Physiological Background of Oxygen Uptake Kinetics At Onset, During And After Exercise

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Declaration of Conflict of Interest
None
Oxygen Flow during Exercise

Muscle Activity

O₂ & CO₂ Transport

Ventilation (VA+VD=VE)

Peripheral Circulation

Pulmonary Circulation

Muscles

Heart Blood

Lungs

Vasodilation

Vasodilation

↑ QCO₂

↑ Stroke volume

↑ Tidal volume

↑ QO₂

↑ Heart rate

↑ Respiratory rate

Physiological Response to Exercise

Prof. Karlman Wasserman

Mito. ṪO₂ ṪCO₂

Expired Inspired
Oxygen Uptake (\(\dot{\text{VO}}_2\)) and Cardiac Output

\[ \dot{\text{VO}}_2 = \text{CO} \times \text{C(a-v)O}_2 \text{ Difference} \]

- Cardiac Output = Oxygen delivery; Central function
- \(\text{C(a-v)O}_2\) Difference = Oxygen utilization; Peripheral function

\(\dot{\text{VO}}_2\): an index of cardiac output during exercise

\(\text{C(a-v)O}_2\) Difference \(\propto\) %Work load

\(\dot{\text{V}}\text{O}_2\): an index of metabolism, energy, and exercise intensity

1 metabolic equivalent (1 MET) = 3.5ml/min/kg \(\dot{\text{V}}\text{O}_2\)

(\(\dot{\text{V}}\text{O}_2\) of 40 y.o., 70 kg, Caucasian male at sitting position)
Parameters from Cardiopulmonary Exercise Test

VO₂ kinetics during and after exercise
**Phase I**

**Phase II**

**Phase III**

VO₂ deficit

\[ \text{\( O_2 \) deficit} \]

\[ \text{\( \tau_{on} \)} \]

\[ \text{\( \dot{\text{VO}}_2 \)} \]

\[ \text{\( \dot{\text{VO}}_2 \) on} \]

\[ \text{\( \dot{\text{VO}}_2 \) off} \]

\[ \text{\( \tau_{off} \)} \]

\[ \text{\( T_{1/2} \)} \]

\[ \text{\( \dot{\text{VO}}_2 \) s-s} \]

\[ \text{\( O_2 \) debt} \]

**Constant Work**

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**\( \dot{\text{VO}}_2 \) Response to the Square Wave Test**
Parameters from Cardiopulmonary Exercise Test with Ramp Protocol

**Beginning of Ex.**
- \( \tau_{on} \)

**During Ex. (Steady-state)**
- \( \dot{\text{VO}}_2 \) at warm-up

**During incremental Ex.**
- \( \Delta \dot{\text{VO}}_2/\Delta \text{WR} \), \( \Delta \dot{\text{HR}}/\Delta \text{WR} \), \( \text{VE} \) vs. \( \dot{\text{VCO}}_2 \) slope, Min. \( \text{VE}/\dot{\text{VCO}}_2 \)
- TV-RR curve, OUES (oxygen uptake efficacy slope)

**Submaximal Ex.**
- AT, PET\( \text{CO}_2 \) at RC point

**Maximal Ex. (Peak Ex.)**
- Peak \( \dot{\text{VO}}_2 \), Ex time, Peak \( \text{O}_2 \) pulse

**Recovery phase**
- \( \tau_{off}, T_{1/2} \)

- Work Rate
  - 10～20 watts/min

- Peak \( \dot{\text{VO}}_2 \)
- \( \Delta \dot{\text{VO}}_2/\Delta \text{WR} \)
- \( \dot{\text{VO}}_2 \)
- \( \dot{\text{VO}}_2s-s \)
- \( \tau_{on} \)
- \( \tau_{off} \)
**VO₂ Response to the Start of the Exercise**

Time constant for VO₂ at the beginning of step exercise

- Cardiac output response
- C(a–v)O₂ response
- Heart rate response
- Vasodilatory response
- Parasympathetic nervous activity
- Endothelial function
**Oxygen uptake (VO₂) Response at the Beginning of Ex.**

Figure 1. Representative tracings of time course changes of VO₂, mixed venous O₂ saturation (SvO₂), and cardiac output at the onset of 20-watt exercise in a patient whose peak VO₂ was <18.0 ml/min/kg.

Figure 2. Relation of $\tau$ of VO₂ with that of cardiac output or with that of AV O₂ difference for a 20-watt work rate. Group A consisted of 6 patients whose peak VO₂ was >18.0 ml/min/kg, and group B consisted of 6 patients whose peak VO₂ was <18.0 ml/min/kg.

Short-term (2W) physical training improves vasodilating capacity and $\tau_{on}$ in cardiac patients (POST CABG)

Cardiac output response at the beginning of step exercise

$\Delta \tau_{on}$ (sec)

$\Delta$ Culff blood flow (ml/min/100ml tissue)

Endothelial function

$y = -3.2066x - 8.1679$

$R = -0.73$

$p < 0.0001$

\( \dot{V}O_2 \) Response to the Square Wave Test: \( \tau \) on Prolonged with Exercise Intensity

\( \tau \) on

Work rate

\( \begin{align*}
\text{10W} & \quad \text{20W} & \quad \text{40W} & \quad \text{60W} & \quad \text{80W} & \quad \text{120W}
\end{align*} \)

\( (\text{sec}) \)

N=6  Normal volunteer
Age: 28±3y


\( \dot{VO}_2 \) Response to the Square Wave Test: \( \dot{VO}_2 \) during Steady-State Exercise

- Cardiac output
- Blood redistribution
- Mechanical exercise efficiency of working muscles

\( \dot{VO}_2 \) during constant exercise
Δ\(\dot{V}O_2/\Delta WR\) and Functional Class

\(\dot{V}O_2\) at rest ↓
\(\dot{V}O_2\) at 20Ws−s ↓
\(\Delta\dot{V}O_2/\Delta WR\) ↓

Data from Itoh H, et al. Jpn Circ J 1992;56:504-508
Change in $\dot{VO}_2$ at 20w before and after Valve Replacement

MR Patients (NYHA class III)

$\dot{VO}_2$ (20Ws·s)

ml/min/kg

Before 1 mon. after 6 mon. after

P<0.01
\[ \Delta \dot{V}O_2/\Delta WR \]

\[ \Delta \dot{V}O_2/\Delta WR \]

\( \dot{V}O_2 \) (Cardiac output) at given WR

\( \dot{V}O_2 \) response to the work

\( \dot{V}O_2 \) increase relative to increase in work rate
Simulation of the Theoretical Relationship: $\dot{\text{VO}}_2$ step and ramp response

$Y = K \left( 1 - e^{-t/\tau} \right)$, where $K$ is the steady-state increase in $\dot{\text{VO}}_2$ and $\tau$ is a time constant. The $\dot{\text{VO}}_2$ ramp response to 15 W/min exercise was mathematically derived.

A) A longer $\tau$ of the step response with an identical $K$ (10ml/min/w) results in a rightward shift of the ramp response. (*solid line; $\tau =$50s, *broken line; $\tau =$80s).

B) A smaller $K$ with an identical time constant ($\tau =$50s) results in a smaller $\Delta \dot{\text{VO}}_2/\Delta \text{WR}$. (*solid line; $K =$10 ml/ min/w, *broken line; $K =$7.5 ml/min/w).

Δ\(\dot{VO}_2\)/ΔWR in Different Ramp Slopes (Normal volunteer)

**Peak Work Rate**

- 10W/min.
- 20W/min.
- 30W/min.
- 40W/min.

**Peak \(\dot{VO}_2\)**

- 10W/min.
- 20W/min.
- 30W/min.
- 40W/min.

\(\Delta \dot{VO}_2/\Delta WR\)

- 10W/min.
- 20W/min.
- 30W/min.
- 40W/min.

**:** P<0.01  *:** P<0.05

Ono T, et al. 1999
Changes of $\Delta \dot{VO}_2/\Delta WR$ in Normal, Ischemic, and Heart Failure

**Normal**
- Skeletal muscle recruited $\uparrow$
- Respiratory muscle work $\uparrow$
- Body temperature $\uparrow$
- Bohr effect

**Angina pectoris**
- Ischemia

**Heart failure**
- Impaired CO increase
Ischemia and $\Delta \dot{V}O_2/\Delta WR$

A Sample of $\dot{V}O_2$ and ST Changes in Multi-vessel Disease

$\Delta \dot{V}O_2/\Delta WR$ before ST dep

$\Delta \dot{V}O_2/\Delta WR$ after ST dep

$\dot{V}O_2$

ST level

ST -1.0mm

Total Extent Score 429/1000
Δ\(\dot{V}O_2/\Delta WR\) and Prognosis Heart Disease Patients

Parameters in Recovery Phase

\[ \tau_{\text{off}} \quad (T_{1/2}) \]

- Time constant (Half time) for \( \dot{\text{VO}_2} \) after the exercise
- Cardiac output decrease
- O₂ deficit during Ex.
- Heart rate decrease
- Parasympathetic nervous activity
$T_{1/2}$ and Severity of Heart failure

\( \tau_{\text{on}} \) and \( \tau_{\text{off}} \) in Low and High Intensity Step Exercise Test

23 MI patients did Low and high intensity exercise.

TC during exercise: \( \tau_{\text{on}} \)

TC during recovery: \( \tau_{\text{off}} \)

(1) The gas exchange kinetics were influenced by the intensity of exercise.

(2) \( \tau_{\text{off}} \) reflected \( \tau_{\text{on}} \) for \( \text{VO}_2 \) and \( \text{VCO}_2 \), but not for \( \text{VE} \).

Low: 80% of AT    High: AT+(peak-AT)x0.4

$T_{1/2}$ in Patients with and without Coronary Artery Disease

$\Delta VO_2 / \Delta WR$ after / before ST dep
Slope Ratio Across ST-dep

\[ p < 0.001 \]

$T_{1/2} \dot{V}O_2$ vs
Slope Ratio Across ST-dep

\[ r = -0.65 \quad p < 0.001 \]

Parasympathetic nervous activity ↓
Heart rate ↑

Endothelial function
Afterload ↓
Stroke volume ↑
Cardiac output ↑

Parasympathetic nervous activity ↑
Sympathetic ↓
Muscle pump ↓
Heart rate ↓
Venous return ↓
Stroke volume ↓
Cardiac output ↓

\[ \Delta VO_2/\Delta WR \uparrow \]

\[ T_{on} \downarrow \]

\[ T_{off}\cdot T_{1/2} \downarrow \]

Cardiac output
Blood redistribution

\[ \dot{V}O_2 \text{ at given WR} \uparrow \]

Itoh H, 2012