Comparison of model estimates of phase two on-transient \( \dot{V}O_2 \) uptake kinetics during submaximal exercise in old men

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RESUMEN

Introducción. El análisis cinético de las respuestas transitorias de captación pulmonar de oxígeno \((\dot{V}O_2)\) durante ejercicio moderado \((\dot{V}O_{2mod})\) e intenso \((\dot{V}O_{2int})\) fueron comparados con estrategias comunes de modelado para evaluar el mejor. Material y métodos. Comparamos el parámetro estimado constante de tiempo para la fase 2 de \(\dot{V}O_2\) \((\tau_{\Phi, \dot{V}O_2})\) en adultos mayores \((n = 9; 71(\pm 5) \text{ años; media (± DE)})\). Estos hicieron una prueba de rampa \((12 \text{ W•min}^{-1})\) hasta el límite de su tolerancia para determinar el \(\dot{V}O_2\) pico y estimar el umbral lático \((\delta_1)\). También hicieron ejercicio de carga constante a 50 Watts \((\dot{V}O_{2mod})\) y a 80% \((\dot{V}O_{2int})\) y 120% \((\delta_1)\). Cada transición de cada carga duró 6 min, fue precedida por 6 min de pedaleo a una línea de base de 20 W y se repitió de 4 a 6 veces por intensidad. El \(\dot{V}O_2\) se medió de respiración por respiración. Los datos de cada transición fueron filtrados, interpolados a intervalos de 1 s y promediados en ensamblado para obtener un perfil de respuesta única por persona e intensidad y ajustados con regresión no lineal a base de modelos exponenciales de uno \((1C)\) ventana apropiada desde 0.3333 min \(\dot{V}O_{2mod}\) hasta su final o hasta la fase de transición 2 \(3 I_{NT}\); dos \((2C)\) y tres componentes \((3C)\) desde el inicio hasta el final del ejercicio. Además, los datos fueron colocados en “bins” discretos de tiempo de 10 s \((10 \text{ s bins})\) para modelarlos con \(1C\). Resultados. El \(1C, 4P_{0.3333 \rightarrow 3 \text{ min}}\) fue el más apropiado para modelar la \(\Phi_{\dot{V}O_2} S_{UB}\) y distinguir \(\Phi_{\dot{V}O_2}\). Los datos de la \(\Phi_{\dot{V}O_2}\) fueron fisiológicamente mejor modelados con \(2C, 7P_{\text{LineaBase} \text{Inicio hasta Final Ejercicio}}\) \(\dot{V}O_{2mod}\) y \(3C, 10P_{\text{LineaBase} \text{Inicio hasta Final Ejercicio}}\) \(\delta_1\), y permitieron describir dentro del modelado la \(\Phi_{\dot{V}O_2}\). Estas \(\tau_{\Phi, \dot{V}O_2}\) fueron similares entre ellas en nuestros voluntarios \((\text{media ± DE; } \tau_{\text{datos de } \dot{V}O_2 \text{ segundo por segundo}} = 46 \pm 15 \text{ s; } \tau_{\text{datos de } \dot{V}O_2 \text{ 10 s bins}} = 43 \pm 7 \text{ s})\).

Palabras clave: Adultos mayores, cinética de la captación de \(O_2\), fase dos del \(O_2\) modelado exponencial, constante de tiempo.

ABSTRACT

Introduction. The kinetic analysis of the \(\dot{V}O_2\) on transient response during moderate \((\dot{V}O_{2mod})\) and heavy \((\dot{V}O_{2int})\) intensity \((\dot{V}O_{2mod} + \dot{V}O_{2int} = S_{UB})\) exercise was compared by using several common modelling strategies to assess the best one. Material and methods. We compared the parameter estimate for the phase 2 \(\dot{V}O_2\) time constant \((\tau_{\Phi, \dot{V}O_2})\) in older male adults \((n = 9; 71(\pm 5) \text{ yrs; mean (± SD)})\). Subjects performed an incremental ramp test \((12 \text{ W•min}^{-1})\) to the limit of tolerance to determine \(\dot{V}O_2\) peak and the estimated lactate threshold \((\delta_1)\). Constant load cycle exercise was performed at 50 W \((\dot{V}O_{2mod})\) and work rates corresponding to 80% \((\dot{V}O_{2mod})\) and 120% \((\delta_1)\). Each transition in work rate lasted 6 min and was preceded by 6 min cycling at a baseline of 20 W; transitions at each intensity were repeated 4 6 times. \(\dot{V}O_2\) was measured breath by breath. Data from each transition were filtered, interpolated to 1 s intervals and ensemble averaged to yield a single response profile for each subject and intensity. Responses were modelled by means of nonlinear regression techniques with one \((1C)\); fitting window 0.3333 min from exercise onset to either end \(\dot{V}O_{2mod}\) or phase 2 transition \(\delta_1\), two \((2C)\) and three component \((3C)\) (fitting window from start exercise to end exercise) exponential models. In addition to this, data were placed into discrete time bins of 10 s \((10 \text{ s bins})\) to be modelled using \(1C\) exponential model. Results. The \(1C, 4P_{0.3333 \rightarrow 3 \text{ min}}\) best fitted \(\Phi_{\dot{V}O_2}\) data for \(S_{UB}\) and allowed us to characterize \(\Phi_{\dot{V}O_2}\). The \(\Phi_{\dot{V}O_2}\) data were physiologically best fitted with models \(2C, 7P_{\text{Base Line Start to End Exercise}}\) for \(\dot{V}O_{2mod}\) and \(3C, 10P_{\text{Base Line Start to End}}\) for \(\dot{V}O_{2int}\) they allowed us an intra modelling characterization of the \(\tau_{\Phi, \dot{V}O_2}\). These \(\tau_{\Phi, \dot{V}O_2}\) were similar to each other in our old male volunteers \((\text{Overall mean ± SD; } \tau_{\text{second by second } \dot{V}O_2 \text{ data}} = 46 \pm 15 \text{ s; } \tau_{\text{10 s bins } \dot{V}O_2 \text{ data}} = 43 \pm 7 \text{ s})\).

Key words: Old men, \(O_2\) uptake kinetics, phase two \(O_2\), exponential modelling, time constant.

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INTRODUCTION

During whole-body exercise in normal people, the increased vascular conductance to improve muscle blood flow and oxygenation is the key to this on-transient elevation in pulmonary oxygen uptake ($\Phi O_2$). At the start (onset) of exercise, muscle blood flow and therefore $O_2$ delivery, increase to meet the metabolic demand of contracting muscle mass. Because $O_2$ delivery can have a profound effect on muscle metabolism and function, it has been of considerable interest to understand the nature of cardiovascular control mechanisms responsible for adjusting muscle blood flow and $O_2$ delivery to muscle metabolic demand in terms of $O_2$ consumption ($\Phi O_2$ consumption), especially in the ageing process of the human beings. A simple and common approach has to investigate the dynamic response of $\Phi O_2$ to step transitions in exercise intensity, by mathematical modelling of this $\Phi O_2$, on-transient response. In consequence, different exponential mathematical models has been used, in studies oriented to the quantification of the dynamic response characteristics of this physiological regulatory $\Phi O_2$ and $\Phi O_2$ consumption system, in the search of unique insight into underlying mechanisms not obtained through examination of the steady state. Quantifying the three parameters of a dynamic response, that is:

1. The time delay ($T_{\text{time Delay}}$) from onset of stimulus to onset of response.
2. Rate of adaptation of the response ($\tau$, the time constant).
3. The magnitude of the response (amplitude or gain); and also determining the number of distinct phases of a $\Phi O_2$ on-transient response.

Three main theoretical phases has been observed ($\Phi_1$, $\Phi_2$, $\Phi_3$) of the on-transient $\Phi O_2$ responses ($\Phi_1\Phi O_2$, $\Phi_2\Phi O_2$, $\Phi_3\Phi O_2$) to an ergometric exercise. The first $\Phi_1\Phi O_2$ named by Whipp cardiodynamic phase, consists in an increased pulmonary perfusion with no significant change in the mixed venous $O_2$ and carbon dioxide (CO$_2$) tensions and Whipp postulated (p) that during $\Phi_1\Phi O_2$, the $\Phi O_2$ increases its response following the onset of exercise lasting approximately 20 s; so that, $\Phi_1\Phi O_2$ starts approximately 20 s after the beginning of exercise and finishes at 3 min exercise ($\Phi_2$ postulated $\Phi O_2$). The $\Phi_2\Phi O_2$ is an exponential instantaneously rate of change that is proportional to the magnitude of response from a baseline or required level and it is of the most importance because it reflects the rate of increasing of $\Phi O_2$. The $\Phi_3\Phi O_2$ begins at the end of $\Phi_1\Phi O_2$ and slows progressively towards its steady-state (asymptotic) value for moderate-intensity exercise ($M_{\text{ODERATE}}$) or unsteady-state (slow component) for heavy-intensity exercise ($H_{\text{EAVY}}$). The end of $\Phi_2\Phi O_2$ is associated with a transient decrease of pulmonary respiratory exchange ratio as a result of increased muscle tissue storage of metabolic CO$_2$. The $\Phi_3\Phi O_2$ is a slow increase in $\Phi O_2$ that ends in a plateau for $M_{\text{ODERATE}}$. The $\Phi_3\Phi O_2$ consists in slow increase in $\Phi O_2$ named slow component for $H_{\text{EAVY}}$ and whether or not the slow component is an exponential response is motive of debate.

These $\Phi_1\Phi O_2$, $\Phi_2\Phi O_2$, and $\Phi_3\Phi O_2$ on-transient responses to ergometric exercise have been described by monoexponential functions that include $T_{\text{time Delay}}$ such as a one-component model (1C), an exponential function with one $T_{\text{time Delay}}$; two-component model (2C), two exponential terms with one $T_{\text{time Delay}}$ each one; and threecomponent model (3C), three exponential terms with a $T_{\text{time Delay}}$ for each one. These exponential empirical 1C, 2C, and 3C models, allow us to screen for $\Phi O_2$ on-transient mass rate of change per unit of time ($\Phi O_2$ kinetics) during $S_{\text{SUBMAXIMAL}}$. The $\Phi O_2$ kinetics assessment is based on the time required for the transient $\Phi O_2$ response to reach 63% of final amplitude named the kinetic parameter, time constant ($\tau$).

The purpose of this work consisted in assessing the best mathematical exponential models, previously published, to characterize the $\Phi_2\Phi O_2$ on-transient response ($\Phi_2$ postulated $\Phi O_2$ and $\Phi_2$ isolated $\Phi O_2$) to $S_{\text{SUBMAXIMAL}}$, in search for determinant mechanisms of the $\Phi O_2$ kinetics in old men. The comparison of modelling assessment techniques have been used to characterise $\Phi O_2$ kinetics during the on-transient of $S_{\text{SUBMAXIMAL}}$ in young but in old men it has not.

On one hand, $\Phi O_2$ $\Phi_2$ on-transient kinetics is slow-age related; on the other hand, body constitution is age-related; and also the $\Phi O_2$ $\Phi_2$ on-transient is characterized by reduced venous oxygen content consequent to the increased muscle oxygen extraction due to the metabolic rate, which leads to a further increase in $\Phi_2$ and pulmonary gas exchange; however, we do not know if the $\Phi O_2$ $\Phi_2$ on-transient response to exercise intensity below estimated lactate threshold (below $\theta_1$) and above $\theta_1$ (above $\theta_1$) ($S_{\text{UBMAXIMAL}}$) could be modelled differently in old men by the empirical exponential mathematical models already tested in young men.

In the search for determinant mechanisms of this $\Phi O_2$ kinetic response and for "simplicity" we decided to assess in this study the $\Phi_2\Phi O_2$ on-transient kinetic ($\Phi_2\Phi O_2$ time constant) response in old men. We addressed the following questions:
• Is there any exponential mathematical model that fitted statistically best \( \Phi_{2\text{postulated}} \) on-transient \( S_{\text{UBMAXIMAL}} \) response?

• Which exponential mathematical model fitted either statistically or physiologically (or both) best the \( \Phi_2 \text{VO}_2 \) into the entire \( \text{VO}_2 \) on-transient \( S_{\text{UBMAXIMAL}} \) (\( \Phi_{2\text{isolated}} \text{VO}_2 \)) response?

• Are the \( \Phi_2 \text{VO}_2 \) time constant values, from best fitting models, different from each other?

**Hypothesis**

If the exponential phase two \( \text{VO}_2 \) on-transient response to \( S_{\text{UBMAXIMAL}} \) is similarly modelled by different fitting models like the single monoeponential function, one-two-, and 3-component models in terms of time constant duration, thus these \( \Phi_2 \text{VO}_2 \) kinetic parameter (\( \tau \Phi_2 \text{VO}_2 \)) estimated values from best fitting models should not be significantly different from each other, in old adults.

**MATERIAL AND METHODS**

The cardiopulmonary methodology used in this study has been already described somewhere else,5,8 However, in brief as follows:

• **Ventilation and pulmonary gas exchange (\( \text{VO}_2 \), \( \text{CO}_2 \)):** Ventilation, \( \text{VO}_2 \), and \( \text{CO}_2 \) were calculated breath-by-breath with a computer based programme (Beaver et al., 1981). Inspired and expired air was sampled continuously (1 mL s\(^{-1}\)) at the mouth, and analysed for fractional concentrations of \( \text{O}_2 \), \( \text{CO}_2 \), and \( \text{N}_2 \) using a respiratory mass spectrometer (Perkin Elmer MGA-1100 or Airspec MGA2000) daily calibrated.5 The electrocardiograph (Harco, Sauborn Model 500-1100) measures the bioelectric potentials of the heart, inputs the ECG signals into a computerized oscilloscope (Perking Elmer EM 530 B), and records these voltages in a microcomputer.5 All the input signals were stored on a hard disc system for later analyses.

• **Testing subjects:** Nine old healthy male adults participated in this study. The University’s Review Board for Research Using Human subjects approved this research.

• **Ramp test:** On the initial visit to the laboratory each subject performed and incremental exercise test in the upright position on an electrically-braked cycle ergometer (Lode, Model H-300-R), in which after initiated at 60 rpm by 4 min “loadless” (actual constant power output approximately 20 W) pedaling, the power output increased as a ramp function at 15 W min\(^{-1}\) to volitional fatigue8 for the determination of the \( \tilde{\Phi}_1 \), peak \( \text{O}_2 \) uptake \( \text{VO}_2\text{peak} \), heart rate peak and maximal work rate.8

• \( \text{VO}_2\text{peak} \): The \( \text{VO}_2 \) averaged over the final 15 s of the incremental test prior to fatigue was taken as \( \text{VO}_2\text{peak} \).

• **Estimated lactate threshold (\( \tilde{\Phi}_1 \)):** The \( \tilde{\Phi}_1 \) as a non-invasive method was expressed as a percentage of the \( \text{VO}_2\text{max} \). The \( \tilde{\Phi}_1 \) was defined as the \( \text{VO}_2 \) at which there was a systematic increase in the ventilatory equivalent for \( \text{VE/VO}_2 \) and end-tidal \( \text{PO}_2 \), with no concomitant increase in the \( \text{VE/VO}_2 \), or decrease in the end-tidal \( \text{PCO}_2 \). The \( \text{VO}_2 \) corresponding to the time of the \( \tilde{\Phi}_1 \) was calculated as Wasserman, et al.,16 as well as, the work rate corresponding to the \( \text{VO}_2 \) at 80% and 120% \( \tilde{\Phi}_1 \) was calculated. For example,5 from the \( \text{VO}_2 \) corresponding to the time of the \( \tilde{\Phi}_1 \) (\( \text{VO}_2 \) 1875, mL min\(^{-1}\) 52.1% \( \text{VO}_2\text{max} \)) it was calculated the work rate corresponding to both the:

  i) \( 80\% \tilde{\Phi}_1 \text{VO}_2 \) expected (mL min\(^{-1}\)) \( \text{VO}_2 \) • 0.8 1875

  • 0.8 1650, mL min\(^{-1}\), and the

  ii) \( 120\% \tilde{\Phi}_1 \text{VO}_2 \) expected (mL min\(^{-1}\)) \( \text{VO}_2 \) • 1.2 1875

  • 1.2 2220, mL min\(^{-1}\); evermore, since the \( \text{VO}_2 \) equivalent (mL min\(^{-1}\)) \( 10 \times \text{Watts}_{\text{Baseline}} + \text{VO}_2\text{Baseline} \) \( (10 \times 20) + 500 = 700 \), mL min\(^{-1}\), then the 100% \( \tilde{\Phi}_1 \text{VO}_2 \) equivalent (power in Watts) \( (\tilde{\Phi}_1 \text{VO}_2 - \text{VO}_2\text{equivalent}) / 10 \) (1875 - 700) / 10 117.5, W; consequently, the

  iii) \( 80\% \tilde{\Phi}_1 \text{VO}_2 \) equivalent (W) \( (\tilde{\Phi}_1 \text{VO}_2 \times 0.8) - \text{VO}_2\text{equivalent} / 10 \) (1650 - 700) / 10 95, W, and the

  iv) \( 120\% \tilde{\Phi}_1 \text{VO}_2 \) equivalent (W) \( (\tilde{\Phi}_1 \text{VO}_2 \times 1.2) - \text{VO}_2\text{equivalent} / 10 \) (2220 - 700) / 10 152, W.

• **Submaximal constant-load leg cycling exercise tests (\( S_{\text{UBMAXIMAL}} \)):** Subjects performed constant-load leg cycling exercise where the power output increased as a step function from “loadless” cycling to a power output corresponding to \( M_{\text{ODERATE}} \) or \( H_{\text{AVY}} \).4,16 Three different intensities of \( S_{\text{UBMAXIMAL}} \) were studied to determine \( \text{VO}_2 \) on-transient kinetics and consisted in square waves of 50 W (absolute power output, \( M_{\text{ODERATE}} \)), power outputs corresponding to 80% \( \tilde{\Phi}_1 \) (relative power output, \( M_{\text{ODERATERel}} \)) and 120% \( \tilde{\Phi}_1 \) (relative power output, \( H_{\text{AVYRel}} \)), with each subject performing all three exercise intensities during the curse of the study. The protocol began with 6 min loadless cycling, followed by a step increase in power output lasting 6 min in duration, and ending with a step decrease in power output back to loadless cycling. Changes in power output were initiated without warning the subject. Each subject performed 4-6 transitions for the \( M_{\text{ODERATE}} \) protocols (Abs and Rel), and two to four repetitions for the \( H_{\text{AVYRel}} \) protocol. During each test, subjects pedalled while breathing to measure the ventilation and gas exchange
calculated breath-by-breath\textsuperscript{14} by a computer based programme.\textsuperscript{5}

- **Data analysis:** The breath by breath $M_{\text{ODERATE}}$ and $H_{\text{VY}}$ data were interpolated to 1 s interval, and each repetition was time aligned and assemble averaged to provide a single response for each subject for determining the kinetics of the $\text{VO}_2$ on-transient response to $S_{\text{UBMAXIMAL}}$.\textsuperscript{5} We determined in $\Phi_3$ the magnitude of the $\Delta\text{VO}_2$ data as the difference between the $\text{VO}_2$ at the end exercise and the $\text{VO}_2$ at 3 min of exercise ($\Delta\text{VO}_2_{(6-3\text{min})}$). The $\text{VO}_2$ at 3 min ($\text{VO}_2_{3\text{min}}$) was taken as mean between 2.75 and 3.15 min, and the end exercise $\text{VO}_2$ ($\text{VO}_2_{6\text{min}}$) was taken as the mean $\text{VO}_2$ during the last 0.25 min exercise. We also calculated the slope subthreshold $\text{VO}_2$- power relationship and the $\text{VO}_2$ during loadless pedalling cycling.\textsuperscript{5,8}

- **Modelling:** The breath-by-breath $\text{VO}_2$ on-transient single response from each subject was modelled by using the 1C, 2C and 3C exponential mathematical expressions with eight different fitting models as follows.\textsuperscript{5} The $M_{\text{monoExponential}}$ function of the form $\text{VO}_2(t) = a_{\text{amplitude0}} + a_{\text{amplitude1}} \cdot e^{-(t/\tau_0)}$, presented as $\text{VO}_2(t)$ is the mass rate of change per unit of time $(\text{dV}_2/\text{dt})$ assuming $T_{\text{timeDelay}1} = 0$; $a_{\text{amplitude0}}$ is the baseline; $a_{\text{amplitude1}}$ is the $\text{VO}_2$ distance value from $a_{\text{amplitude0}}$ to the $\text{VO}_2$ required, or the difference between unloaded pedalling and end exercise $\text{VO}_2$ response ($\text{VO}_{2\text{EE}}$); $1-e^{-t/\tau_0}$ is the negative exponential distribution,\textsuperscript{17} $e^{-t/\tau_0}$ is the die-away factor with the time constant $\tau_0$ for an exponential on-transient $\text{VO}_2$ response increase, $t$ is the time in which the transient $\text{VO}_2$ response is gradually (exponentially) dying away; when $t = \tau_0$ it means that the time required for the transient $\text{VO}_2$ response to die away to $e^{-1}$ part ($e^{-1}$) was 1/2.71828 0.3678 of its original value, thus, $\tau_0 = 0.3678 0.63$, and $e^{-2.718281} = (1 + n)^{-1}$, $n \geq 10$ and ‘e’ is incommensurable with 1. This single $M_{\text{monoExponential}}$ function models with three parameters (3P: $a_{\text{amplitude0}}$, $a_{\text{amplitude1}}$, and $\tau_0$) (1C,3P). The 1C is the $M_{\text{oneExponential}}$ function with the inclusion of $T_{\text{timeDelay1}}$ (named onecomponent)\textsuperscript{7} that it brought about the 1C with 4P ($a_{\text{amplitude0}}$, $a_{\text{amplitude1}}$, $T_{\text{timeDelay1}}$, and $\tau_0$),\textsuperscript{5,18,19} expressed as follows (1C,4P): $\text{VO}_2(t) = a_{\text{amplitude0}} + a_{\text{amplitude1}} \cdot [1-e^{-(t/\tau_0)}]$. The 2C consists in a doble $M_{\text{OneExponential}}$ function with $T_{\text{timeDelay1}}$ and $T_{\text{timeDelay2}}$ included, and for this reason it models two gapped exponential transient periods of time with 7P ($a_{\text{amplitude0}}$, $a_{\text{amplitude1}}$, $T_{\text{timeDelay1}}$, $T_{\text{timeDelay2}}$, $\tau_1$, $a_{\text{amplitude2}}$, $T_{\text{timeDelay2}}$, and $\tau_2$),\textsuperscript{5,18,19} expressed as follows (2C,7P): $\text{VO}_2(t) = a_{\text{amplitude0}} + a_{\text{amplitude1}} \cdot [1-e^{-(t/\tau_1)}] + a_{\text{amplitude2}} \cdot [1-e^{-(t/\tau_2)}]$. The 3C consists in a triple $M_{\text{OneExponential}}$ function with $T_{\text{timeDelay1}}$, $T_{\text{timeDelay2}}$, and $T_{\text{timeDelay3}}$ included, and for this reason it models three gapped exponential transient periods of time with 10P ($a_{\text{amplitude0}}$, $a_{\text{amplitude1}}$, $T_{\text{timeDelay1}}$, $\tau_1$, $a_{\text{amplitude2}}$, $T_{\text{timeDelay2}}$, $\tau_2$, $a_{\text{amplitude3}}$, $T_{\text{timeDelay3}}$, $\tau_3$),\textsuperscript{5} expressed as follows (3C,10P): $\text{VO}_2(t) = a_{\text{amplitude0}} + a_{\text{amplitude1}} \cdot [1-e^{-(t/\tau_1)}] + a_{\text{amplitude2}} \cdot [1-e^{-(t/\tau_2)}] + a_{\text{amplitude3}} \cdot [1-e^{-(t/\tau_3)}]$. When 3C,10P is constrained to $T_{\text{timeDelay2}} = T_{\text{timeDelay3}}$ then the threecompoment model is identified as 3C,9P (constrained 3C,10P).\textsuperscript{22} The $\Phi_3$ $\text{VO}_2$ $\tau$ estimate parameter of the response was compared together with a statistical analysis of how well each model fit the $\text{VO}_2$. We specifically addressed:

- The effect of incorporating the analysis of $\Phi_1$ $\text{VO}_2$ data within a model to physiologically isolate $\Phi_2$.
- The effect of incorporating the analysis of $\Phi_1$ $\text{VO}_2$ data within a model to physiologically isolate $\Phi_2$ and to statistically isolate $\Phi_3$, based on Fisher test.\textsuperscript{23}
- Differences between fitting entire $\text{VO}_2$ on-transient response versus a fitting window for $\Phi_2$ $\text{VO}_2$ on-transient data.

The acceptability of the fitting models were also assessed primarily on whether the information provided by the models was consistent with current understanding of the $\text{VO}_2$ on-transient response ($\Phi_3_{\text{PhysBestFit}}$, $\text{VO}_2$); as well as, statistical merits ($\Phi_2_{\text{StatBestFit}}$, $\text{VO}_2$). In addition to this, data were placed into discrete time-bins of 10 s (10 s bins $\text{VO}_2$ data) to be modelled using 1C exponential mathematical expression. Eight fitting models were expressed as follows: 1C,4P$^0_{3333}$ to 3 min, 1C,4P$^0_{3333}$ to 6 min, 1C,4P$^1_{7\text{BL2}}$ to 3 min (BL2, two min baseline) to estimate $\tau_{\Phi2_{postulated}}$, 2C,7P$^0_{2\text{BL2}}$ to 6 min, 3C,9P$^0_{7\text{BL2}}$ to 6 min, and 3C,10P$^0_{10\text{BL2}}$ to 6 min to estimate $\tau$ from an isolated $\Phi_2$ ($\tau\Phi_2_{isolated}$) with the second exponential term of these multi-component fitting models. These multi-component fitting models were used to assess the best physiological ($\Phi_2_{\text{isolatedPhysBestFit}}$), statistical ($\Phi_2_{\text{StatBestFit}}$) and both ($\Phi_2_{\text{isolatedPhysStatBestFit}}$) fit of $\Phi_2$ $\text{VO}_2$ on-transient response to submaximal exercise. The 1C,4P$^0_{7\text{BL2}}$ to 6 min and 1C,3P$^0_{7\text{BL2}}$ to 6 min that fitted the entire on-transient $\text{VO}_2$ data set, were used to assess the best fit compared to multiple component models. The kinetic analysis of phase two $\text{VO}_2$ was assessed in terms of the $\tau\Phi_2$ ($\tau_2$, time constant two).

- **Statistical analyses:** The goodness of fit for each fitting model was assessed using the lowest residual sum of squares (RSS values) from a computerized nonlinear regression technique:\textsuperscript{24}

$$F = \frac{(SS_1 - SS_2)(df_1 - df_2))}{(SS_2 df_2)}$$
Where $SS$ is the residual sum of squares of each fit, $df$ is the number of degrees of freedom, the suffixes 1 and 2 refer to the models being compared where suffix 1 refers to the model with the fewest parameters. The best statistical fit exponential mathematical model was assessed using the RSS values for models that fit the same number of experimental data points or the mean square error (MSE values, RSS values for models that fit the same number of experimental data points by performing a Fisher’s test ($F_{\text{value}}$ at 0.05 level of significance and one tailed),$^{5,23,25}$ The number of circular permutations for model comparisons ($nP'x$) was calculated according to Zar$^{25}$ and expressed as a factorial function: $^5$

$$nP'x = n! / [(n - x) ! (x)]$$

Where $n$ is the number of different ways of arranging two out (x 2) of n (n 8) mathematical models in circular “arrangement”. For example,$^{5,23,25}$ on the assessment of the:

i) $2C,7P_{\text{Baseline, 0 to 6 min for Hvy}}$ (data: RSS$^1_{1}$ 19743532, NDP$^1_{1}$ 360, NP$^1_{1}$ 7, df$^1_{1}$ 360 - 7 353) versus $3C,10P_{\text{from MinBaseline, 0 to 6 min for Hvy}}$ (data: RSS$^2_{2}$ 11826244, NDP$^2_{2}$ 360, NP$^2_{2}$ 10, df$^2_{2}$ 360 - 10 350) with $F_{\text{valueRSS}} = [(RSS^1 - RSS^2) / (df^1 - df^2)] / (RSS^2 / df^2)$ ($19743532 - 11826244) / (353 - 350)$) resulted significantly high compared $F_{\text{tab,1a}}$ (1.10, $P < 0.05$); consequently, complex model ($3C,10P$) statistically best fitted experimental data for heavy intensity exercise.$^5$ On the assessment$^{25}$ of the

ii) $1C,4P_{\text{from 0.3333 to 3 min for ModAbs}}$ (data: MSE$^1_{1}$ 280528, NDP$^1_{1}$ 160, NP$^1_{1}$ 4, df$^1_{1}$ 160 - 4 156) versus $2C,7P_{\text{from Baseline, 0 to 6 min for ModAbs}}$ (data: MSE$^2_{2}$ 1348, NDP$^2_{2}$ 360, NP$^2_{2}$ 10, df$^2_{2}$ 360 - 7 353) with $F_{\text{valueMSE}} = [(MSE^1 - MSE^2) / (df^1 - df^2)] / (MSE^2 / df^2)$ ($280528 - 1348) / (156 - 7)$ results significantly high compared $F_{\text{tab,1a}}$ (1.23, $P < 0.05$); consequently, complex model ($2C,7P$) statistically best fitted $\text{Vo}_2$ on-transient experimental data for moderate absolute intensity exercise.$^5$ The eight exponential mathematical fitting models used in this study were four simple ($1C,4P_{0.3333}$ → $3 \text{min}$, $1C,4P_{0.3333}$ → $6 \text{min}$, $1C,3P_{BL2}$ → $6 \text{min}$, $1C,4P_{BL2}$ → $6 \text{min}$) and four complex ($2C,7P_{BL2}$ → $3 \text{min}$, $2C,7P_{BL2}$ → $6 \text{min}$, $3C,9P_{BL2}$ → $6 \text{min}$ and, $3C,10P_{BL2}$ → $6 \text{min}$) models. Data treatment consisted of group analyses performed using either an ANOVA with Student-Newman-Keuls and Tukey post-hoc analyses or Kruskal-Wallis ANOVA on Ranks procedure Dunns’ Method when variances of the dependent variable were unequal or the distribution of the dependent variable was not normal, to compare kinetic temporal parameters from the exercise square waves.$^{25}$ Student t-test was used to assess for significant differences between the estimated parameter means from two groups with the same number of parameters.$^{25}$ The probability level denoted significance at $p \leq 0.05$. Except where otherwise stated, the estimated parameters are presented as mean ± standard deviation.

### RESULTS

**Physical characteristics and ramp exercise test**

The physical characteristics, maximal cardiorespiratory and $R_l$ values are presented in table 1. The $\text{Vo}_2$ peak exercise intensity expressed as absolute power output ($\text{MODerateAbs}$) and relative ($\text{MODerateRel}$, $H_{\text{EAVYRel}}$) to the $R_l$ (% $R_l$) are presented in table 2. The power output ($W$), significantly lasted $\text{MODerate}$ low compared $H_{\text{EAVY}}$ (Table 2). The square wave test $\text{Vo}_2$ endExercise significantly lasted ($\text{MODerate}$ lower than $H_{\text{EAVY}}$) (Table 2) different from $\text{Vo}_2$ pl ($\text{MODerate}$) (Table 1). The $\text{Vo}_2$ relative exercise intensity the $R_l$ (% $R_l$) lasted $\text{MODerate}$ low compared $H_{\text{EAVY}}$ (Table 2). The W relative exercise intensity the $R_l$, calculated as $W_{\text{intensity exercise}} / W_{\text{pl}}$, lasted (%): $\text{MODerateAbs}$ (82.2 ± 16.3) lower than $\text{MODerateRel}$ (57.0 ± 4.6) lower than $H_{\text{EAVYRel}}$ (143.2 ± 4.7) (F ratio = 29, $P < 0.0001$). The $\text{Vo}_2$ 6min on-transient significantly lasted $\text{MODerate}$ low compared $H_{\text{EAVY}}$ ($F_{\text{ratio}}$

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Total Body Mass (kg)</th>
<th>Work Rate (Watts)</th>
<th>$\text{Vo}_2$ peak (L min⁻¹) (mL kg⁻¹ min⁻¹)</th>
<th>Heart Rate Experimental 220 Age (beats min⁻¹)</th>
<th>$E_{\text{estimated lactate}}$ (mL min⁻¹ (% $\text{Vo}_2$ peak))</th>
</tr>
</thead>
<tbody>
<tr>
<td>70.7 ± 4.7</td>
<td>173.9 ± 5.5</td>
<td>79.8 ± 10</td>
<td>128.4 ± 20.8</td>
<td>2.2 ± 0.4</td>
<td>28.3 ± 7.2</td>
<td>158.3 ± 14.9</td>
</tr>
</tbody>
</table>

Numeric values are mean ± sd.
Table 2. Data for exercise at the same absolute power output (PO), and during relative intensity exercise below (moderate) and above (heavy) the estimated lactate threshold (θ_L) in nine old men.

<table>
<thead>
<tr>
<th>PO (W)</th>
<th>%θ_L</th>
<th>%VO_2 peak</th>
<th>VO_2 (mL.min^-1)</th>
<th>%θ_L</th>
<th>%VO_2 peak</th>
<th>VO_2 (mL.min^-1)</th>
<th>%θ_L</th>
<th>%VO_2 peak</th>
<th>VO_2 (mL.min^-1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate Relative (80%)</td>
<td>Heavy relative (120%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1180±</td>
<td>89i</td>
<td>57k</td>
<td>1050±</td>
<td>79i</td>
<td>49k</td>
<td>90i</td>
<td>1770±</td>
<td>121i</td>
<td>81i</td>
</tr>
<tr>
<td>±145</td>
<td>±15</td>
<td>±15</td>
<td>±11</td>
<td>±198</td>
<td>±12</td>
<td>±11</td>
<td>±17</td>
<td>±333</td>
<td>±17</td>
</tr>
</tbody>
</table>

Numeric values are mean ± sd. Significant differences between means with different letter, allocated by ANOVA procedure Tukey test: a,b,c,d,F_ratio = 19.5, P < 0.001 (included differences from mean VO_2 V/IT = 1333 ± 139±d, mL.min^-1); Kruskal Wallis ANOVA based on Ranks: e,F_ratio = 26.8, P < 0.001; Student Newman Keuls test: i,F_ratio = 12, P < 0.001 (included differences from mean VO_2 V/IT %VO_2 peak = 62 ± 7.8%, %). %V/IT calculated as (VO_2 exercise intensity)/VO_2 V/IT • 100. %VO_2 peak calculated as (VO_2 exercise intensity)/VO_2 peak • 100.

Experimental data
- 1C, 4P_0.3333 → 3 min: τF_2P = 36 s
- 2C, 7P_BL2 → 6 min: τF_2Iso_Phys = 41 s

Figure 1. Oxygen uptake (VO_2) time course during the on transient moderate intensity (50 W) exercise. Exercise onset (start) is at six min. Exercise offset (end) is at six min. The best intra phase two data fit for the postulated (p) phase two (F_2postulated) VO_2 was 1C,4P_0.3333 → 3 min (F_2postulated) fitting model. The best physiologically (Phys) fit for the isolated phase two (F_2iso) VO_2 was the 2C,7P_BL2 → 6 min (F_2Iso_Phys) fitting model (2C,7PBASELINE Offset to Offset). Estimates for the time required to re reach 63% of final amplitude (τ) are with reference to phase two (τF_2postulated, τF_2Iso_Phys). The characteristic seven parameters (7P) of a twocomponent exponential model (2C) describing this VO_2 time course data are as followed: a_0 is the baseline VO_2 (VO_2 model started fitting from 2 min baseline, BL2, before the onset to the offset of the exercise); a_1 and a_2 (long dashed lines) are the increases in the amplitude of VO_2 above the baseline value; τ_1 and τ_2 are the time constants; TD_1 and TD_2 are the time delays; and A_Tot = a_1 + a_2. The 2C,7P_BL2 → 6 min Phys differentiates F_2 VO_2 from both F_1, VO_2 and F_3 VO_2 on transient entire response data.

7.5, P < 0.0001) (Table 2), and the VO_2 manpower on-transient also lasted as followed (mL.min^-1): 1MODERATEAbs (1119 ± 153) similar MODERATERel (1022 ± 193) lower than H_EAR_VRel (1574 ± 235) (F_ratio 13, P < 0.0001). Finally, only H_EAR_VRel showed VO_2 6min (mL.min^-1) on-transient significantly (F_ratio 4, P < 0.03) higher (1770 ± 333) than VO_2 2min on-transient (1574 ± 235), confirming that this exercise intensity was below θ_L (ΔVO_2[2min-3min] 197 ± 70).

VO_2 linear regression

The slope (coefficient) of the MODERATE VO_2-power output relationship and the VO_2 during loadless cycling (constant) were: VO_2MODERATE 569.53 + (12.43 • W), n 18, R 0.98, P < 0.001 and VO_2loadless 751 ± 127 mL.min^-1.

Mathematical Modelling

We have compared estimates of on-transient phase two pulmonary VO_2 uptake time constant (F_2 VO_2) by eight empirical exponential mathematical fitting models of VO_2 data during moderate- and heavy-intensity exercise in old men. For MODERATE, the most convenient best intra F_2 VO_2 fit was provided by onecomponent exponential model, which omitted F_1 VO_2 data, that fitted from 20 s after the exercise onset to a presumed steady-state at 3 min and underestimated T_immediate Delay2. The estimate of F_2 VO_2 and τ provided by onecomponent exponential model was similar to that provided by the best physiologically F_2 VO_2 fit, a two exponential model, that fitted from baseline exercise onset to exercise offset. Both models (1C and 2C) had phy-
siological significance as they focussed, 1C,4P_0.3333 → 3 min modelling intra-Φ₂ VO₂ and 2C,7P Baseline_Onset to Offset modelling into the entire data and also physiologically isolating Φ₂ VO₂, upon the area of the on-transient data which reflected working muscle VO₂. For H_EAVY, VO₂ was best modelled with a three-component exponential model that was fit throughout the entire data set. The 3C,10P Baseline_Onset to Offset modelling H_EAVY response data was both statistically best compared 2C,7P Baseline_Onset to Offset and physiologically best compared 1C,4P_0.3333 → 3 min, 2C,7P Baseline_Onset to Offset and 3C,9P Baseline_Onset to Offset. These more convenient (1C,4P_0.3333 → 3 min modelling S_SUBMAXIMAL response data) and best physiological fitting models (2C,7P Baseline_Onset to Offset modelling M_ODERATE response data or 3C,10P Baseline_Onset to Offset modelling H_EAVY response data) showed on-transient Φ₂ VO₂ τ estimated values similar in older men, that seem to be correct in order to kinetically compare the on-transient pulmonary Φ₂ VO₂ data (Φ₂ VO₂ τ) of submaximal exercise in young versus old men. Our research on this topic is guaranteed.

An example of the VO₂ time course for M_ODERATEAbs, M_ODERATERel and H_EAVYRel tests are presented in figures 1-3 respectively. Examples of the best fitting models for Φ₂ postulated with 1C,4P_0.3333 → 3 min and Φ₂ Is0 with 2C,7P BL2 → 6 min.

![Image](image_url)

**Figure 2.** Oxygen uptake (VO₂) time course during the on transient of moderate intensity (80% VO₂) exercise. Exercise onset (start) is at six min. Exercise offset (end) is at six min. The best intra phase two data fit for the postulated (p) phase two (Φ₂postulated) VO₂ was 1C,4P_0.3333 → 3 min (Φ₂postulated) fitting model. The best physiologically (Phys) fit for the isolated phase two (Φ₂iso) VO₂ was the 2C,7P BL2 → 6 min (Φ₂iso_Phys) fitting model (2C,7P Baseline_Onset to Offset). Estimates for τ (time required to reach 63% of final amplitude) are with reference to phase two (τ Φ₂postulated: τ Φ₂iso_Phys). θ₂, estimated lactate threshold.

![Image](image_url)

**Figure 3.** Oxygen uptake (VO₂) time course during the on transient of heavy intensity (120% VO₂) exercise. Exercise onset (start) is at six min. Exercise offset (end) is at six min. The best intra phase two data fit for the postulated (p) phase two (Φ₂postulated) VO₂ was 1C,4P_0.3333 → 3 min (Φ₂postulated) fitting model. The best both physiologically (Phys) and statistically (Stat, based on Fisher’s test) fit for the isolated phase two (Φ₂iso) VO₂ was the 3C,10P BL2 → 6 min (Φ₂iso_PhysStat) fitting model (3C,10P Baseline_Onset to Offset). Estimates for τ (time required to reach 63% of final amplitude) are with reference to phase two (τ Φ₂postulated: τ Φ₂iso_Phys). The characteristic ten parameters (10P) of a threecomponent exponential model (3C) describing this VO₂ time course data are as followed: a₀ is the baseline VO₂ (3C model started fitting from 2 min baseline, BL2, before the onset to the offset of the exercise); a₁, a₂, a₃, and a₄ (long dashed lines) are the increases in the amplitude of VO₂ above the baseline value; τ₁, τ₂ and τ₃ are the time constants; TD₁, TD₂ and TD₃ are the time delays; and A₁tot = a₁ + a₂ + a₃. The 3C,10P BL2 → 6 min Phys differentiates Φ₂ VO₂ from both Φ₁ VO₂ and Φ₃ VO₂ on transient entire response data. θ₂, estimated lactate threshold.
are presented in figures 1 and 2 for \( M_{\text{ODERATE}} \). Examples of the best fitting models for \( \Phi_2 \text{postulated} \) with \( 1C,4P_{0.3333 \rightarrow 3 \text{ min}} \) are shown in figures 3 and 4 and for \( \Phi_2 \text{isolated} \) are also presented in figure 3 with \( 3C,10P_{\text{BL2} \rightarrow 6 \text{ min}} \) (\( \Phi_2 \text{isolated}_{\text{PhysStatBestFit}} \)) and figure 4 with \( 3C,9P_{\text{BL2} \rightarrow 6 \text{ min}} \) (\( \Phi_2 \text{isolated}_{\text{StatBestFit}} \)) for \( H_{\text{EAVY}} \) during the on-transient of steady-state \( S_{\text{UBMAXIMAL}} \) as estimated by eight different fitting models are presented in table 3. The mathematical model permutations of \( 1C,2C \) and \( 3C \) comparisons for the on-transient \( \text{VO}_2 \) \( S_{\text{UBMAXIMAL}} \) responses are presented in table 4. The amplitude and the parameter estimates determined from kinetic analyses of \( \text{VO}_2 \) during the on-transient of steady-state exercise, as estimated by the best fitting models from these study, are presented in table 4 for \( M_{\text{ODERATE}} \) and \( H_{\text{EAVY}} \). Amplitudes from \( \Phi_2 \text{isolated}_{\text{VO}_2} \) and \( \Phi_2 \text{VO}_2 \) during the on-transient of steady-state \( H_{\text{EAVY}} \) were different in model \( 3C,9P_{\text{BL2} \rightarrow 6 \text{ min}} \) compared to model \( 3C,10P_{\text{BL2} \rightarrow 6 \text{ min}} \) (Table 5).

### One component fitting model comparisons

Both \( 1C,4P_{\text{BL2} \rightarrow 6 \text{ min}} \) and \( 1C,3P_{\text{BL2} \rightarrow 6 \text{ min}} \) were not physiologically useful for fitting \( \text{VO}_2 \) on-transient entire responses data to characterize \( \Phi_2 \text{VO}_2 \) for \( S_{\text{UBMAXIMAL}} \). The simple one model \( 1C,4P_{0.3333 \rightarrow 3 \text{ min}} \) fitted (Figures 1-3).

### Figure 4. Oxygen uptake (\( \text{VO}_2 \)) time course during the on transient of heavy intensity (120% \( \theta_i \)) exercise. Exercise onset (start) is at six min. Exercise offset (end) is at six min. The best fit for the postulated (p) phase two (\( \Phi_2 \text{postulated} \)) \( \text{VO}_2 \) was the simple \( 1C,4P_{0.3333 \rightarrow 3 \text{ min}} \) (\( \Phi_2 \text{postulated} \)) fitting model. The best statistically fit for “isolated” phase two (\( \Phi_2 \)) \( \text{VO}_2 \) was the restricted (\( T_{\text{onset}}D_{\text{delay}2} = T_{\text{onset}}D_{\text{delay}3} \)) \( 3C \) or \( 3C,9P_{\text{BL2} \rightarrow 6 \text{ min}} \) (\( \Phi_2 \text{isolated}_{\text{Phys}} \)) fitting model (\( 3C,9P_{\text{Baseline,Onset to Offset}} \)). Estimates for \( \tau \) (time required to reach 63% of final amplitude) are with reference to phase two (\( \tau \Phi_2 \text{postulated} \), \( \tau \Phi_2 \text{isolated}_{\text{Phys}} \)). The \( 3C,9P_{\text{BL2} \rightarrow 6 \text{ min}} \) Phys differentiates \( \Phi_2 \text{VO}_2 \) from \( \Phi_1 \text{VO}_2 \) but not from \( \Phi_1 \text{VO}_2 \) on transient entire response data. \( \theta_i \), estimated lactate threshold.

### Table 3. Residual sum of squares and mean square error estimates for kinetic analysis of \( \text{VO}_2 \) during the on transient of steady state submaximal exercise as estimated by eight different exponential mathematical models in nine old men.

<table>
<thead>
<tr>
<th>Fitting Model</th>
<th>RSS (x10^5)</th>
<th>50 Watts</th>
<th>( M_{\text{mean}} )</th>
<th>S_\text{square}</th>
<th>E_\text{error}</th>
</tr>
</thead>
<tbody>
<tr>
<td>( 1C,4P_{0.3333 \rightarrow 3 \text{ min}} )</td>
<td>2.07 ± 0.64</td>
<td>1324 ± 408</td>
<td>3.07 ± 2.70</td>
<td>1965 ± 1731</td>
<td>6.31 ± 8.31</td>
</tr>
<tr>
<td>( 1C,4P_{0.3333 \rightarrow 6 \text{ min}} )</td>
<td>4.73 ± 1.75</td>
<td>1409 ± 522</td>
<td>6.29 ± 4.60</td>
<td>1870 ± 1369</td>
<td>14.85 ± 20.15</td>
</tr>
<tr>
<td>( 1C,3P_{\text{BL2} \rightarrow 6 \text{ min}} )</td>
<td>7.61 ± 3.47</td>
<td>1536 ± 619</td>
<td>7.77 ± 5.61</td>
<td>1787 ± 1155</td>
<td>18.96 ± 23.76</td>
</tr>
<tr>
<td>( 1C,4P_{\text{BL2} \rightarrow 6 \text{ min}} )</td>
<td>6.77 ± 2.61</td>
<td>1402 ± 504</td>
<td>7.12 ± 5.30</td>
<td>1643 ± 1094</td>
<td>17.65 ± 21.12</td>
</tr>
<tr>
<td>( 2C,7P_{\text{BL2} \rightarrow 6 \text{ min}} )</td>
<td>3.79 ± 1.50</td>
<td>1294 ± 512</td>
<td>4.61 ± 2.86</td>
<td>1666 ± 1118</td>
<td>8.82 ± 9.37</td>
</tr>
<tr>
<td>( 2C,7P_{\text{BL2} \rightarrow 3 \text{ min}} )</td>
<td>6.43 ± 2.61</td>
<td>1359 ± 552</td>
<td>6.98 ± 5.05</td>
<td>1657 ± 1103</td>
<td>15.86 ± 20.68</td>
</tr>
<tr>
<td>( 3C,9P_{\text{BL2} \rightarrow 6 \text{ min}} )</td>
<td>It did not fit these data</td>
<td>It did not fit these data</td>
<td>It did not fit these data</td>
<td>It did not fit these data</td>
<td>15.97 ± 19.93</td>
</tr>
<tr>
<td>( 3C,10P_{\text{BL2} \rightarrow 6 \text{ min}} )</td>
<td>It did not fit these data</td>
<td>It did not fit these data</td>
<td>It did not fit these data</td>
<td>It did not fit these data</td>
<td>17.70 ± 17.83</td>
</tr>
</tbody>
</table>

Numeric values are mean ± sd. RSS: Residual Sum of Squares and is expressed as RSS x 10^5. 1C, 2C, and 3C are the one component, two component, and three components exponential mathematical models. 3P: three parameters. 4P: four parameters. 7P: seven parameters. 9P: nine parameters. 10P: ten parameters. BL2: two min baseline. \( T_{\text{onset}}D_{\text{delay}2} = T_{\text{onset}}D_{\text{delay}3} \) fitting period of time window: \( 0.3333 \rightarrow 6 \text{ min} \), from 20 s after start to end exercise; BL2: 6 min, from two min baseline to end exercise.
Fisher’s test ($F$ test) is a statistical test used to compare the means of two groups. It is often used in conjunction with an analysis of variance (ANOVA) to determine whether the variances of two groups are significantly different. In this context, Fisher’s test is applied to assess the physiological significance of the residual sum of squares and is expressed as $\text{RSS} \times 10^5$.

Table 4. The best statistical fit from the two out mathematical model permutations of onecomponent, twocomponent and threecomponent mathematical exponential models for the on transient $\text{VO}_2$ submaximal exercise in nine old men.

<table>
<thead>
<tr>
<th>Number of Permutations</th>
<th>“S”</th>
<th>“C”</th>
<th>“O”</th>
<th>50 Watts</th>
<th>Estimated Lactate</th>
<th>Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$S_{\text{simple}}$</td>
<td>$C_{\text{complex}}$</td>
<td>$O$</td>
<td>$F_{\text{value}}$</td>
<td>$F_{\text{RSS}}$</td>
<td>$F_{\text{MSE}}$</td>
</tr>
<tr>
<td>Oneocomponent model vs. Onecomponent model.</td>
<td>1</td>
<td>1C,3P_{BL2} → 6 min</td>
<td>1C,4P_{BL2} → 6 min</td>
<td>42*,C$_o$</td>
<td>28*,C$_o$</td>
<td>17*,C$_o$</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1C,3P_{BL2} → 6 min</td>
<td>1C,4P_{0.3333} → 6 min</td>
<td>1.33*,C$_o$</td>
<td>0.01,S$_i$</td>
<td>0.21,S$_i$</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1C,3P_{BL2} → 6 min</td>
<td>1C,4P_{0.3333} → 3 min</td>
<td>0.01,S$_i$</td>
<td>0.01,S$_i$</td>
<td>0.07,S$_i$</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>1C,4P_{0.3333} → 3 min</td>
<td>1C,4P_{0.3333} → 6 min</td>
<td>0.08,S$_i$</td>
<td>0.04,S$_i$</td>
<td>0.17,S$_i$</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>1C,4P_{0.3333} → 3 min</td>
<td>1C,4P_{BL2} → 6 min</td>
<td>0.06,S$_i$</td>
<td>0.71,S$_i$</td>
<td>0.01,S$_i$</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>1C,4P_{0.3333} → 6 min</td>
<td>1C,4P_{BL2} → 6 min</td>
<td>0.17,S$_i$</td>
<td>0.77,S$_i$</td>
<td>0.74,S$_i$</td>
</tr>
</tbody>
</table>

Table 5. Amplitude and parameter estimates determined for kinetic analysis of $\text{VO}_2$ during the on transient of steady state submaximal exercise as estimated by the best fit exponential mathematical models in nine old men.

<table>
<thead>
<tr>
<th>$W_{\text{on}}$</th>
<th>$R_{\text{rate}}$</th>
<th>Fitting Model</th>
<th>Estimated parameters (Baseline (a$_0$, mL•min$^{-1}$))</th>
<th>$A_{\text{amplitude}_{\Phi_1}}$ (a$_1$, mL•min$^{-1}$)</th>
<th>$A_{\text{amplitude}_{\Phi_2}}$ (a$_2$, mL•min$^{-1}$)</th>
<th>$A_{\text{amplitude}_{\Phi_3}}$ (a$_3$, mL•min$^{-1}$)</th>
<th>$A_{\text{amplitude}_{\text{total}}}$ (mL•min$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50W</td>
<td>1C,4P_{0.3333} → 3 min</td>
<td>1C,4P_{BL2} → 6 min</td>
<td>860.4 ± 131.6</td>
<td>299.5 ± 52.5</td>
<td>438.7 ± 52.5</td>
<td>281.5 ± 150.4</td>
<td>1073.4 ± 315.2</td>
</tr>
<tr>
<td>80%_{ <code>$\Phi$</code> }</td>
<td>2C,7P_{BL2} → 6 min</td>
<td>741.5 ± 129.8</td>
<td>192.6 ± 55.1</td>
<td>245.2 ± 51.5</td>
<td>438.7 ± 52.5</td>
<td>281.5 ± 150.4</td>
<td>1073.4 ± 315.2</td>
</tr>
<tr>
<td>120%_{ <code>$\Phi$</code> }</td>
<td>3C,9P_{BL2} → 6 min</td>
<td>750.6 ± 130.6</td>
<td>138.3 ± 63.6</td>
<td>142.7 ± 94.3</td>
<td>281.5 ± 150.4</td>
<td>1073.4 ± 315.2</td>
<td>1067.8 ± 325.5</td>
</tr>
</tbody>
</table>

: No estimated parameter value. `$\Phi$`: Estimated lactate threshold. $a \neq b$ (t = 9) and $c \neq d$ (t = 57) Student $t_{0.05}$ P < 0.05. `$\Phi$`: Phases of the increase in $\text{VO}_2$ during the on transient of submaximal exercise. [ ] “virtual” either baseline $\text{VO}_2$ or TD2. TD: time delay. $\tau$: time constant. MRT$_{\text{exp}}$: exponential mean response time (the time required for the transient $\text{VO}_2$ response to reach 63% of final amplitude); MRT$_{\text{exp}}$: 1C = TD + $\tau$ of $\text{VO}_2$; MRT$_{\text{exp}}$: 2C = [a$_1$ + a$_2$] + (TD1 + T1) + [a$_3$ + a$_4$] + (TD2 + T2); MRT$_{\text{exp}}$: 3C = [a$_1$ + a$_2$ + a$_3$] + (TD1 + T1) = [a$_4$ + a$_5$ + a$_6$] + (TD2 + T2) + [a$_7$ + a$_8$ + a$_9$] + (TD3 + T3). 1C, 2C, and 3C, One, Two, and three component exponential mathematical model. RSS: residual sum of squares and is expressed as RSS x 10$^5$. MSE: mean square error. $p$: postulated. $S$: statistical best. P: physiological best. *: no physiological sense.
best intra $\Phi_2V_{O_2}$ data ($\Phi_{2\text{postulated}}V_{O_2}$) for $S_{\text{SUBMAXIMAL}}$ (Table 4).

**One-, two-, and three-component fitting model comparisons**

The $2C,7P_{BL2\rightarrow6min}$ showed physiological best fit $\Phi_2V_{O_2}$ on-transient response data to $M_{\text{MODERATE}}$ (Table 4, Figures 1 and 2); $\Phi_2$ Isolated PhysBestFit$V_{O_2}$. The $3C$ model ($3C,9P$, $3C,10P_{BL2\rightarrow6min}$ fitted statistically better (based on Fisher’s test) than $2C,7P_{BL2\rightarrow6min}$ (Table 4) the $\Phi_2V_{O_2}$ on-transient response data for $H_{\text{EAVY}}$. The $3C,9P_{BL2\rightarrow6min}$ was neither physiologically nor statistically better than $3C,10P_{BL2\rightarrow6min}$ (Tables 4 and 5, Figure 4) on fitting $\Phi_2V_{O_2}$ on-transient response data for $H_{\text{EAVY}}$. The $3C,10P_{BL2\rightarrow6min}$ showed physiological sense in terms of amplitude and temporal parameter estimates of the three $V_{O_2}$ phases of response data for $H_{\text{EAVY}}$ and allowed us to physiologically characterize the $\Phi_2V_{O_2}$ (Table 5, Figure 3) response data for $H_{\text{EAVY}}$.

**Phase Two $V_{O_2}$ On-Transient Kinetics ($\tau \Phi_2V_{O_2}$)**

The $1C,4P_{0.3333\rightarrow3min}$ characterized $\Phi_{2\text{postulated}}V_{O_2}$ on-transient data for $M_{\text{MODERATE Abs}}$ ($\Phi_{2\text{postulated}}33 \pm 4.95s$).

### Table 6. Parameter estimated by the best fit one component mathematical model from kinetic analysis of $V_{O_2}$ data placed into discrete time bins of 10 s during the on transient of steady state submaximal exercise in nine old men.

<table>
<thead>
<tr>
<th>Work Rate</th>
<th>Baseline($a_0$) (mL•min$^{-1}$)</th>
<th>Amplitude($a_1$) (mL•min$^{-1}$)</th>
<th>$\Phi_2T_{\text{max Delayed}}(TD2)$ (s)</th>
<th>$\Phi_{2\text{postulated}}\tau (T2)$ (s)</th>
<th>$\pm 95$ (confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 Watts</td>
<td>[740 ± 137]</td>
<td>438 ± 55</td>
<td>[10.32 ± 12]</td>
<td>42.61 ± 9.1</td>
<td>3 ± 0.9</td>
</tr>
<tr>
<td>80% $\bar{V}_{\text{L}}$</td>
<td>[727 ± 87]</td>
<td>293 ± 134</td>
<td>[7.94 ± 8.8]</td>
<td>42.73 ± 4.83</td>
<td>6 ± 2.2</td>
</tr>
<tr>
<td>120% $\bar{V}_{\text{L}}$</td>
<td>[741 ± 112]</td>
<td>922 ± 260</td>
<td>[7.08 ± 5.5]</td>
<td>43.70 ± 7.8</td>
<td>2 ± 0.7</td>
</tr>
</tbody>
</table>

$\bar{V}_{\text{L}}$: estimated lactate threshold. $\Phi_2$: refers to phase 2 of the increase in $V_{O_2}$ during the on transient of submaximal exercise. $a_0$ represents the baseline $V_{O_2}$ prior to the transition to submaximal exercise. The $a_0$ shown in square brackets is the $V_{O_2}$ corresponding to 0.3333 min (20 s) with the exercise transient, and thus represents a “virtual” baseline $V_{O_2}$. Data was fitted with one component exponential mathematical model of four parameters ($a_0, a_1, TD1, TD2$). Fitting window: 20 s from exercise onset to either end exercise (MOD: 50 Watts, 80% $\bar{V}_{\text{L}}$) or phase 2.3 transition (HVY: 120% $\bar{V}_{\text{L}}$). $T_{\text{max Delayed}}$ shown in square brackets represent a “virtual” TD2. $\tau$: time constant. $\Phi_{2\text{postulated}}V_{O_2}$ started 20 s after de onset of the exercise and end at 3 min on transient response to submaximal exercise.

### Table 7. Final summary best fit exponential mathematical models that characterized the Phase two $V_{O_2}$ during the on transient of steady state moderate intensity (50 W, 80% $\bar{V}_{\text{L}}$) and heavy intensity (120% $\bar{V}_{\text{L}}$) exercise, respectively, in nine old men.

<table>
<thead>
<tr>
<th>Exponential Mathematical Model</th>
<th>Fitting Model</th>
<th>$\tau \Phi_2V_{O_2}$</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_{O_2}(t) = a_0(\text{virtual}) + a_1 \cdot [1 e^{-[\text{TD}]/\tau}]$</td>
<td>Submaximal Exercise</td>
<td>$\tau\Phi_{2\text{postulated}}$ (Practical Phys $\Phi_2V_{O_2}$)</td>
<td>$1C,4P_{0.3333\rightarrow3min}$ Exercise</td>
</tr>
<tr>
<td>$V_{O_2}(t) = a_0 + a_1 \cdot [1 e^{-[\text{TD}]/\tau}] + a_2 \cdot [1 e^{-[\text{TD}2]/\tau}]$</td>
<td>$\Phi_2$ Isolated PhysBestFit $V_{O_2}$</td>
<td>$2C,7P_{\text{Baseline}\rightarrow\text{End Exercise}}$</td>
<td>$\Phi_1$, $\Phi_2$ Phys BestFit, $\Phi_3$</td>
</tr>
<tr>
<td>$V_{O_2}(t) = a_0 + a_1 \cdot [1 e^{-[\text{TD}]/\tau}] + a_2 \cdot [1 e^{-[\text{TD}2]/\tau}] + a_3 \cdot [1 e^{-[\text{TD}3]/\tau}]$</td>
<td>Heavy-Intensity Exercise</td>
<td>$3C,10P_{\text{Baseline}\rightarrow\text{End Exercise}}$</td>
<td>$\Phi_1$, $\Phi_2$ Phys BestFit, $\Phi_3$</td>
</tr>
</tbody>
</table>

$\tau$: Fitting period of time arrow. On transient, the output of a system from the onset to the offset of the exercise; Onset and Offset, the start and end, respectively, of an application of an ergometric forced function. $\Phi_2$: Ventilatory threshold. Phys: physiological sense (it differentiated $\Phi_2 V_{O_2}$ from both $\Phi_1 V_{O_2}$ and $\Phi_3 V_{O_2}$). $V_{O_2}$: Pulmonary oxygen uptake. $V_{O_2}(t)$: Mass rate of change per unit of time ($dV_{O_2}/dt$), mL•min$^{-1}$. $TD$: Time delay, s. $a_0$: Baseline (the $V_{O_2}$ at the start of the model); $a_1$: the $V_{O_2}$ distance value from $a_0$ to the $V_{O_2}$ required for phase one ($a_1$), phase two ($a_2$) and phase three ($a_3$) amplitudes, mL, $1 e^{-[\text{TD}]/\tau}$: The negative exponential distribution (Evans, Hastings and Peacock, 1993), $1 e^{-[\text{TD}2]/\tau}$: The die away factor with the time constant $\tau$, s, for an exponential increase (on transient $V_{O_2}$ response), $t$: The time in which the transient $V_{O_2}$ response is gradually (exponentially) dying away, when $t = \tau$ means the time required for the transient $V_{O_2}$ response to die away to $e^{1}$ part ($e^{1} = 1/2.71828 = 0.3678$) of its original value, thus, $\tau = 10.3678 = 0.63$, $e = 2.718281 = [1 + n^{10}]^{\Phi}$, $n \geq 10$ and 'e' is incommensurable with 1. One component (1C), $TD1$: Two components (2C), $TD1$ and $TD2$; Three components (3C), 2C and $TD3$. $4P$: Four parameters ($a_0$, $a_1$, $TD1$, $\tau$). $7P$: Seven parameters ($7P$, $a_2$, $TD2$, $\tau$).
DISCUSSION

Physical characteristics, ramp exercise test, and constant load tests

The physical characteristics, maximal cardiorespiratory and \( \hat{\theta}_1 \) values from all of our subjects were above average fitness.26 In this study the observations were that subject showed low power output and low square wave test \( \text{VO}_2\text{end} \) Exercise for \( \text{MODERATE} \) compared to \( \text{HEAVY} \). Subjects showed \( \text{MODERATE}_{\text{Abs}} \text{VO}_2 \left( \% \hat{\theta}_1 \right) \) similar to \( \text{VO}_2 \text{abs} \). \( \text{MODERATE} \) Rel \( \text{VO}_2 \left( \% \hat{\theta}_1 \right) \) resulted lower compared \( \text{VO}_2 \text{rel} \), and they were lower that the \( \text{HEAVY} \),Rel \( \text{VO}_2 \left( \% \hat{\theta}_1 \right) \). However, these differences in the numeric values of these variables, showed \( \text{PH}_2 \text{VO}_2 \tau \) values not to be kinetically different between the work rates of \( \text{MODERATE} \). Our study showed the well known observation that cycle exercise resulted in a linear increase in \( \text{VO}_2 \) of approximately 10 mL\( \cdot \)min\(^{-1}\) (this study 12 mL\( \cdot \)min\(^{-1}\) for \( \text{MODERATE} \) for every one W increase in work rate.27 The \( \text{HEAVY} \) showed a positive on-transient \( \Delta \text{VO}_2 \) (6-3 min) value because the metabolic requirement for performance of this heavy work rate, is known to be over and above that predicted from below \( \hat{\theta}_1 \) \text{VO}_2 - work rate relationship.4

Mathematical Modelling

- One component fitting model comparisons: The 1C fitting models 1C,4P,0.3333 min to Offset 1C,4P BaseLine, Onset to Offset and 1C,3P BaseLine, Onset to Offset oversimplifying the \( \text{VO}_2 \) response data for \( \text{MODERATE} \) and \( \text{HEAVY} \),28 they poorly fitted in terms of large MSE through the phase due to an increase in pulmonary blood flow.15,19,27 followed by a further exponential increase in pulmonary \( \text{VO}_2 \) that reflects muscle \( \text{VO}_2 \).29,30 and they showed also no physiological sense of the estimates of \( \Phi_2 \text{VO}_2 \tau \). All these observations are in agreement with those ones observed in a similar study done with young adults.8,9 Thus, from 1C fitting model comparisons, the most convenient best intra-fit \( \Phi_2 \text{postulated \text{VO}_2 \text{on-transient response data to} \text{SUBMAXIMAL} \right) \) in terms of both \( \tau_2 \) value and physiological meaning, was the 1C,4P,0.3333 min to 3 min, in agreement with previous observations in young adults.8,9 The fact that 1C,4P,0.3333 to 3 min physiologically best intra-fitted \( \Phi_2 \text{VO}_2 \) on-transient response data to \( \text{SUBMAXIMAL} \), compared to either 2C,7P for \( \text{SUBMAXIMAL} \) or 3C for \( \text{HEAVY} \), is explained because this \( \Phi_2 \text{VO}_2 \) is an exponential transient response.27 and also because the shorter the period of time modelled the better both the fit and the simple the mathematical model.8,23

- Two component fitting model comparisons: We fit the same \( \text{SUBMAXIMAL} \) data set with three different 2C fitting models (2C,7P BaseLine, Onset to 3 min, and 2C,7P BaseLine, Onset to Offset) which varied mainly in their fitting window and consideration of the phases of increase in \( \text{VO}_2 \) in our group of old men. Taking in consideration that the \( \text{VO}_2 \) response data during the on-transient of \( \text{MODERATE} \), culminating in a steady-state value, is less complicated relative to the response during the on-transient of \( \text{HEAVY} \); the 2C,7P BaseLine, Onset to 3 min omitted \( \Phi_1 \text{VO}_2 \) and arbitrary limits of 3 min the \( \Phi_2 \text{VO}_2 \) end, had the inconvenient, that did not neither physiologically differentiate nor isolate \( \Phi_2 \text{VO}_2 \) from the \( \text{MODERATE} \) entire data in young,8,9 and old men in this study. Thus, the 2C,7P BaseLine, Onset to Offset fitting models was physiologically best fit in old men for the \( \text{MODERATE} \), \( \text{PH}_2 \text{isolated \text{VO}_2 \text{on-transient entire response data, because this model included a baseline when it differentiated this \( \Phi_2 \text{isolated \text{VO}_2 \text{with its second exponential term from the three phases of this entire \text{MODERATE} \text{VO}_2 \text{on-transient response.}} \)8,9 If \( \text{MODERATE} \) \( \Phi_2 \text{VO}_2 \) were and exponential response, then the fitting model 2C,7P BaseLine, Onset to Offset would probably perfectly match the entire \( \text{VO}_2 \) morphology of this \( \text{MODERATE} \) response data. Nevertheless, 2C,7P BaseLine, Onset to Offset, supported in both physiological and kinetical terms the isolation
of the $M_{\text{ODERATE}} \phi_2 \overline{V}_O_2 (\phi_2 \text{isolated}_\text{Phys}_1 \overline{V}_O_2 \tau)$ response data to constant-load leg cycling. In consequence, we preferred $2C,7P_{\text{Baseline Onset to Offset}}$ to characterize $\tau\phi_2 \text{isolated}_\text{Phys}_2 \overline{V}_O_2$ on-transient response data to $M_{\text{ODERATE}}$ in old men, because it properly fitted with double exponential functions (with two-component included: TD1 and TD2)\(^7\) the cardiodynamic ($\phi_1$), exponential ($\phi_2$), and steady state ($\phi_3$) $\overline{V}_O_2$ responses to $M_{\text{ODERATE}}$. \(^{21}\) These observations are in agreement with the fact that $\phi_2$ being less complicated response thus it may be described adequately by relatively less complex ($2C$ instead $3C$) mathematical models. In consequence, the $2C,7P_{\text{Baseline Onset to Offset}}$ fitting model was physiologically best fit in old men for the $M_{\text{ODERATE}} \phi_2 \text{isolated}_\text{Phys}_2 \overline{V}_O_2$ on-transient entire response data, because it differentiated this $\phi_2 \text{isolated}_\text{Phys}_2 \overline{V}_O_2$ with its second exponential term from the three phases of this entire $M_{\text{ODERATE}} \overline{V}_O_2$ on-transient response data.\(^8\)

### Three component fitting model comparisons: The $3C$ models fitted statistically better than $2C,7P_{\text{Baseline Onset to Offset}}$ for $H_{\text{EAVY}}$ constant-load leg cycling, because the superimposed morphology of the slow component in the $H_{\text{EAVY}} \phi_2 \overline{V}_O_2$ on-transient response data cannot be properly fitted by $2C$ models.\(^{8,9,32,33}\) These assessments lead us from the physiological system, $\overline{V}_O_2$ on-transient $S_{\text{UBMAXIMAL}}$, to a mathematical formulation, modelling $\phi_2 \overline{V}_O_2$, with the best fitting exponential mathematical models, and to the physiological interpretation of the results in terms of $\phi_2 \overline{V}_O_2 \tau$.

### Phase Two $\overline{V}_O_2$ On-Transient Kinetics ($\tau\phi_2 \overline{V}_O_2$): The $1C,4P_{0.3333 \rightarrow 3 \text{min}}$ kinetically ($\tau$) characterized $S_{\text{UBMAXIMAL}} \phi_2 \text{postulated}_\text{Phys}_2 \overline{V}_O_2$ on-transient response data to constant-load leg cycling, because this $S_{\text{UBMAXIMAL}} \phi_2 \overline{V}_O_2$ on-transient response data is an exponential one\(^7\) and also because by fitting the period of time from 20 s after the onset of the exercise to 3 min exercise, we were mainly modelling in the whole $\phi_2$ experimental data, as well as because the probability of kinetic influences on $\phi_2 \overline{V}_O_2$ from both $\phi_1 \overline{V}_O_2$ and $\phi_3 \overline{V}_O_2$\(^6\) were minimized; in particular $\phi_3 \overline{V}_O_2$ that it has been considered to overlap $\phi_2 \overline{V}_O_2$ during $H_{\text{EAVY}}$ constant-load leg cycling.\(^6,9\) In consequence, the $1C,4P_{0.3333 \rightarrow 3 \text{min}}$ fitting model seems to be closely implying dependence in nature, because there is a high probability that this $\phi_2 \text{postulated}_\text{Phys}_2 \overline{V}_O_2$ on-transient kinetic ($\phi_2 \text{postulated}_\text{Phys}_2 \overline{V}_O_2 \tau$) response data to $S_{\text{UBMAXIMAL}}$ is related at peripheral level (energy- metabolism kinetics) in terms of $\overline{V}_O_2$ consumption $\tau$ and PCR $\tau$ (cause) and $\phi_2 \overline{V}_O_2$ pulmonary uptake $\tau$ (effect).\(^{14}\)

We preferred $2C,7P_{\text{Baseline Onset to Offset}}$ to kinetically characterize $S_{\text{UBMAXIMAL}} \phi_2 \text{isolated}_\text{Phys}_2 \overline{V}_O_2$ on-transient response data, because it showed also physiological sense as a fitting model that isolated the $M_{\text{ODERATE}} \phi_2 \overline{V}_O_2$ on-transient response data ($\phi_2 \text{isolated}_\text{Phys}_2 \text{PhysBestFit}_2$) to constant-load leg cycling. This $2C,7P_{\text{Baseline Onset to Offset}}$ properly fits with double exponential functions (with $T_{\text{time Delay 1}}$ and $T_{\text{time Delay 2}}$ included)\(^7\) the cardiodynamic ($\phi_1$), exponential ($\phi_2$), and steady state ($\phi_3$) $\overline{V}_O_2$ responses to $M_{\text{ODERATE}}$.\(^{31}\) The $T_{\text{time Delay 2}}$ from both the $M_{\text{ODERATE}}$ $\overline{V}_O_2$ (26 s) and the $M_{\text{ODERATE}}$ $\text{Rel}$ (27 s) were different from that assumed prior to phase two of approximately 20 s for fitting model $1C,4P_{20s \rightarrow 3 \text{min}}$ because $\phi_1 \overline{V}_O_2$ on-transient response data finished approximately 20 s after the onset $M_{\text{ODERATE}}$ but individual variability and the intensity of the $M_{\text{ODERATE}}$ test may be responsible for small significant differences like those observed of 6 s for $M_{\text{ODERATE}} \text{Abs}$ and 7 s for $M_{\text{ODERATE}} \text{Rel}$ power output. If $\phi_1 \overline{V}_O_2$ were and exponential response to $M_{\text{ODERATE}}$, then the fitting model $2C,7P_{\text{Baseline Onset to Offset}}$ would probably perfectly match the entire $\overline{V}_O_2$ morphology of response to $M_{\text{ODERATE}}$. Nevertheless, $2C,7P_{\text{Baseline Onset to Offset}}$ supported in physiological and in kinetical terms the isolation of the $M_{\text{ODERATE}} \phi_2 \overline{V}_O_2$ ($\phi_2 \text{isolated}_\text{PhysStat BestFit}_2 \overline{V}_O_2 \tau$) on-transient response data. The $3C,10P_{\text{Baseline Onset to Offset}}$ showed both statistical merits and physiological sense in kinetically characterizing the isolated $H_{\text{EAVY}} \phi_2 \tau$($\phi_2 \text{isolated}_\text{PhysStat BestFit}_2 \overline{V}_O_2 \tau$) $\overline{V}_O_2$ on-transient response data to constant-load leg cycling. The $3C,10P_{\text{Baseline Onset to Offset}}$ characterized with its second exponential term the $H_{\text{EAVY}} \phi_2 \tau$($\phi_2 \text{isolated}_\text{PhysStat BestFit}_2 \overline{V}_O_2 \tau$) $\overline{V}_O_2$ on-transient response data to constant-load leg cycling.\(^{4,7,9,28}\) The $3C,9P_{\text{Baseline Onset to Offset}}$ did not model in physiological terms the estimated parameters (i.e., $\tau$) of the entire $\overline{V}_O_2$ on-transient response data to $H_{\text{EAVY}}$ because it was $3C,10P_{\text{Baseline Onset to Offset}}$ restricted to $T_{\text{time Delay 2}}$ $T_{\text{time Delay 3}}$. Evermore, during $H_{\text{EAVY}}$ both the amplitude $\phi_2$ and amplitude $\phi_3 \overline{V}_O_2$ were different in $3C,9P_{\text{Baseline Onset to Offset}}$ Compared to $3C,10P_{\text{Baseline Onset to Offset}}$. And these amplitude value differences, particularly the one from the slow component (amplitude $\phi_3 \overline{V}_O_2$), is one of the reasons for the lack of physiological sense in the way of modelling entire $\overline{V}_O_2$ on-transient response data to $H_{\text{EAVY}}$ by the fitting model $3C,9P_{\text{Baseline Onset to Offset}}$.\(^{5,8,9}\) These no sense in the estimated values of the temporal parameters, is explained because the $\phi_3 \overline{V}_O_2$ on-transient response data to $H_{\text{EAVY}}$, elicited no steady- state ($\Delta \overline{V}_O_2$)\(^{6,3-3\text{min}}\) positive, slow component.\(^4\) In $M_{\text{ODERATE}}$, not only is $\phi_1 \overline{V}_O_2$ a non exponential response\(^7\) but the $\phi_3 \overline{V}_O_2$ has been questioned of whether this slow component is or not an exponential response data to $H_{\text{EAVY}}$.\(^9\) Nevertheless and since we were interested for this
study in kinetically characterizing $\Phi_2 \text{VO}_2$ only, then $3C,10P_{\text{BaseLine Onset to Offset}}$ characterized $H_{EAVY} \Phi_2$ isolated. PhysBestFit $\text{VO}_2 \tau$ response data to constant-load leg cycling. When modelling the $\Phi_2 \text{VO}_2$ on-transient response data to $M_{\text{MODERATE}}$, it is useful to use the fitting model $1C,4P_{20 \text{ s } \rightarrow 3 \text{ min}}$ as we did in this study, $1C,4P_{0.3333 \rightarrow 3 \text{ min}}$ and did also previously$^{5,6,9}$ as a general reference of $\tau$ values of the postulated on-transient $\Phi_2 \text{VO}_2$ to feedback the kinetic ($\tau$) values from the isolated $\Phi_2 \text{VO}_2$ with either $2C,7P_{\text{BaseLine Onset to Offset}}$ for $S_{\text{UB-MAXIMAL}}$ or $3C,10P_{\text{BaseLine Onset to Offset}}$ for $H_{EAVY}$; these $\tau$ values should be similar to each other, as it was observed in young adults$^{5,6,9}$ and in this study for $S_{\text{UB-MAXIMAL}}$ as well.

The $\Phi_2 \text{VO}_2$ on-transient data of response to $S_{\text{UB-MAXIMAL}}$ is very important from the kinetically and physiologically points of view because they allow us to study the oxygen mass rate of change per unit of time during a non steady-state condition response to exercise, in terms of mathematical modelling of this response, to assess the dynamics of the blood,$^{35}$ cardiovascular and energy metabolism$^{4,18}$ in human beings. The $\tau$ for expired ventilation exceeds that of $\text{VO}_2$ by some 50-70%.$^3$ This kinetic dissociation of expired ventilation from phase two of a constant-load exercise, and it has been demonstrated.$^{20,36}$ Interestingly, pulmonary $\tau \Phi_2 \text{VO}_2$ uptake seems to be similar to the kinetics of $\text{VO}_2$ consumption by the exercising body mass.$^{29,37}$ Finally, whether the rate of increase in oxidative phosphorylation is limited by the adaptation of oxygen utilization or oxygen transport mechanisms, is motive of debate.$^{30,34,38,39}$ In consequence, there is a need for a consensus in the way to model the oxygen uptake on-transient kinetics of the response to different intensities of exercise, in search of a cause-effect relationship, underlaying the mechanisms of the non steady-state response in exercise physiology, to match the mathematical model with the physiological one to come. Finally, these findings in old men seem to be correct in order to kinetically compare them properly with those from young men.

**CONCLUSIONS**

The simple (practically) onecomponent, four parameters, exponential mathematical model ($1C,4P$), conveniently best intramodelled and fitted $\text{VO}_2$ on-transient data and allowed us to kinetically characterize the estimated $\text{VO}_2$ on-transient time constant for postulated phase two $\text{VO}_2$ on-transient data of submaximal exercise (fitting model $1C,4P_{0.3333 \rightarrow 3 \text{ min exercise}}$). The complexes twocomponent seven parameters ($2C,7P$) and threecomponent, ten parameters ($3C,10P$) exponential mathematical models, were physiologically and statistically best fit, respectively, on kinetically characterizing the estimated $\text{VO}_2$ on-transient time constant for the isolated phase two $\text{VO}_2$ on-transient data, for moderate-intensity exercise with the fitting model $2C,7P_{\text{from baseline } \rightarrow \text{end exercise}}$ and for heavy exercise intensity with the fitting model $3C,10P_{\text{from baseline } \rightarrow \text{end exercise}}$. These $2C,7P$ and $3C,10P$ fitting models differentiated from the three $\text{VO}_2$ phases of the entire on-transient data and kinetically characterized, the estimated $\text{VO}_2$ on-transient time constant for phase two of response by intra modelling the phase two $\text{VO}_2$ into the entire on-transient data with their second exponential term. The phase two $\text{VO}_2$ on-transient time constant estimated values from these one-, two- and three-component best fitting models of the $\text{VO}_2$ on-transient response data to submaximal exercise, were similar to each other.

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