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Difference in Physiological Components of $VO_{2\ Max}$ During Incremental and Constant Exercise Protocols for the Cardiopulmonary Exercise Test

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Abstract. [Purpose] VO_2 is expressed as the product of cardiac output and O_2 extraction by the Fick equation. During the incremental exercise test and constant high-intensity exercise test, VO_2 results in the attainment of maximal O_2 uptake at exhaustion. However, the differences in the physiological components, cardiac output and muscle O_2 extraction, have not been fully elucidated. We tested the hypothesis that constant exercise would result in higher O_2 extraction than incremental exercise at exhaustion. [Subjects] Twenty-five subjects performed incremental exercise and constant exercise at 80% of their peak work rate. [Methods] Ventilatory, cardiovascular, and muscle oxygenation responses were measured using a gas analyzer, Finapres, and near-infrared spectroscopy, respectively. [Results] VO_2 was not significantly different between the incremental exercise and constant exercise. However, cardiac output and muscle O_2 saturation were significantly lower for the constant exercise than the incremental exercise at the end of exercise. [Conclusion] These findings indicate that if both tests produce a similar VO_2 value, the VO_2 in incremental exercise would have a higher ratio of cardiac output than constant exercise, and VO_2 in constant exercise would have a higher ratio of O_2 extraction than incremental exercise at the end of exercise.
Key words: Cardiopulmonary exercise test, Fick equation, Near-infrared spectroscopy

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INTRODUCTION

The cardiopulmonary exercise test (CPX) is the gold standard for evaluating the cause of exercise intolerance in patients with pulmonary and cardiac disease[1)]. Various tests are available, each being more or less suitable as a stressor of a particular component of the patient's pathophysiology. According to the American Thoracic Society/American College of Chest Physicians statement on CPX, the incremental exercise test (IET) is most widely used in clinical practice, but the constant high-intensity exercise test (CET) is gaining popularity because of its clinical applicability, particularly for monitoring responses to a spectrum of therapeutic interventions[2)].

The IET is used to calculate the aerobic threshold (AT)[3)], respiratory compensation point, and O_2 at peak work rate (PW; $VO_{2\ peak}$ or $VO_{2\ max}$)[4)]. On the other hand, the CET is useful for the analysis of gas exchange kinetics[5)] and dynamic hyperinflation[6)]. In addition, the change in time to the limit of tolerance in CET (also known as endurance time [ET]) at 75–80% load of PW has been shown to provide a more sensitive index of improvement than PW, or $VO_{2\ peak}$, in IET[1, 7–10)]. Most recent studies of CET have used an 80% load of PW[7, 8, 11–13)].

VO_2 is determined by the variables in the Fick equation:

$$VO_2 = Q \times (CaO_2 - CvO_2)$$

where Q is the cardiac output (CO; the product of heart rate [HR] and stroke volume [SV]), and CaO_2 and CvO_2 are the O_2 contents of arterial and mixed venous blood, respectively. Thus, VO_2 is expressed as the product of CO and O_2 extraction. The VO_2 value during CET reaches $VO_{2\ max}$, as assessed by IET, in the case of symptom limit and load (higher critical power) during CET[14, 15)]. However, we conjectured that even if both tests reach $VO_{2\ peak}$ at exhaustion, the component ratios are different because of the different exercise load patterns. We hypothesized that CET would reach a higher O_2 extraction at exhaustion because of progressive fatigue due to a higher ATP turnover rate[16, 17)]. Therefore, the purpose of this study was to compare the physiological changes during IET and CET at 80% load of PW in healthy human subjects.

SUBJECTS AND METHODS

Twenty-five young men (mean ± standard deviation [SD]; age = 23.3 ± 1.48 years, height = 169.4 ± 5.9 cm, body

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mass = 61.6 ± 6.4 kg) participated in this study. None of the subjects had routine fitness habits or were smokers. The subjects were informed of the potential risks and discomfort associated with the experiments before giving their written consent to participate in this study, which was approved by the ethical review committee of Kio University (Koryo-cho, Japan) and performed in accordance with the ethical principles of the Declaration of Helsinki.

Subjects reported to the laboratory on two separate occasions. An IET (work rate of 25 W/min, pedal revolution rate of 60 rpm/min) was performed using a braked cycle ergometer (Lode; Corival, Groningen, The Netherlands) on the first day of testing for the determination of estimated PW and other respiratory and metabolic factors. On a separate day, subjects returned to the laboratory for a CET at 80% of PW (pedal revolution rate of 60 rpm/min).

During both tests, we measured physiological responses, namely, ventilatory, metabolic, and cardiovascular responses, and muscle oxygenation. Ventilatory and metabolic variables were recorded breath-by-breath with a gas analyzer; cardiovascular responses were recorded with Finapres; and muscle oxygenation was recorded by near-infrared spectroscopy (NIRS).

Ventilatory and metabolic variables were recorded breath-by-breath with a computerized metabolic cart (MetaMax3B; Cortex, Leipzig, Germany). Oxygen uptake (VO_2), carbon dioxide output (VCO_2), minute ventilation (VE), the ventilator equivalent for carbon dioxide (VE/VCO_2), the ratio of dead space to tidal volume (VD/VT), end-tidal carbon dioxide pressure ($P_{ET}CO_2$), the respiratory exchange ratio (RER), and HR were determined from values averaged every 30 s.

Noninvasive continuous arterial systolic blood pressure (SBP) was measured beat-to-beat using the Finapres finger cuff (PORTEPRESS; FMS, Amsterdam, The Netherlands) on the index finger along with a height correction system attached to the top of the finger. The Finapres finger cuff uses the volume-clamp technique to measure finger arterial pressure[18]. Together with Beatscope software (Beatscope Easy; FMS, Amsterdam, The Netherlands), the Finapres finger cuff determines left ventricular SV; SV and HR values are used to calculate CO.

Oxygenation changes in the vastus lateralis muscle were evaluated by NIRS (BOM-L1TRW; Omegawave, Tokyo, Japan) at rest and during exercise. The NIRS probe was placed on the muscle approximately 14–20 cm above the knee joint. This instrument uses 3 light-emitting diodes (wavelengths: 780, 810, and 830 nm) and calculates the relative tissue levels of oxygenated hemoglobin (O_2Hb), deoxygenated hemoglobin (HHb), and total hemoglobin (THb) according to the Beer-Lambert law. The absorption coefficients of hemoglobin (Hb) are based on previously reported data[19], and individual values are proportional to the Hb levels. Levels of O_2Hb, HHb, and THb are expressed in μmol/L, but Hb concentrations are expressed in arbitrary units (AU) because they do not represent actual physical volumes. We calculated muscle O_2 saturation (SmO_2) from the O_2Hb and THb values with the following formula: SmO_2 (%) = (O_2Hb/THb) × 100.

Table 1. The results of exercise capacity

Variables	
Incremental exercise test (IET)	
VO_2max (L/min)	2.55±0.47
Peak Watt: PW (W)	202.9±22.6
HR max (bpm)	185.3±8.58
VO_2AT (L/min)	1.32±0.22
AT (W)	98.7±18.8
Constant high-intensity exercise test (CET)	
Work rate; 80% of PW (W)	162.3±18.1
Exercise tolerance time (sec)	634.3±73.7

Variables are presented as mean±SD. VO_2: oxygen uptake, HR: heart rate, AT: anaerobic threshold

Data analysis was performed using SPSS® version 19.0 statistical software (SPSS Inc., Chicago, IL, USA). The peak value for each of the measurements was defined as the mean of values acquired during the last 30 s of the test. All data are presented as the mean ± SD. Comparisons between the IET and CET results were analyzed using the paired t-test. A value of $p < 0.05$ was considered to be statistically significant.

RESULTS

Table 1 shows the exercise capacity, and Table 2 shows the results of the comparison of end-exercise responses of the IET and CET. All subjects completed the IET, reaching exhaustion levels; HR_{max} was 94.2 ± 4.23% of the age-predicted value, and RER was 1.17 ± 0.01[20]. The $VO_{2\ max}$ of IET was 2.55 ± 0.47 L/min, and there was no significant difference in VO_2 between the IET and CET. SBP and CO were significantly higher in the IET than in the CET ($p < 0.05$). HHb was significantly higher and SmO_2 was significantly lower in the CET than in the IET ($p < 0.01$).

DISCUSSION

In the present study, all subjects completed the IET and reached exhaustion levels[20]. Therefore, we believe that the IET was performed until exhaustion and that VO_2 reached $VO_{2\ max}$. In addition, there were no significant differences in VO_2 between the IET and CET. Therefore, we believe that VO_2 during the CET also reached $VO_{2\ max}$.

SBP and CO in the IET were significantly higher than in the CET. These results suggest that the IET might have a higher cardiac load than the CET. This hypothesis is supported by the fact that $VO_{2\ max}$ during the IET is mainly limited by the cardiovascular system in normal healthy subjects[21] and that muscle blood flow is correlated linearly and positively with work rate[22, 23]. Further, the IET would demand a greater O_2 delivery than the CET.

By the end of the exercises, HHb in the CET was higher than in the IET. HHb is considered to be similar to O_2 extraction[24, 25], and the increasing rate of HHb in venous occlusion can be used as a muscle O_2 consumption index[26]. In addition, SmO_2 was significantly lower in the CET than

Table 2. Comparison of exercise testing variables at end of exercise between IET and CET

Variables	IET	CET
VO_2 (L/min)	2.55±0.47	2.63±0.41
VCO_2 (L/min)	2.92±0.43	2.71±0.37*
VE (L/min)	68.9±12.3	67.5±12.1
VE/VCO_2	24.8±3.18	26.7±2.92*
VD/VT	0.11±0.03	0.13±0.04*
$P_{ET}CO_2$	45.2±6.26	42.5±4.30*
RER	1.17±0.10	1.21±0.12
HR (bpm)	185.3±8.58	186.5±5.01
SBP (mmHg)	199.09±16.67	186.01±24.27*
SV (ml)	96.93±17.85	82.2±20.07
CO (L/min)	16.1±3.23	13.23±3.02*
TPR	0.68±0.28	0.57±0.25
O_2Hb (A.U.)	7.63±1.68	7.24±1.88
HHb (A.U.)	9.07±2.86	9.53±2.74**
THb (A.U.)	16.8±2.90	16.77±3.21
SmO_2 (%)	46.4±0.09	43.6±0.09**

p value of the paired t-test: *$p<0.05$, **$p<0.01$
Variables are presented as mean±SD. Each value was obtained at the end of exercise. IET: incremental exercise test, CET: constant high-intensity exercise test, VO_2: oxygen uptake, VCO_2: carbon dioxide output, VE: minute ventilation, VE/VCO_2: ventilator equivalent for carbon dioxide, V_D/V_T: ratio of dead space to tidal volume, $P_{ET}CO_2$: end-tidal carbon dioxide pressure, RER: respiratory exchange ratio, HR: heart rate, SBP: arterial blood pressure, SV: stroke volume, CO: cardiac output, O_2Hb: oxygenated hemoglobin, HHb: deoxygenated hemoglobin, THb: total hemoglobin, SmO_2: muscle oxygen saturation

in the IET. SmO_2 signals provide a reliable estimate of the dynamic balance between O_2 supply and O_2 consumption in the area of investigation[27]. These findings suggest that the CET has a higher muscle O_2 extraction rate than the IET at the end of exercise. Interestingly, the findings may be explained by HHb kinetics at the end of the tests. At the end of the IET, the HHb response displays a slowdown or plateau point[28–30], whereas at the end of the CET, the HHb response displays a progressive rise following the HHb "slow component"[31, 32]. We found that the HHb showed these trends in the present study (Fig. 1). The HHb slow component has been reported to be strongly correlated with lactate concentrations during running[33]. Lactic acidosis favors a greater release of O_2 from Hb due to the rightward displacement of the oxyhemoglobin dissociation curve (Bohr effect), consequently facilitating O_2 extraction from the blood. The physiological mechanisms of these HHb responses in relation to the IET and CET are still not fully understood and cannot be explained using the results of the present study, but it is likely that metabolic changes in the muscles play a role.

In conclusion, the present study demonstrated that there are differences in physiological responses between the IET and CET at the end of exercise. Although both exercise tests induced similar responses with respect to VO_2, the factors determining VO_2 changes were different: cardiac load was lower and muscle O_2 extraction was higher in CET than IET. These results suggest that if both tests produce a similar VO_2 value, VO_2 in the IET would have a higher ratio of cardiac output than the CET, and VO_2 in the CET would have a higher ratio of O_2 extraction than the IET at the end of exercise. These findings may be useful for further assessment of individual exercise-limiting factors.

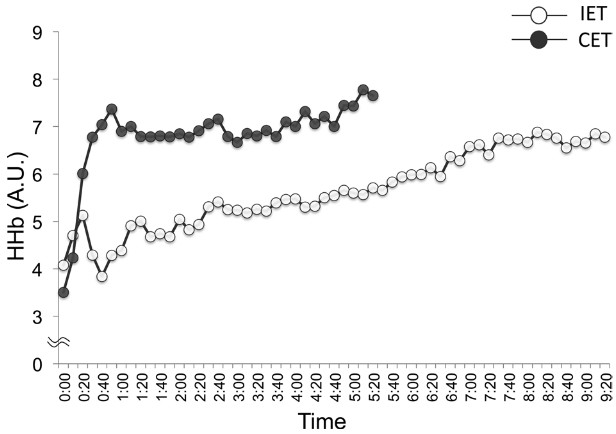

Fig. 1. An example of deoxygenated hemoglobin (HHb) kinetics during exercise tests in a representative subject.

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