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Determination of both the time constant of \dot{V}_{O_2} and $\Delta\dot{V}_{O_2}/\Delta W$ from a single incremental exercise test: validation and repeatability

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Summary

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A single incremental cycle exercise test including a steady-state load, combined with respiratory gas exchange, was performed with the objective of determining the time constant ($\tau\dot{V}_{O_2}$) and the amount of oxygen required at each load ($\Delta\dot{V}_{O_2}/\Delta W$) by using a novel equation. The protocol was validated using four exercise tests at different constant loads and conventionally fitted mono-exponential functions to determine $\tau\dot{V}_{O_2}$, and interpolation of \dot{V}_{O_2} versus load to determine $\Delta\dot{V}_{O_2}/\Delta W$. No significant differences were seen between the means of either $\tau\dot{V}_{O_2}$ or $\Delta\dot{V}_{O_2}/\Delta W$ determined with the two protocols. The correlation coefficient was 0.62 for $\tau\dot{V}_{O_2}$ and 0.48 for $\Delta\dot{V}_{O_2}/\Delta W$. The absolute differences (2 SD) were 11.6 s for $\tau\dot{V}_{O_2}$ and 1.1 ml min⁻¹ W⁻¹ for $\Delta\dot{V}_{O_2}/\Delta W$. The equations were compared in the same steady-state test and good agreement of $\tau\dot{V}_{O_2}$ was obtained ($R = 0.99$). The 5–6-week repeatability (incremental test) was evaluated. No statistical differences were seen between the mean of the repeated tests. The difference between the tests (2 SD) were 20 s for $\tau\dot{V}_{O_2}$ and 1.2 ml min⁻¹ W⁻¹ for $\Delta\dot{V}_{O_2}/\Delta W$. In conclusion, $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ can be determined from a single incremental test. The validation showed an acceptable agreement, although the variations in absolute values were not negligible. This could partly be explained by the natural day-to-day variation and fluctuations in incoming raw data. The test–retest variation in absolute values was considerable, which must be taken into account when using $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ for evaluation of aerobic function.

Introduction

The exercise capacity and aerobic function are commonly defined by measuring maximal oxygen uptake ($\dot{V}_{O_{2max}}$). To gain information on the functional capacity, the increasing contribution of the anaerobic metabolism can be determined from gas exchange responses by using different thresholds during an incremental cycle exercise test (Wisén & Wohlfart, 2004). In addition to these measurements the time constant of \dot{V}_{O_2} ($\tau\dot{V}_{O_2}$) and the amount of O_2 required at each load ($\Delta\dot{V}_{O_2}/\Delta W$) give improved information on the aerobic profile. The $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ are useful in cardiac, pulmonary and peripheral diagnostics, as described by several investigators (Hansen et al., 1987; Itoh et al., 1989, 1992; Whipp & Ward, 1990; Koike et al., 1992; Mettaufer et al., 2000; Toyofuku et al., 2003). Both the $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ can be of importance in characterizing performance capacity or in the evaluation of exercise (Hagberg et al., 1980; Babcock et al., 1994; Phillips et al., 1995).

The time constant of \dot{V}_{O_2} reflects the time required for the body functions to adjust to a change in workload. This process includes the time for the oxygen uptake in the muscle cell but also the time it takes to detect this uptake at the measuring site, which is the lung ventilation. In this study, we define the time constant as a functional constant of the oxygen uptake with the transfer delay included. Endurance training can reduce $\tau\dot{V}_{O_2}$, while physical de-conditioning prolongs $\tau\dot{V}_{O_2}$ (Hagberg et al., 1980; Chilibeck et al., 1996; Cooper & Storer, 2001). The $\Delta\dot{V}_{O_2}/\Delta W$ reflects the efficiency of the body in utilizing oxygen to produce external work during cycling. Recently, Barstow et al. (2000) showed that a high proportion of fibre type I gave an increased $\Delta\dot{V}_{O_2}/\Delta W$. It has also been shown that aerobically fit subjects, have an increased $\Delta\dot{V}_{O_2}/\Delta W$, while physical de-conditioning or cardiopulmonary diseases decrease $\Delta\dot{V}_{O_2}/\Delta W$ (Itoh et al., 1989; Koike et al., 1992; Mallory et al., 2002).

The most commonly used method to determine the time constant is based on calculations of a mono-exponential function describing the rise and adaptation of \dot{V}_{O_2} in a single

steady-state exercise test (Wasserman et al., 1994a; Cooper & Storer, 2001). This model is used primarily to determine the time constant for exercise in the moderate intensity domain, while at higher intensities there is an addition of a slow component of \dot{V}_{O_2} (Roston et al., 1987; Whipp et al., 2002; Ozyener et al., 2003). The amount of O_2 required at each load, is commonly determined either from a constant load test (Åstrand & Rodahl, 1986) or from a linear function of \dot{V}_{O_2} versus load obtained during an incremental exercise test. The latter is performed either by fitting a line to the data from the entire ramp test (Hansen et al., 1987) or by fitting a line to different segments of the data collected (Hansen et al., 1988; Lucia et al., 2002). It has also been shown that various workload increment protocols give different values of $\Delta\dot{V}_{O_2}/\Delta W$ (Hansen et al., 1988). Additionally, the determination of the work efficiency was shown to be different above and below the lactate threshold (Roston et al., 1987). The requirement of several tests to determine the aerobic profile is a disadvantage; it would be more desirable to be able to determine several parameters in a single test. This was recognized early on and equations to determine aerobic parameters from a ramp exercise test were introduced (Whipp et al., 1981). We have a slightly different approach adding a period of a constant load into the conventional ramp exercise protocol. This allows determination of multiple parameters at the same time such as several thresholds (such as the lactate and ventilatory threshold as well as the point $RER = 1.0$ (Wisén & Wohlfart, 2004) submaximal values, maximal values (Wergel-Kolmert et al., 2002) as well as $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$. All these variables combined give improved information of the aerobic capacity, which should be useful, both in exercise prescription, and evaluation of an exercise period.

The repeatability of measurements of $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ using ramp exercise tests has been reported as mean and SD (Whipp et al., 1981). The repeatability of $\tau\dot{V}_{O_2}$ and the η (the work efficiency) has been reported earlier (Hughson & Inman, 1986; Swansson & Hughson, 1988) but is not directly applicable to the present study which is based on another exercise protocol and other parameters. For repeated tests it is of clinical value to determine the repeatability in absolute values and to gain knowledge about long-term variations. The rationale for this is to better be able to, i.e. evaluate physical training effects.

The aim of this study was to implement a new method using equations to determine: (i) the time constant of \dot{V}_{O_2} and (ii) the $\Delta\dot{V}_{O_2}/\Delta W$, from a single exercise test. The new method was validated in this study by comparison with a conventional

method. The 5–6-week repeatability of the measurements was studied in a group of healthy men.

Method

Test groups

Two test groups were recruited. In order to validate the method, 10 healthy men and women (group I) performed two exercise tests with different protocols on two successive days. These subjects were recruited from the medical staff by internal advertisement. A medical examination was performed before the test. To analyse the repeatability of the measurements 19 healthy non-smoking men (group II) performed a second test 5–6 weeks after the first test. The study group II, test procedure and inclusion pretest were the same as described previously (Wergel-Kolmert et al., 2002; Wisén & Wohlfart, 2004). The Ethics Committee of Lund University approved the studies.

All the participants were instructed not to take part in any sporting activities 48 h before the test, not to eat 3 h before the test and not to drink coffee or any beverage containing caffeine 2 h before the test. The members of group I were also asked not to smoke 2 h before the test (all subjects in group II were non-smokers by the inclusion criteria). The members of group II were asked not to alter their general level of activity between the test sessions. Prior the test it was ascertained whether the subject had followed the pretest instructions.

Body weight and height were determined and the body mass index (BMI) was calculated. Characteristics are given in Table 1.

Test measurements

All the tests were performed at the same place, with the same equipment and supervised by the same investigators.

The exercise test was performed on an ergometer cycle (Rodby 380; Siemens-Elcoma, Solna, Sweden). The settings of the handlebars and seat were individually adjusted, documented and applied on the retest occasions. A pedalling rate of 60 rpm was maintained during the test. For the men the test started with a workload of 50 W and increased by 5 W/20 s, while for the women the test started at 30 W and the load was increased by 5 W/30 s, which are the protocols used in the clinical routine. A period of 4 min constant load was included in the incremental exercise test, which is necessary to be able to calculate $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ with the equations proposed. In group I, the constant load was set at a respiratory

Table 1 Characteristics of the subjects. In group I, the new method was validated against a conventional method, $n =$ five men and five women. In group II, the new method was tested for repeatability, $n =$ 19 men. Weight and BMI are given for each of the repeated tests in group II.

Group	Age (years)	Height (cm)	Weight (kg)	BMI
I	42.9 (10.8) 26–55	174 (10) 160–197	70.8 (12.4) 59–98	23.3 (1.8) 20–26
II	27.4 (7.0) 20–48	180 (6) 167–189	75.6 (7.3) 66–92/75.7 (7.5) 66–93	23.4 (2.2) 20–27/23.6 (2.2) 20–28

Mean (SD) and range of selected variables are given.

exchange ratio ($RER = \dot{V}_{CO_2}/\dot{V}_{O_2}$) slightly below 1.0 determined on basis of the online screen report of the RER values. In group II, the load was set at a constant at a level of 40% of the maximal load achieved in the inclusion pretest (which was below RER 1.0). According to the clinical routine, ECG was monitored continuously and blood pressure (BP) and the rating of perceived exertion (RPE) were determined every 2 min (Borg, 1982). In addition, the subjects in group I performed a 6-min, constant-load cycling test at four different loads. The level of the loads was individually determined from the ramp exercise test and in general the difference between the four loads was 30 or 50 W. One load was above PX (the point of crossing of \dot{V}_{O_2} and \dot{V}_{CO_2} where $RER = 1.0$ for the last time during the incremental test, Wisén & Wohlfart, 2004), one load was \leq PX, and two loads were below PX. It was ascertained that the resting levels of \dot{V}_{O_2} and RER were reached between each of the constant-load tests.

Continuous respiratory gas analysis and volume measurements were performed breath-by-breath during the test, as described previously (Wisén & Wohlfart, 2004). In short, a facemask placed tightly over the mouth and nose of the test subject was connected to an Oxycon[®] gas analyser (Jaeger Oxycon Champion, Höchberg, Germany). Flow and gas concentration were measured online. Sitting on the cycle, data collection started with a 2-min resting phase, to allow the participant to become accustomed to breathing through the mask. After the test, the participant was asked to remain sitting on the cycle for 3 min, still with the facemask in place.

Volume and gas concentration calibration were carried out every day according to the instruction manual, and was supervised by medical engineers. Before each test, an automatic zero adjustment of the gas analysers was performed.

\dot{V}_{O_2} in relation to load and time

\dot{V}_{O_2} during a steady-state tests is higher than the \dot{V}_{O_2} during incremental test at the same load, because \dot{V}_{O_2} lags behind the increase in work rate during the incremental test. Thus, during the incremental exercise test it was assumed that \dot{V}_{O_2} at each moment in time strived to reach a steady-state value of \dot{V}_{O_2} ($\dot{V}_{O_{2ss}}$) and that this steady-state value was linearly related to the load (P) at that moment:

$$\dot{V}_{O_{2ss}} = b \cdot P + \dot{V}_{O_{2rest}} \quad (1)$$

where b is the slope of the relation between \dot{V}_{O_2} and load, i.e. $\Delta\dot{V}_{O_2}/\Delta W$.

The kinetics of \dot{V}_{O_2} during the ramp exercise was described by a differential equation, where \dot{V}_{O_2} was assumed to be a function of both time and load according to,

$$d\dot{V}_{O_2}/dt = 1/\tau \cdot (\dot{V}_{O_{2ss}} - \dot{V}_{O_2}) \quad (2)$$

where τ is the time constant of \dot{V}_{O_2} .

Using time series where each observation was a function of the previous observation, solved the equation:

$$\dot{V}_{O_2}(n + 1) = \Delta t/\tau[\dot{V}_{O_{2ss}}(n) - \dot{V}_{O_2}(n)] + \dot{V}_{O_2}(n) \quad (3)$$

where Δt is the time interval between each recorded value.

The parameters $\dot{V}_{O_{2rest}}$, $\tau\dot{V}_{O_2}$ and b ($=\Delta\dot{V}_{O_2}/\Delta W$) were determined by minimizing the difference between the function (method of least squares) and the recorded values using Matlab[®] (The Math Works Inc., Natick, MA, USA). Values of \dot{V}_{O_2} from start of the test to the level of PX were used. The slope of $\Delta\dot{V}_{O_2}/\Delta W$ is highly dependent on the recorded value of \dot{V}_{O_2} at rest and \dot{V}_{O_2} at steady state. The shape of the curve between $\dot{V}_{O_{2rest}}$ and $\dot{V}_{O_{2ss}}$ determines the value of $\tau\dot{V}_{O_2}$. The values of the parameters were obtained together with graphs for each of the subjects tested, using Matlab[®].

The conventional method of determining the time constant of \dot{V}_{O_2} is to perform one or more constant load tests and then apply a mono-exponential equation (Cooper & Storer, 2001):

$$\dot{V}_{O_2} = A(1 - e^{-t/\tau}) + b \quad (4)$$

where $A + b$ is \dot{V}_{O_2} at steady state and b is \dot{V}_{O_2} at rest. It has been proposed that the first part of the transition should be excluded and the function applied with a time delay (Paterson & Whipp, 1991). To explore the influence of this we in addition calculated the time constant excluding the first values corresponding to 0–30 s.

The conventional method of determining the oxygen expenditure per unit workload, $\Delta\dot{V}_{O_2}/\Delta W$, during dynamic conditions, as incremental exercise test, is to use linear functions (Hansen et al., 1988). Another possibility, described previously, is to interpolate between \dot{V}_{O_2} measurements achieved at several constant loads (Åstrand & Rodahl, 1986). In this study, we interpolated the values obtained from $\dot{V}_{O_{2ss}}$ for each of the four loads tested and $\dot{V}_{O_{2rest}}$. The $\dot{V}_{O_{2rest}}$ values were determined from the means of the four registered values in the resting position on the cycle prior to the exercise. In order to explore if any differences in the slopes ($\Delta\dot{V}_{O_2}/\Delta W$) between different intensities of the test exist, we interpolated values obtained below the lactate threshold as well as the values obtained \leq PX. The lactate threshold were determined using crossing of the derivatives (DX) where the rate of \dot{V}_{CO_2} increase just exceeds the rate of \dot{V}_{O_2} increase during the exercise test (for details see Wisén & Wohlfart, 2004).

Statistics

Data were collected breath-by-breath using the gas analyser (Oxycon[®]), and time-based averages (10 s) (whole-breath average) were obtained as raw data and were further analysed on a personal computer. Signal processing, analysis of data, and generation of preliminary graphs were performed in Matlab[®]. The mean, SD and range of selected variables were calculated. The repeatability of the measurements obtained from each of the exercise sessions was analysed by plotting the differences between the individual measurements against their mean (Bland & Altman, 1986). The mean of the differences between the repeated measurements was calculated, and the hypothesis of

zero bias was tested using Student's *t*-test. A significance level of $P = 0.05$ was chosen. Graphs were created in Sigmaplot® (SPSS Inc., Chicago, IL, USA).

Results

The two exercise protocols

During the first exercise test (Fig. 1) \dot{V}_{O_2} started from a resting level and increased to match the increasing loads. At fixed load \dot{V}_{O_2} reached into a plateau. Then there was a linear increase as the load rose towards a maximum. After this, the load was again zero and \dot{V}_{O_2} fell towards $\dot{V}_{O_{2rest}}$. It can be seen in Fig. 1a that the proposed equation (Eq. 3, line) followed the original \dot{V}_{O_2}

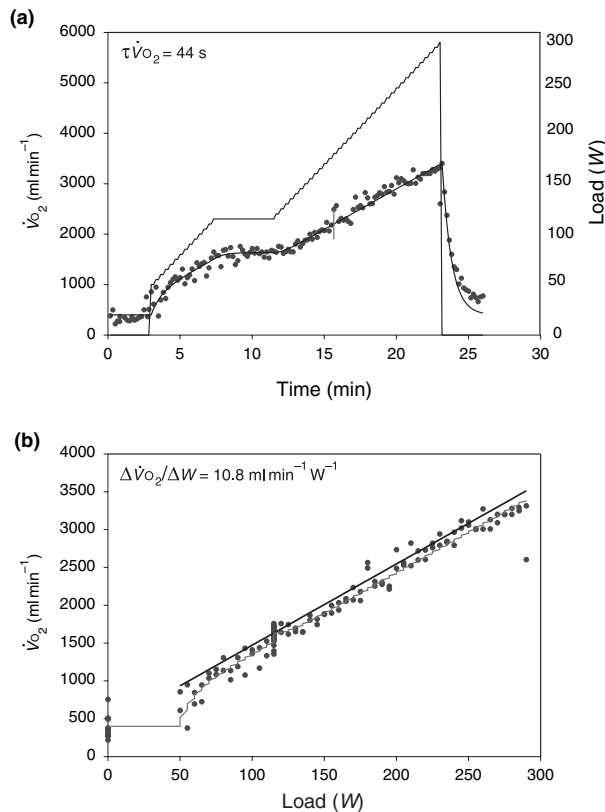


Figure 1 (a) A representative recording of the relation between \dot{V}_{O_2} and time during the incremental exercise test. The load (upper solid line) started at 50 W and increased by 15 W min⁻¹ – a 4-min constant level was also included. It can be seen that the fitted curve (solid line) based on Eq. (3) followed the measured \dot{V}_{O_2} well. The equation was based on values up to PX (vertical line), and extrapolated above PX. The time constant ($\tau\dot{V}_{O_2}$) estimated from Eq. (3), is given in the figure. (b) Measured \dot{V}_{O_2} (dots) and \dot{V}_{O_2} obtained from the fitted Eq. (3) (light solid line) versus load during the incremental exercise test, together with the steady-state \dot{V}_{O_2} ($\dot{V}_{O_{2ss}}$, heavy solid line) calculated from Eq. (1). It can be seen that during the incremental exercise \dot{V}_{O_2} was lower than the calculated values of $\dot{V}_{O_{2ss}}$, except during the 4-min constant load, where the measured values of \dot{V}_{O_2} increased to the level of $\dot{V}_{O_{2ss}}$. The values of $\Delta\dot{V}_{O_2}/\Delta W$ estimated from Eq. (1) is given in the figure. Equations (2) and (3) were formulated based on the assumption that \dot{V}_{O_2} at each moment during the incremental test strived to reach $\dot{V}_{O_{2ss}}$, as a first-order time-dependent process.

(dots) during the exercise and the calculated $\tau\dot{V}_{O_2}$ is given. The proposed equation describes the striving of \dot{V}_{O_2} to reach steady state. This is shown in Fig. 1b where the dots represent original \dot{V}_{O_2} data and the line $\dot{V}_{O_{2ss}}$ in relation to load, according to Eq. (1). The slope ($\Delta\dot{V}_{O_2}/\Delta W$) is given.

The second exercise protocol depicted in Fig. 2, showing four different steady-state exercise tests. An exponential function (Eq. 4) followed the original \dot{V}_{O_2} recordings in each of the panels and the associated values of $\tau\dot{V}_{O_2}$ are shown. Calculations of $\tau\dot{V}_{O_2}$ with the first 10 s excluded showed exactly the same values as the calculation with this time interval included. Excluding 30 s (at high intensity where RER was ≤ 1.0) showed no difference compared with the calculation with this time period included [the mean of the difference (SD), excluded – included, was -0.7 (1.3)]. \dot{V}_{O_2} at each steady state (using Eq. 4) was related to load in Fig. 3 and the slope ($\Delta\dot{V}_{O_2}/\Delta W$) was calculated using these four loads. No differences were seen between slope calculations including two loads (below DX, i.e. the lactate threshold) and the calculation including all four loads. The mean of the differences (SD) (calculation based on two loads – calculation based on four loads) were 0.1 (0.05). Neither were there differences between calculations based on three (below RER = 1.0) and four loads [mean of the difference (SD) 0 (0.3)].

Ten subjects (group I) performed the incremental exercise test and on the following day the four steady-state tests. The mean \dot{V}_{O_2} at each of the four loads corresponded to 44, 59, 73 and 91% of mean $\dot{V}_{O_{2max}}$. The two lower loads were below DX. As determined from the incremental exercise test; the highest load was chosen to be above PX (the point of crossing of \dot{V}_{O_2} and \dot{V}_{CO_2} where RER = 1.0 for the last time during the incremental test) mean \dot{V}_{O_2} at PX was 75% of $\dot{V}_{O_{2max}}$.

The values of $\tau\dot{V}_{O_2}$ obtained in the incremental exercise test (using Eq. 3) were compared with $\tau\dot{V}_{O_2}$ at each of the four different loads (using Eq. 4) (Table 2). As can be seen, $\tau\dot{V}_{O_2}$ from the incremental exercise test and the values from the high load are the most alike. It can also be seen that the lowest value of $\tau\dot{V}_{O_2}$ was associated with the low load and the highest value with the highest load. In the latter case, \dot{V}_{O_2} often continued to rise slightly during the 6 min constant load. Values of $\tau\dot{V}_{O_2}$ from the incremental exercise test and from the high load had a correlation coefficient of 0.62. The corresponding correlation for $\Delta\dot{V}_{O_2}/\Delta W$ between the two protocols was 0.48. No significant difference was seen between the means of either $\tau\dot{V}_{O_2}$ or $\Delta\dot{V}_{O_2}/\Delta W$ between the two protocols. The differences between the values achieved from each of the methods were plotted against the means for each individual (Fig. 4). Two SD of the difference were calculated: 11.6 s for $\tau\dot{V}_{O_2}$ and 1.1 ml min⁻¹ W⁻¹ for $\Delta\dot{V}_{O_2}/\Delta W$. These variations can be explained by (i) the difference in exercise protocol, (ii) the natural day-to-day variation and (iii) the difference in the equations used. The latter was tested by calculating $\tau\dot{V}_{O_2}$ for each subject at each constant load using Eqs (3) and (4). The correlation coefficient was high (0.99), but the mean value of $\tau\dot{V}_{O_2}$ calculated with Eq. (4) was 5 s shorter than that found using Eq. (3).

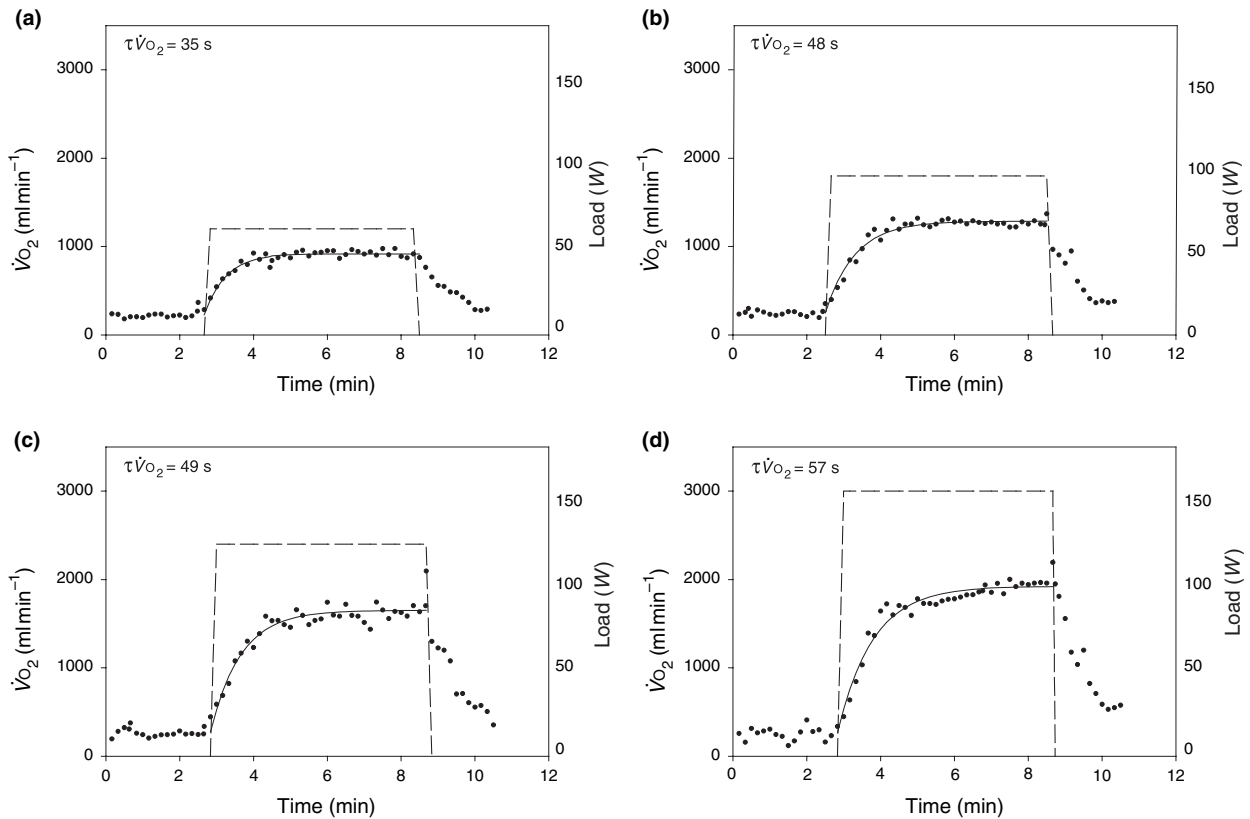


Figure 2 Four typical recordings of \dot{V}_{O_2} (dots) and relation between \dot{V}_{O_2} and time during the constant-load exercise test (dotted line). The load was set at 60, 90, 120 and 150 W in (a), (b), (c) and (d), respectively. As can be seen, \dot{V}_{O_2} increased to a steady state to match the load. The exponential function from Eq. (4) (solid line) followed the raw data. $\tau\dot{V}_{O_2}$ calculated from Eq. (4) is given in each of the panels.

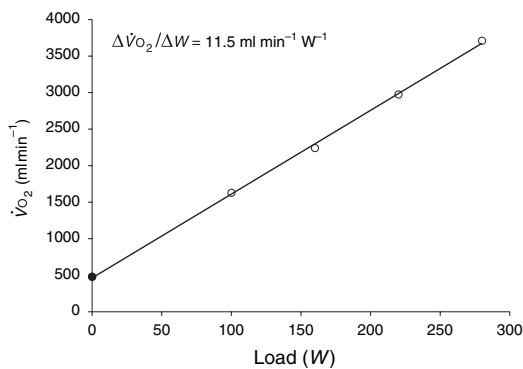


Figure 3 \dot{V}_{O_2} (dots) versus load based on mean of $\dot{V}_{O_{2rest}}$ from the four tests (filled circle) and \dot{V}_{O_2} at each of the four constant load tests (open circles). A linear relation is apparent and the value of $\Delta\dot{V}_{O_2}/\Delta W$ is given in the figure.

Repeatability

The repeatability of $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ measurements using the incremental test and Eq. (3) was tested in a group of 19 men (group II). Body weight did not vary between the repeated tests, which were 5–6 weeks apart (Table 1).

The mean values of $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ were not significantly different between the repeated tests (Table 3). However,

the correlation coefficients between the tests were low for $\tau\dot{V}_{O_2}$ ($r = 0.39$) and somewhat higher for $\Delta\dot{V}_{O_2}/\Delta W$ ($r = 0.47$). Likewise the mean values of both $\dot{V}_{O_{2rest}}$ and $\dot{V}_{O_{2max}}$ were not significantly different between the tests. The correlation coefficients were higher for $\dot{V}_{O_{2rest}}$ and much higher for $\dot{V}_{O_{2max}}$. The mean values (SD) of the two tests were 4.6 (0.6) and 39 (6.3) $\text{ml min}^{-1} \text{kg}^{-1}$ of $\dot{V}_{O_{2rest}}$ and $\dot{V}_{O_{2max}}$, respectively.

The 5–6-week repeatability of $\tau\dot{V}_{O_2}$ is shown in Fig. 5a where the difference in $\tau\dot{V}_{O_2}$ is plotted against the mean value for each subject. The repeatability, ± 2 SD as shown by the two horizontal lines, was 20 s. It can be seen that the variation in $\tau\dot{V}_{O_2}$ was not dependent on the magnitude of $\tau\dot{V}_{O_2}$. The corresponding repeatability of $\Delta\dot{V}_{O_2}/\Delta W$ was 1.2 $\text{ml min}^{-1} \text{W}^{-1}$ (Fig. 5b).

Also given in Table 3 are 1 SD values of the individual differences between the repeated tests. The corresponding SD values were 0.7 and 2.9 $\text{ml min}^{-1} \text{kg}^{-1}$ for $\dot{V}_{O_{2rest}}$ and $\dot{V}_{O_{2max}}$, respectively.

Discussion

It is an advantage to be able to determine aerobic function including capacity from a single exercise test. We have earlier described the special incremental exercise protocol used, including a resting period, an increasing load and a period of constant load followed by increasing load to maximum. This

Table 2 Values of $\tau\dot{V}_{O_2}$ (s), $\Delta\dot{V}_{O_2}/\Delta W$ ($\text{ml min}^{-1} \text{W}^{-1}$) and $\dot{V}_{O_{2\max}}$ (ml min^{-1}) from the ramp exercise test and from the four different constant loads for each of the subjects ($n = 10$, subject 1–5 are men, subject 6–10 are women).

Subject	Ramp exercise test			6 min constant load				
	$\tau\dot{V}_{O_2}$	$\Delta\dot{V}_{O_2}/\Delta W$	$\dot{V}_{O_{2\max}}$	$\tau\dot{V}_{O_2}$				$\Delta\dot{V}_{O_2}/\Delta W$
				Low	Moderate	High	Very high	
1	39	10.6	2701	44	49	46	57	11.8
2	44	11.1	4488	30	37	51	52	11.5
3	32	10.7	2937	18	45	44	56	11.2
4	40	10.9	3595	33	37	40	44	10.6
5	45	12.0	2976	39	35	43	38	11.6
6	46	11.1	1540	44	49	39	50	11.4
7	50	11.9	1723	26	59	47	56	11.4
8	32	10.3	2234	31	33	33	46	10.1
9	41	11.3	2008	35	48	49	57	11.3
10	27	11.1	2574	29	33	33	46	11.3
Mean (SD)	39.6 (7.3)	11.1 (0.5)	2678 (890)	32.9 (8.1)	42.5 (8.8)	42.1 (7.0)	48.8 (8.7)	11.3 (0.5)

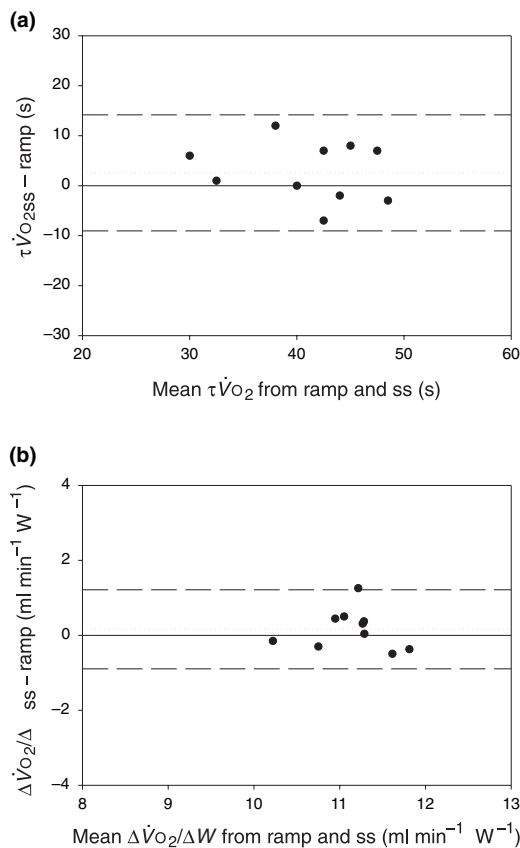


Figure 4 (a) The difference in $\tau\dot{V}_{O_2}$ calculated from the constant-load test (steady state, ss) using Eq. (4) and from the incremental test (ramp) using Eq. (3) versus the mean of $\tau\dot{V}_{O_2}$ from both the tests. Each subject ($n = 10$) is represented by a dot. The mean difference (dotted line) and 2 SD (pairs of horizontal dashed lines) was 2.6 (11.6) s. (b) The difference in $\Delta\dot{V}_{O_2}/\Delta W$ between the constant-load tests and the incremental test for each individual. The mean difference (dotted line) and 2 SD (pairs of horizontal dashed lines) was 0.2 (1.1) $\text{ml min}^{-1} \text{W}^{-1}$.

exercise protocol together with the equation described provides the possibility to calculate $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ in a new and

Table 3 $\tau\dot{V}_{O_2}$, $\Delta\dot{V}_{O_2}/\Delta W$, $\dot{V}_{O_{2\text{rest}}}$ and $\dot{V}_{O_{2\max}}$ at test–retest.

	$\tau\dot{V}_{O_2}$ (s)	$\Delta\dot{V}_{O_2}/\Delta W$ ($\text{ml min}^{-1} \text{W}^{-1}$)	$\dot{V}_{O_{2\text{rest}}}$ (ml min^{-1})	$\dot{V}_{O_{2\max}}$ (ml min^{-1})
Test 1/test 2	38/38	10.80/10.90	340/356	2910/2963
Mean (SD)	38 (8)	10.8 (0.5)	348 (50)	2936 (410)
SD between the tests	10	0.6	56	166
Correlation coefficient	0.39	0.47	0.52	0.92

Mean values of test 1 and 2 and means (SD) for the two tests are given, as well as the correlation between the two tests. 1 SD of the individual differences between the tests is presented ($n = 19$).

more versatile manner. In addition, at the constant load, extra measurements like blood samples can be made. Submaximal values (like \dot{V}_{O_2} , VE, HR, etc.) can be followed which can be useful when evaluating effects of, e.g. an exercise period. The increased contribution of anaerobic metabolism can be quantified as we have described in a previous study where we used different analyse techniques but the same exercise protocol (Wisén & Wohlfart, 2004). Altogether it is possible to get an integrated analysis of aerobic function using this protocol. However, a disadvantage could be that the test duration will be longer than if a continuous ramp is used.

Calculations of $\Delta\dot{V}_{O_2}/\Delta W$ are based on the assumption that the oxygen cost versus workload is linear. It has also been shown that the oxygen cost per unit workload is higher for steady state than for incremental exercise (Wasserman et al., 1994b). Based on this we included a steady-state load in the incremental protocol to be able to determine $\dot{V}_{O_{2\text{ss}}}$ (from the resting value of \dot{V}_{O_2} and the value reached at the end of the constant load, see Method). The assumption was that \dot{V}_{O_2} at each moment in time strived to reach the steady state by means of a first-order, time-dependent process. A similar approach has earlier been described (Whipp et al., 1981). We chose to register raw data at 10 s intervals. Other sampling rates are

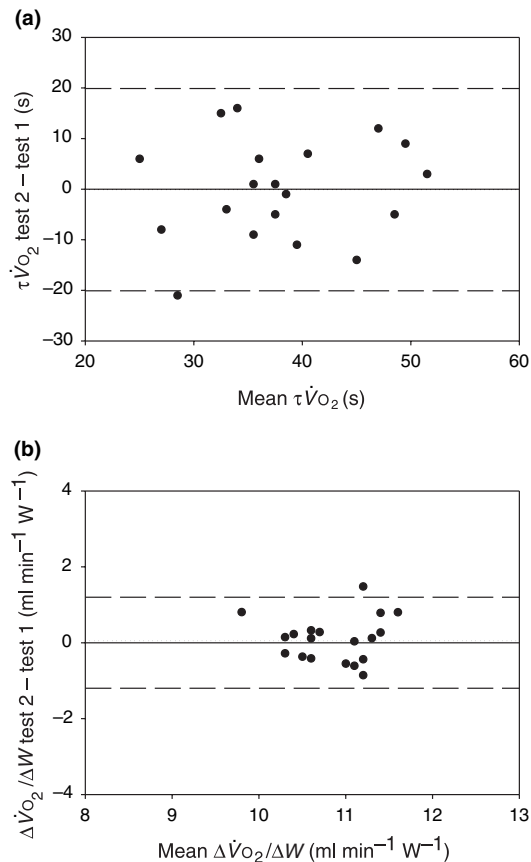


Figure 5 Values of $\tau\dot{V}_{O_2}$ (a) and $\Delta\dot{V}_{O_2}/\Delta W$ (b) from the two repeated incremental exercise tests 5–6 weeks apart. The difference (test 2 – test 1) versus the mean of the tests for each individual is shown (dots) ($n = 19$). The mean differences were zero for both $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ [solid lines in (a) and (b)]. The difference (2 SD) for $\tau\dot{V}_{O_2}$ was 20 s, as shown by the pair of horizontal dashed lines in (a). The difference (2 SD) for $\Delta\dot{V}_{O_2}/\Delta W$ was 1.2 ml min⁻¹ W⁻¹ and is shown in an analogous way in (b).

possible even collection breath-by-breath. We also decided to apply the equation only up to PX during the incremental exercise test. We have chosen to include all four loads at the determination of $\Delta\dot{V}_{O_2}/\Delta W$. This was based on that we did not find any differences between the cases when the slope was calculated using the two loads below the lactate threshold, the three loads below PX or when all four loads were included. In contrast, it has been shown that the $\Delta\dot{V}_{O_2}/\Delta W$ is different above the lactate threshold (Casabury et al., 1989; Paterson & Whipp, 1991) and that the determination of $\Delta\dot{V}_{O_2}/\Delta W$ during dynamic conditions using linear functions gives varying results, depending on which part of the curve that is analysed (Hansen et al., 1988; Xu & Rhodes, 1999). Differences of the efficiency (in the unit $\dot{V}_{O_2} \text{ min}^{-2}$) in ramp exercise tests with different step increase have been observed (Swansson & Hughson, 1988). However, if these efficiencies are transformed to $\Delta\dot{V}_{O_2}/\Delta W$ the differences are minor at lower and moderate loads, and only at extreme ramp inclinations, such as 80 W min⁻¹, $\Delta\dot{V}_{O_2}/\Delta W$ was reduced slightly.

It has earlier been shown that at constant load exercise tests at an intensity above the lactate threshold (which correspond to DX determined in this study), \dot{V}_{O_2} continues to slowly increase, which prolongs the $\tau\dot{V}_{O_2}$ (Roston et al., 1987; Casabury et al., 1989). In contrast we found that the slow increase appeared only at loads above PX. It has been suggested that there is a lag time before \dot{V}_{O_2} starts to increase (Paterson & Whipp, 1991). Applying the mono-exponential equation with a delayed onset to workload change was examined. However, it is clear from Fig. 2 that there was no lag time. Neither were there any differences in $\tau\dot{V}_{O_2}$ when one or three data points (corresponding to 10 or 30 s) were excluded prior to applying the equation to the constant load. The lack of the lag time in the present study might be conditioned responses of the subjects since the change of the load was made apparent by a count down (3, 2, 1, now). The same procedure was used at the start of the incremental test.

The mean values of $\tau\dot{V}_{O_2}$, determined from the incremental exercise test, was 38 s, which for \dot{V}_{O_2} gives a time to reach steady state of around 2.5 min ($4\tau\dot{V}_{O_2}$, implying that the increase in \dot{V}_{O_2} will be 98% of the total increase). The period of fixed load (4 min) in our protocol was thus sufficiently long to ensure a steady state of \dot{V}_{O_2} . A lower mean value of $\tau\dot{V}_{O_2}$ of 30 s has previously been reported (Whipp & Ward, 1990).

Our mean value of $\Delta\dot{V}_{O_2}/\Delta W$, of 10.8 ml min⁻¹ W⁻¹, is in agreement with values for normal men presented by (Hansen et al., 1987), 10.3 ml min⁻¹ W⁻¹. Both higher values, 11.7 ml min⁻¹ W⁻¹ (Jones et al., 1985), and lower values, 9.3 ml min⁻¹ W⁻¹ (Hansen et al., 1984), have been presented for healthy men.

Validation of the equations

Good agreement was observed between $\tau\dot{V}_{O_2}$ determined from the incremental test and the steady-state test when Eqs (3) and (4) were applied at the same steady-state loads. We have chosen to validate the incremental protocol with the constant load test at high intensity, which is \leq PX. The mean and SD of $\tau\dot{V}_{O_2}$ obtained with the two methods (incremental test and Eq. 3, steady-state test at the high intensity and Eq. 4) were almost the same. However, the absolute variation of $\tau\dot{V}_{O_2}$ and of $\Delta\dot{V}_{O_2}/\Delta W$ between the methods was considerable. It should be noted that the incremental and steady-state tests respectively were performed on two successive days and therefore the day-to-day variation was added to the variation between the methods.

Another reason for the observed variation is that the evaluation of $\tau\dot{V}_{O_2}$ is sensitive to the raw data variation. This has previously been analysed in detail by Lamarra et al. (1987) who studied fluctuations during breath-by-breath registrations and found that by fitting a non-linear model to the transition from one workload to another the mean (of the time delay + the mean response time) was independent of the noise level but that the SD increased at higher noises. In this study we simulated variations within a fixed SD applied to the mono-exponential function based on 10 s values. The robustness of $\tau\dot{V}_{O_2}$ obtained from Eq. (4) was explored. A fixed SD of 100 ml

of \dot{V}_{O_2} was programmed and random series of \dot{V}_{O_2} from 10 simulations following the mono-exponential function were created. Ten new equations were solved as described giving 10 values of $\tau\dot{V}_{O_2}$. Using the SD = 100 ml, the variation of $\tau\dot{V}_{O_2}$ could be as high as 6 s (SD) which would correspond to a COR of 12 s. This high variation is not obvious from inspecting graphs or figures and thus requires attention.

In the constant load tests the values of $\tau\dot{V}_{O_2}$ were different at each load. This might be due to prior exercise speeding up the \dot{V}_{O_2} kinetics (di Prampero et al., 1989). In addition, the level at which the load was set influenced the value of $\tau\dot{V}_{O_2}$ (Xu & Rhodes, 1999).

Repeatability

The mean values of $\tau\dot{V}_{O_2}$ from the repeated incremental tests were not significantly different. Previously reported similarities of the means of repeated tests have been taken as indications of good reproducibility (Whipp et al., 1981). The correlation coefficient between $\tau\dot{V}_{O_2}$ from the repeated tests was low compared with the correlation coefficient for $\dot{V}_{O_{2max}}$. The small range of the values from test 1 versus test 2 can explain this in part. Nevertheless, there are noticeable differences in $\tau\dot{V}_{O_2}$ between the tests (2 SD = 20 s), which certainly need to be accounted for in clinical practice. However, the mean value of $\tau\dot{V}_{O_2}$ of 38 s should be compared with the value of $\tau\dot{V}_{O_2}$ observed in patients with cardiopulmonary diseases, reported to be 70 s (Wasserman et al., 1994a), and in well-trained subjects, 20 s (Cooper & Storer, 2001), which indicate that the actual range of $\tau\dot{V}_{O_2}$ is wider than the test–retest variation reported here.

The mean values of $\Delta\dot{V}_{O_2}/\Delta W$ obtained from the repeated incremental tests were not significantly different, and the correlation coefficient was somewhat higher than for $\tau\dot{V}_{O_2}$. The variation (2 SD) of test–retest values for $\Delta\dot{V}_{O_2}/\Delta W$ was 1.2 ml min⁻¹ W⁻¹. This is a fairly high variation. However, patients with pulmonary vascular diseases or peripheral vascular diseases, or those with an abnormal ECG during exercise had been reported to have a significantly lower $\Delta\dot{V}_{O_2}/\Delta W$, 8.3 ml min⁻¹ W⁻¹, than normal men (Hansen et al., 1987). This indicates that, despite the variation, the measurements of $\Delta\dot{V}_{O_2}/\Delta W$ could be valuable. It has also been proposed that a low proportion of muscle fibre type 1 gives rise to a lower value of the $\Delta\dot{V}_{O_2}/\Delta W$ than a higher proportion of type 1 fibres (9 and 11 ml min⁻¹ W⁻¹, respectively) (Barstow et al., 2000).

Conclusions

Equations have been developed to calculate $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ from a single exercise test. This provides a valuable possibility to obtain a detailed description of the aerobic function. This equation/protocol was validated versus a mono-exponential equation using a series of constant load tests. The agreement between the equations was acceptable. The considerable variations in the difference in absolute values of $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ between the protocols are, however, not negligible.

The variation could be partly explained by the natural day-to-day variation. A considerable difference in absolute values was seen for $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ between repeated tests of the incremental test, 5–6 weeks apart. This must be taken into account when using the estimated values of $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}/\Delta W$ for evaluation of aerobic function. A more solid baseline could be established by calculating the mean of several repeated tests.

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