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**COMPARISON OF OXYGEN UPTAKE ON-KINETIC CALCULATIONS DURING
SUBMAXIMAL EXERCISE**

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ABSTRACT

COMPARISON OF OXYGEN UPTAKE ON-KINETIC CALCULATIONS DURING SUBMAXIMAL EXERCISE. **Ross Arena, Reed Humphrey, Mary Ann Peberdy, Michael Madigan. JEPonline.** 2003;6(2):1-7. The mean response time (MRT) and time constant (TC) are two oxygen uptake (VO_2) on-kinetic calculations whose values are presumed to be interchangeable. This study tests the assumption of uniformity among different VO_2 on-kinetic calculations. Nineteen (13 male/6 female) apparently healthy subjects were recruited for this study. Mean age ($\pm$ SD) for this group was 44.1 ± 10.1 years. Subjects underwent a progressive exercise test and six-minute exercise session (1.6 m/hr, 3.0% grade) on separate days. Both breath-by-breath (bb) and 10-second averaged (avg) ventilatory expired gas data were used to produce four VO_2 on-kinetic calculations (MRT_{bb} , MRT_{avg} , TC_{bb} , TC_{avg}). There were statistically significant differences ($p < 0.05$) between TC_{bb} (17.6 s) and TC_{avg} (22.7 s), MRT_{bb} (22.9 s), and MRT_{avg} (24.7 s). Comparisons amongst TC_{avg} (22.7 s), MRT_{bb} (22.9 s), and MRT_{avg} (24.7 s) did not reach statistical significance ($p > 0.05$). All VO_2 on-kinetic calculations were significantly correlated with peak VO_2 , age, and each other. These results indicate that all MRT and TC calculations may not be interchangeable. All VO_2 uptake on-kinetic expressions did, however, appear to represent aerobic capacity and were highly correlated with each other indicating that calculation method may not have an excessively negative impact.

Key Words: Mean Response Time, Time Constant, Ventilatory Expired Gas

INTRODUCTION

Oxygen uptake (VO_2) on-kinetics during steady-rate exercise, at workloads below an individual's anaerobic threshold, fits the mono-exponential regression equation illustrated in Figure 1. Whipp (1) developed an algebraic expression from this mono-exponential equation that solves for the time constant (TC), otherwise known as the mean response time (MRT). The MRT equation is illustrated in figure two.

To demonstrate equality of the TC, derived through non-linear regression, and the MRT, solved algebraically, Whipp (1) conducted 15-minute steady-rate exercise sessions on a lower extremity ergometer at 50 and 75 Watts in eight healthy subjects (6 male/2 female, 26.4 ± 4.2 years). VO_2 was determined by collecting expired gas via a Douglas Bag at rest, 30-second intervals during the first three minutes of exercise, and every minute thereafter for the remainder of the session. The author calculated the rate constant both algebraically and graphically. The inverse of the rate constant equates to the time constant (regression method) and MRT (algebraic method) (2). The mean TC/MRT for the 50 and 75 Watt sessions were 45.45/44.44 and 44.44/44.44 s, respectively. From these findings, Whipp (1) concluded the algebraic calculation accurately represents the regression calculation and was therefore a valid measure of VO_2 on-kinetics during steady-rate exercise below one's anaerobic threshold.

Several investigations have used either the TC (3,4) or MRT (5-7) to examine O_2 uptake on-kinetics in apparently healthy subjects. While not stated directly, there is an assumption that the TC and MRT are interchangeable based upon the original work by Whipp (1). Furthermore, ventilatory expired gas analysis systems have changed significantly since the MRT equation was derived and compared to the TC (1). The present study therefore compares TC-MRT calculations using a ventilatory expired gas system capable of breath-by-breath analysis.

METHODS

Subject Characteristics

Virginia Commonwealth University's Institutional Review Board approved the study and informed written consent was obtained. Nineteen apparently healthy subjects (13 males/6 females) were recruited for this study. Mean age ($\pm$ SD) for this group was 44.1 ± 10.1 years. All subjects were rigorously screened for risk/evidence of cardiac disease. Pre-test exclusion criteria consisted of a history of tobacco use, total cholesterol ≥ 240 mg/dL (if data were available), resting systolic blood pressure ≥ 140 mmHg, resting diastolic blood pressure > 90 mmHg, diabetes, and/or any past diagnosis of cardiac disease/dysfunction. Exclusion criteria during testing consisted of evidence of an abnormal hemodynamic response, electrocardiographic changes suggestive of myocardial ischemia or arrhythmia, and/or the subject reporting symptoms suggestive of myocardial ischemia. No subject was rejected for these reasons.

Testing Procedure and Data Collection

Subjects participated in two exercise testing sessions. The metabolic cart (Sensormedics Vmax29, Yorba Linda, CA) used for ventilatory expired gas analysis was calibrated prior to each exercise session. The first exercise session consisted of a progressive ramping protocol to determine peak VO_2 in ml O_2 /kg/min. The ramping protocol selected for testing consisted of approximately 2 ml O_2 /kg/min increases in workload every 30 s (8,9). Stage one began at 1.0 mi/hr and a 0% grade. Stages increased by 0.1 mi/hr and 0.5% grade thereafter. The same treadmill protocol was used to test all subjects. The second exercise session consisted of steady-rate treadmill ambulation at 1.6 mi/hr and a 3.0% grade without warm-up creating a square wave protocol. Since exercise was immediately started at the desired steady-rate workload (1.6 mi/hr and 3% grade), accounting for a time delay in VO_2 on-kinetic calculations secondary to a period of exercise at a lower intensity was unnecessary. VO_2 in L/min was recorded prior to and during exercise.

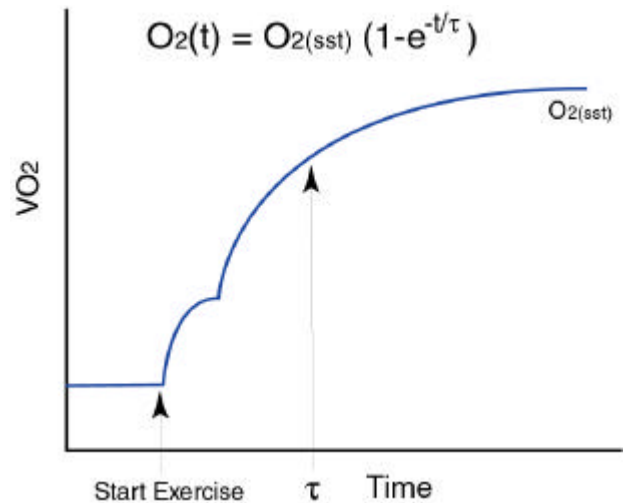


Figure 1. The algebraic equation for and profile of the exponential change in VO_2 over time during a rest-to-steady state exercise transition.
 $\text{O}_2(t)$ = oxygen uptake at any time ; $\text{O}_{2(\text{sst})}$ = steady-state VO_2 ; τ = time taken to reach 63% of the steady-rate value ; t = any time value

The determination and administration of steady-state exercise intensities used for analysis of VO_2 on-kinetics have not been standardized. The steady-state intensity used in this study optimized the likelihood of subjects completing the protocol before volitional fatigue, allowed a sufficient rise in VO_2 above resting value to calculate VO_2 on-kinetics, and minimized the potential of exercising above the maximal steady state intensity. Subjects were asked to ambulate at this workload for 6 min. Monitoring for both sessions consisted of continuous 5-lead electrocardiography (Cardiosoft, Yorba Linda, CA), manual blood pressure pre, during and post exercise, and continuous heart rate monitoring via the electrocardiogram. A qualified exercise physiologist conducted the exercise tests with a cardiologist available onsite for consultation. Based on ACSM guidelines for exercise termination criteria (10), none of the exercise tests were terminated prematurely. The primary endpoint during progressive exercise testing was volitional fatigue. All subjects completed the six min, steady-state exercise session.

Calculation of O_2 uptake on-kinetics

VO_2 on-kinetics was calculated algebraically (MRT) and through non-linear regression (TC). The MRT was derived from the equation illustrated in Figure 2. Breath-by-breath and 10-second averaged data were used to produce two MRT calculations (MRT_{BB} and MRT_{AVG}). Resting O_2 uptake was the average of all data prior to exercise (≥ 2 min). Steady-rate VO_2 was the averaged value over the last two min of exercise. The difference between rest and steady-state VO_2 , multiplied by exercise time (six min), is the expected amount of VO_2 for the exercise session. The sum of measured VO_2 above rest is the actual amount of VO_2 during the exercise session. The difference between expected and summed VO_2 (in liters) is the oxygen deficit. Division of the oxygen deficit by the difference between rest and steady-rate VO_2 (in liters) equals the MRT. The resultant MRT, multiplied by 60, produced a value expressed in seconds. The TC was determined by curve fitting breath-by-breath (TC_{BB}) and 10-second averaged (TC_{AVG}) data according to the equation illustrated in Figure 1. A graphical software package (SigmaPlot 5.0, SPSS Science, Chicago, IL) curve fit the data and derived the TC in seconds.

Statistical Analysis

Repeated measures analysis of variance (ANOVA) assessed differences in the VO_2 on-kinetic calculations: $\text{MRT}_{\text{BB}} - \text{MRT}_{\text{AVG}}$, $\text{TC}_{\text{BB}} - \text{TC}_{\text{AVG}}$, $\text{MRT}_{\text{BB}} - \text{TC}_{\text{BB}}$, and $\text{MRT}_{\text{AVG}} - \text{TC}_{\text{AVG}}$. Tukey's honestly significant difference (HSD) was used to assess significant differences defined by repeated measures ANOVA. The Pearson product-moment correlation was used to determine the relationship among the four on-kinetic calculations and age as well as peak VO_2 . The correlation between the four VO_2 on-kinetic calculations was additionally assessed. A p-value ≤ 0.05 was considered significant for all statistical tests. A statistical software program was used for data analysis (SPSS 10.0 for Windows, SPSS Science, Chicago, IL). All data are presented as mean $\pm$ SD.

RESULTS

Data of the four VO_2 on-kinetic calculations are listed in Figure 3. Repeated measures ANOVA demonstrated a statistically significant difference between the four VO_2 on-kinetic calculations ($F = 4.5$, $p < 0.05$, effect size = 0.23). Tukey's HSD revealed TC_{BB} was significant less than all other VO_2 on-kinetic calculations. All other

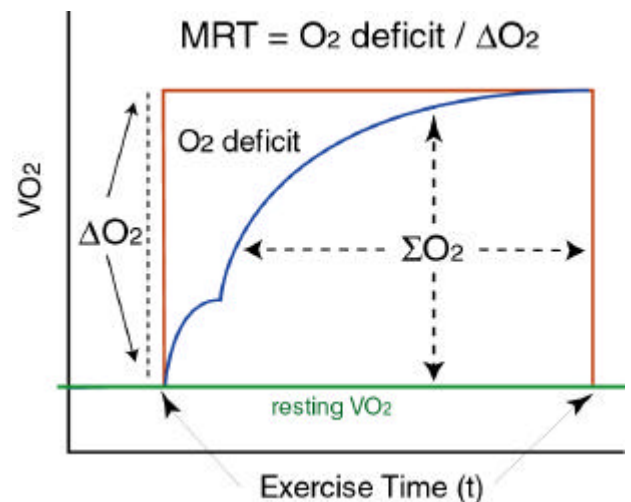


Figure 2. The algebraic equation for, as well as an illustration of the concept, describing VO_2 on-kinetics during steady-state exercise.

O_2 deficit = oxygen deficit = $t * \Delta\text{O}_2 - \Sigma\text{O}_2$, where t : exercise time ; ΔO_2 = difference between rest and steady-state VO_2 ; ΣO_2 = sum of measured oxygen uptake, above rest, during exercise

Table 1. Results from the Tukey's HSD paired mean comparisons.

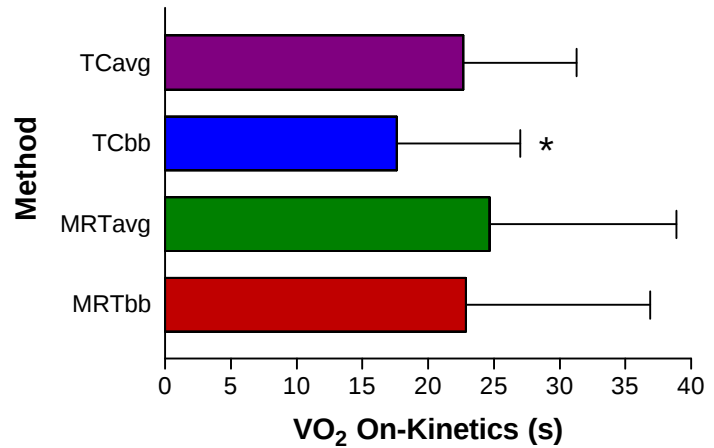
Comparison	Mean difference
$TC_{BB} - TC_{AVG}$	5.1*
$MRT_{BB} - MRT_{AVG}$	1.8 ^{NS}
$MRT_{BB} - TC_{BB}$	5.1*
$MRT_{AVG} - TC_{AVG}$	2.0 ^{NS}
$MRT_{AVG} - TC_{BB}$	7.1*
$MRT_{BB} - TC_{BB}$	5.3*
$MRT_{BB} - TC_{AVG}$	0.2 ^{NS}

p<0.05 ; NS = not significant

Table 2. Results from correlation analysis between VO₂ on-kinetic calculations and both peak VO₂ and age

	Peak VO ₂	Age
MRT_{BB}	-0.73*	0.59*
MRT_{AVG}	-0.74*	0.64*
TC_{BB}	-0.52 *	0.58*
TC_{AVG}	-0.50*	0.67*

* p<0.05

**Figure 3. Mean±SD VO₂ data for the four conditions. X-axis values are as follows: 1 = TCbb ; 2 = TCavg ; 3 = MRTbb ; 4 = MRTavg****Table 3. Results from correlation analyses between VO₂ on-kinetic calculations.**

	MRT_{BB}	MRT_{AVG}	TC_{BB}	TC_{AVG}
MRT_{BB}	-----	0.90*	0.72*	0.68*
MRT_{AVG}	-----	-----	0.72*	0.75*
TC_{BB}	-----	-----	-----	0.79*
TC_{AVG}	-----	-----	-----	-----

* p<0.05

comparisons did not reach statistical significance. Results from the repeated measures ANOVA and Tukey's HSD are outlined in Table 1 and Figure 3.

There were statistically significant correlations between all of the VO₂ on-kinetic calculations and both peak VO₂ and age. Furthermore, all four VO₂ on-kinetic calculations were significantly correlated with each other. The correlation analyses are listed in Tables 2 and 3.

DISCUSSION

The results indicated that not all VO₂ on-kinetic calculations were interchangeable. The common denominator for these differences appears to be the un-averaged, exponential calculation (TC_{BB}). Variability in breath-by-breath data is a well-documented phenomenon (11). These breath-by-breath fluctuations in VO₂ may have significantly altered exponential curve fitting thereby producing a significant difference between TC_{BB} - TC_{AVG} . Data sampling did not significantly alter MRT values and both were similar to TC_{AVG} . The latter result is not surprising considering the MRT calculation itself entails data averaging.

A portion of these findings conflict with the assumption derived from the original work by Whipp (1) and has implications for generalization of findings using different VO₂ on-kinetic calculations. The findings in the present study do not support interchangeability of the TC and MRT when the TC is calculated via un-averaged VO₂ data. Interchangeability of the TC and MRT is, however, supported when data is averaged over 10 s intervals. Additionally, MRT calculations appear to maintain comparability irrespective of data sampling. The latter two observations support the intention of the original work by Whipp (1), which was to produce a simple algebraic derivation that accurately represents a more complex exponential calculation (TC) of O₂ uptake on-kinetics.

The present study was undertaken subsequent to a similar investigation in a group of patients diagnosed with heart failure by the same group of authors (12). The initial investigation in the heart failure group revealed the four VO_2 on-kinetic calculations (MRT_{BB} , MRT_{AVG} , TC_{BB} , and TC_{AVG}) were all significantly different from one another. The disparity between findings in the original investigation and the findings reported in the present study may be secondary to ventilatory expired gas responses unique to the heart failure population. A number of patients with heart failure demonstrate ventilatory expired gas oscillations; the mechanism of which is not entirely clear (13,14). This oscillatory pattern, unique to patients with heart failure, can clearly have an impact on VO_2 on-kinetic calculations. The authors therefore caution readers in generalizing findings of the present study outside of apparently healthy populations.

A question raised from these findings is which VO_2 on-kinetic calculation most accurately reflects physiology in apparently healthy subjects? Previous evidence indicates faster VO_2 on-kinetics is associated with higher levels of aerobic capacity (15-20) and younger age groups (16,21). In the present study, all four VO_2 on-kinetic calculations were significantly correlated with age and aerobic capacity as well as each other. With respect to the latter finding, however, coefficient of determination (r^2) values find that a great deal (>50%) of variance between the VO_2 on-kinetic calculations is left unexplained. The authors therefore do not feel comfortable in defining an optimal VO_2 on-kinetic calculation from these findings. The correlation analysis does indicate that while all VO_2 on-kinetic calculations were not interchangeable, they may all accurately represent one's physiology. Such a conclusion would presently validate the use of several VO_2 on-kinetic calculations in assessing aerobic fitness via transitions between steady state exercise intensities, although additional study is required. Specifically, future investigations addressing reliability and sensitivity features (discriminating between healthy and unhealthy populations or detecting changes in cardiovascular function in a given individual over time) of several VO_2 on-kinetic calculations would facilitate the determination of a standardized expression.

The fact that only un-averaged and 10 s averaged data, collected during a single exercise session, was used for the VO_2 on-kinetic calculations is considered a weakness of the present study. Other averaging intervals may produce different values that prove superior. The authors do feel 10 s averaging is a reasonable compromise between un-averaged data, which may result in unacceptable variability, and larger averaging intervals, which may produce too few data points to adequately represent the on-kinetic response. Additionally, several investigations have calculated VO_2 on-kinetics by averaging breath-by-breath data from several exercise sessions at the same steady-rate intensity (22). Other investigations have reduced noise by time-interpolating breath-by-breath data to produce second-by-second values (19,23). These techniques improve exponential curve fitting of data and, if employed in the present study, may have negated the differences between the TC and MRT. Serial measures and additional data processing do, however, increase the complexity of calculating VO_2 on-kinetics and should be avoided if comparable information is obtained from simpler techniques. Maximally simplifying the calculation of VO_2 on-kinetics, without sacrificing the usefulness of information gained from this measure, will greatly facilitate clinical application. To support simplification by employing a single session measure of VO_2 on-kinetics, a reliability analysis must be conducted and demonstrate adequate repeatability over several days in subjects whose physiologic function remains stable.

Conclusions

Several methods are presently used to calculate VO_2 on-kinetics. The TC and MRT are presumed to be interchangeable. The findings reported here do not completely support this assumption. Given the demonstrated potential VO_2 on-kinetics has in differentiating between varying levels of aerobic fitness (15-20), efforts should be directed toward determining optimal expression and standardizing this non-invasive, simple measure.

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REFERENCES

1. Whipp BJ. Rate constant for the kinetics of oxygen uptake during light exercise. *J Appl Physiol* 1971;30:261-63.
2. Sietsema KE, Ben Dov I, Zhang YY, Sullivan C, Wasserman K. Dynamics of oxygen uptake for submaximal exercise and recovery in patients with chronic heart failure. *Chest* 1994;105:1693-700.
3. Hill DW. Effect of time of day on aerobic power in exhaustive high-intensity exercise. *J Sports Med Phys Fitness* 1996;36:155-60.
4. Yano T, Yunoki T, Ogata H. Relationship between the slow component of oxygen uptake and the potential reduction in maximal power output during constant-load exercise. *J Sports Med Phys Fitness* 2001;41:165-69.
5. Padilla J, Martinez E, Olvera G, Ojeda CP, Caudillo PD. [Cardiopulmonary dynamics during a maximal exertion test in Mexican endurance athletes]. *Arch Inst Cardiol Mex* 2000;70:268-84.
6. Hayashi N, Yoshida T. Water immersion delays the oxygen uptake response to sitting arm- cranking in humans. *Eur J Appl Physiol Occup Physiol* 1999;80:132-38.
7. Macdonald M, Pedersen PK, Hughson RL. Acceleration of VO₂ kinetics in heavy submaximal exercise by hyperoxia and prior high-intensity exercise. *J Appl Physiol* 1997;83:1318-25.
8. Arena R, Humphrey R. Comparison of ventilatory expired gas parameters used to predict hospitalization in patients with heart failure. *Am Heart J* 2002;143:427-32.
9. Arena R, Humphrey R. Relationship between ventilatory expired gas and cardiac parameters during symptom-limited exercise testing in patients with heart failure. *J Cardiopulm Rehabil* 2001;21:130-34.
10. Balady G, Berra KA, Lawrence A, Gordon NF, Mahler DA, Myers J *et al*. Clinical Exercise Testing. In: Franklin BA, Whaley MH, Howley ET, editors. **ACSM's Guidelines For Exercise Testing and Prescription, 6th ed.** Baltimore, MD: Lippincott Williams and Wilkins, 2000:91-114.
11. Myers J. Instrumentation: Equipment, Calculations, and Validation. In: Washburn RA, editor. **Essentials of Cardiopulmonary Exercise Testing.** Champaign, IL: Human Kinetics; 1996:59-81.
12. Arena R, Humphrey R, Peberdy MA, Madigan M. Comparison of oxygen uptake on-kinetic calculations in heart failure. *Med Sci Sports Exerc* 2002;34:1563-69.
13. Ben Dov I, Sietsema KE, Casaburi R, Wasserman K. Evidence that circulatory oscillations accompany ventilatory oscillations during exercise in patients with heart failure. *Am Rev Respir Dis* 1992;145:776-81.
14. Francis DP, Davies LC, Piepoli M, Rauchhaus M, Ponikowski P, Coats AJ. Origin of oscillatory kinetics of respiratory gas exchange in chronic heart failure. *Circulation* 1999;100:1065-70.
15. Cerretelli P, Pendergast D, Paganelli WC, Rennie DW. Effects of specific muscle training on VO₂ on-response and early blood lactate. *J Appl Physiol* 1979;47:761-69.
16. Xu F, Rhodes EC. Oxygen uptake kinetics during exercise. *Sports Med* 1999;27:313-27.
17. Zhang YY, Johnson MC, Chow N, Wasserman K. The role of fitness on VO₂ and VCO₂ kinetics in response to proportional step increases in work rate. *Eur J Appl Physiol Occup Physiol* 1991;63:94-100.
18. Yoshida T, Udo M, Ohmori T, Matsumoto Y, Uramoto T, Yamamoto K. Day-to-day changes in oxygen uptake kinetics at the onset of exercise during strenuous endurance training. *Eur J Appl Physiol Occup Physiol* 1992;64:78-83.
19. Barstow TJ, Jones AM, Nguyen PH, Casaburi R. Influence of muscle fiber type and pedal frequency on oxygen uptake kinetics of heavy exercise. *J Appl Physiol* 1996;81:1642-50.
20. Phillips SM, Green HJ, MacDonald MJ, Hughson RL. Progressive effect of endurance training on VO₂ kinetics at the onset of submaximal exercise. *J Appl Physiol* 1995;79:1914-20.

21. Babcock MA, Paterson DH, Cunningham DA, Dickinson JR. Exercise on-transient gas exchange kinetics are slowed as a function of age. ***Med Sci Sports Exerc*** 1994;26:440-46.
22. Lamarra N, Whipp BJ, Ward SA, Wasserman K. Effect of interbreath fluctuations on characterizing exercise gas exchange kinetics. ***J Appl Physiol*** 1987;62:2003-12.
23. Engelen M, Porszasz J, Riley M, Wasserman K, Maehara K, Barstow TJ. Effects of hypoxic hypoxia on O₂ uptake and heart rate kinetics during heavy exercise. ***J Appl Physiol*** 1996;81:2500-08.