. (1987) is dependent on the degree of estimating VB and eventually the estimation of oxygen stores change. Accordingly when VB is smaller than estimation of INMAN et al. (1987), the response rate of $m\dot{V}O_2$ can be calculated as slower response. In the present study, VB and time constant of $m\dot{V}O_2$ were determined with seeking the optimal curve for the date of $\dot{V}O_2$. The determined VB (1.5 l) was actually smaller than that by INMAN et al.

(1987).

Thus the present result at the onset of step exercise could not suggest evidence supporting the transport limitation hypothesis of oxygen uptake kinetics.

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