Unit of oxygen uptake efficiency slope

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Abstract The oxygen uptake efficiency slope (OUES) is the slope of a regression line of oxygen uptake ($\dot{V}O_2$) on logarithmically converted minute ventilation ($\dot{V}E$) measured during incremental exercise: $\dot{V}O_2 = a\log_{10}\dot{V}E + b$. Here, $a$ is the OUES. The higher the OUES, the more efficient the uptake of oxygen. The OUES has been widely accepted to estimate maximum oxygen uptake without maximal exercise. Nevertheless, the unit of OUES is unsettled in the literature having eight different descriptions. We introduced a new equation for the OUES using resting $\dot{V}O_2 (\dot{V}O_2_{\text{rest}})$ and resting $\dot{V}E (\dot{V}E_{\text{rest}})$: $\dot{V}O_2 = a\log_{10}(\dot{V}E/\dot{V}E_{\text{rest}}) + \dot{V}O_2_{\text{rest}}$. This equation is based on the mathematical principle that an antilogarithm such as $\dot{V}E/\dot{V}E_{\text{rest}}$ is dimensionless. It is clear from this equation that OUES has the same unit as $\dot{V}O_2$, because $\log_{10}(\dot{V}E/\dot{V}E_{\text{rest}})$ is just a numerical value without the unit. The new equation is written as $\dot{V}O_2 = a\log_{10}\dot{V}E - a\log_{10}\dot{V}E_{\text{rest}} + \dot{V}O_2_{\text{rest}}$. The OUES value is obtained from Baba’s original equation with $\dot{V}O_2$ and $\dot{V}E$ during incremental exercise. The new equation is useful to identify the unit of OUES and the $y$-intercept $b$.

Keywords: incremental exercise, oxygen uptake efficiency slope (OUES), unit of OUES

Introduction

Baba et al.\(^1\) showed a linear correlation between the logarithm of minute ventilation ($\dot{V}E$) and oxygen uptake ($\dot{V}O_2$) during incremental exercise:

$$\dot{V}O_2 = a\log_{10}\dot{V}E + b. \quad (1)$$

They called the slope $a$ as oxygen uptake efficiency slope (OUES) and found a positive correlation between OUES and maximum oxygen uptake ($\dot{V}O_2_{\text{max}}$). Baba et al.\(^1\) showed a relation between $\dot{V}O_2_{\text{max}}$ (mL/min) and OUES for young male and female subjects that $\dot{V}O_2_{\text{max}} = -143 + 1.03\text{OUES}, r = 0.941$. The OUES can be determined from $\dot{V}E$ and $\dot{V}O_2$ measured during submaximal incremental exercise, and has been widely utilized to estimate $\dot{V}O_2_{\text{max}}$ without maximal exercise.

The OUES has been applied to evaluate cardiorespiratory fitness in patients with various diseases as well as in healthy individuals\(^1,3,9,11,15,17,24-26,32-35,44\), these various diseases include heart diseases\(^1,4,6,8-9,12-16,18,21,28,29,33,38,40-44,46\), orthopedic surgery\(^5\), gastroenterological surgery\(^7\), intellectually disabled young people\(^40\), multiple sclerosis\(^19,23,33,39,45\), chronic obstructive pulmonary disease\(^5,27,33,48\), pulmonary arterial hypertension\(^9,20,30,36\), lung cancer\(^22\), severely overweight people\(^3,32\) and cystic fibrosis\(^3,35\).

Despite the high concern regarding the value of OUES, its unit is still unsettled. There are eight patterns for describing the unit of OUES in the literature. In this review, a new equation for OUES is derived from the mathematical principle that an antilogarithm is dimensionless\(^47\). Using the new equation, the unit of OUES is shown to be the same as that of $\dot{V}O_2$.

A new equation for OUES

According to the mathematical principle for logarithms, an antilogarithm is dimensionless\(^47\). Concerning the antilogarithm in equation (Eq.) (1), $\dot{V}E$ should be divided by a value with the same unit as $\dot{V}E$. As for the value with the same unit as $\dot{V}E$, we adopted the resting $\dot{V}E (\dot{V}E_{\text{rest}})$, which gives a ratio of $\dot{V}E$ during exercise to basal $\dot{V}E$ at rest. Such treatment is analogous to that of the metabolic equivalents (METs), which take $\dot{V}O_2$ at rest as a basal value. When $\dot{V}E = \dot{V}E_{\text{rest}}$ and $\log_{10}(\dot{V}E/\dot{V}E_{\text{rest}}) = 0$, the left side of Eq. (1) becomes $\dot{V}O_2$ at rest ($\dot{V}O_2_{\text{rest}}$). Therefore, we have a new equation for OUES as

$$\dot{V}O_2 = a\log_{10}(\dot{V}E/\dot{V}E_{\text{rest}}) + \dot{V}O_2_{\text{rest}}. \quad (2)$$

In cardiopulmonary exercise testing $\dot{V}O_2_{\text{rest}}$ and $\dot{V}E_{\text{rest}}$ are usually measured before exercise, so Eq. (2) does not require any additional measurements other than those of $\dot{V}O_2$ and $\dot{V}E$. The new equation is written as $\dot{V}O_2 = a\log_{10}\dot{V}E - a\log_{10}\dot{V}E_{\text{rest}} + \dot{V}O_2_{\text{rest}}$. Comparing Eq. (1) with the above transformed Eq. (2), we have the $y$-intercept $b$ as

$$b = - a\log_{10}\dot{V}E_{\text{rest}} + \dot{V}O_2_{\text{rest}}. \quad (3)$$

Baba et al.\(^1\) obtained the OUES values from $\dot{V}O_2$ and $\dot{V}E$ during exercise irrespective of the resting $\dot{V}O_2$ and $\dot{V}E$. On the other hand, Eq. (2) requires $\dot{V}O_2$ and $\dot{V}E$ at rest and
The authors wrote that because the OUES value is calculated as a regression slope, the unit is arbitrary.

**Table 1.** Eight patterns for describing the unit of OUES in the literature.

| Unit | Study (published year) | Formula etc. to obtain OUES |
|------|------------------------|-----------------------------|
| Not described | Baba et al. (1996) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Baba (2000) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Mollard et al. (2008) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Giardini et al. (2009) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Tordi et al. (2010) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Woods et al. (2011) | \( VO_2, \text{L/min} = a (\log_{10} \dot{V}_E) + b \) |
| | Plypers et al. (2011) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Toste et al. (2011) | \( VO_2 (\text{L/min}) = a (\log_{10} \dot{V}_E) + b \) |
| | Fu et al. (2016) | a natural logarithm plot of \( \dot{V}_E \) vs. \( VO_2 \) |
| | Yabumoto et al. (2012) | \( VO_2 (\text{mL/min}) \) and \( \log_{10} \dot{V}_E (\text{L/min}) \) |
| | Ramos et al. (2012) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Dufay-Bougon et al. (2013) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Cardozo et al. (2015) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Coocekelbergs et al. (2016) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Barron et al. (2016) | \( \log_{10} \text{ minute ventilation} \) and \( \dot{V}_E \) |
| | Kosmala et al. (2016) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Edwards et al. (2017) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Czubaszewski et al. (2017) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Zhao et al. (2017) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Tang et al. (2017) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Canada et al. (2017) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Yakal et al. (2018) | \( VO_2 = a \log \dot{V}_E + b \) |
| | dimensionless | Heine et al. (2014) | \( VO_2 (\text{mL/min/kg}) = a \log \dot{V}_E (\text{L/min}) + b \) |
| arbitary unit | Dougherty et al. (2018) | \( VO_2 (\text{mL/min}) = a \log \dot{V}_E (\text{L/min}) + b \) |
| L/min/log(L/min) | Williamson et al. (2012) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Rogowski et al. (2012) | \( VO_2 (\text{mL/kg/min})/\log_{10} \dot{V}_E (\text{mL/kg/min}) \) |
| | Müller et al. (2012) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Niemeijer et al. (2014) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Ammenwerth et al. (2014) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Shi et al. (2016) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Onofre et al. (2017) | \( VO_2 = a \log \dot{V}_E + b \) |
| L/min/log(L) | Drinkard et al. (2007) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Terzifski et al. (2009) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Gruet et al. (2010) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Williams et al. (2018) | \( VO_2 = a \log \dot{V}_E + b \) |
| L/min/log(\dot{V}_E) | Ramos et al. (2014) | \( VO_2 = a \log \dot{V}_E + b \) |
| (L/min \( O_2 \))/(L/min \( \dot{V}_E \)) | Hollenberg and Tager (2000) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Stein et al. (2009) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Riks fjord et al. (2017) | \( VO_2 (\text{mL/min}) = a \log \dot{V}_E (\text{L/min}) + b \) |
| L/min | Davies et al. (2006) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Van Laethem et al. (2007) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Arena et al. (2008) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Barron et al. (2010) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Kunz et al. (2012) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Teopompi et al. (2014) | \( VO_2 = a \log \dot{V}_E + b \) |
| | Prado et al. (2016) | \( VO_2 = a \log \dot{V}_E + b \) |

a) The authors wrote that because the OUES value is calculated as a regression slope, the unit is arbitrary.
b) The units L/min/log(L/min) and mL/min per 10-fold increase in \( \dot{V}_E \) were both used.
c) The units L and L/min/log(L/min) were both used.
d) The units mL/min/log(L) and mL/min/log(L)/body surface area were both used.
e) The units L/min and L/min per 10-fold ventilation increase were both used.
during exercise. The OUES values can be obtained from Eq. (1) with \( \dot{V}_{O2} \) and \( \dot{V} \) during exercise alone. Equations (2) and (3) are useful to identify the unit of OUES and the \( y \)-intercept \( b \).

The unit of OUES

In Eq. (2) the logarithm term \( \log_{10}(\dot{V}/\dot{V}_{E\text{rest}}) \) is a numerical value without the unit. In any equation, the unit of each term on both sides must be identical. Therefore, \( a \) (OUES) has the same unit as \( \dot{V}_{O2} \) and \( \dot{V}_{O2\text{rest}} \).

There are eight patterns for describing the unit of OUES in the literature (Table 1). Among them, L/min is the correct unit for OUES because OUES has the same unit as \( \dot{V}_{O2} \) as shown by Eq. (2). Modified units of \( \dot{V}_{O2} \), for example, mL/min, mL/min/body weight, or mL/min/body surface area can be used for the unit of OUES as well.

Baba et al.\(^{31} \) converted the base of \( \log V \) from 10 to Napier’s constant \( e \) to differentiate \( \dot{V}_{O2} \) with respect to \( \dot{V}_{E} \), indicating that they used \( \log \dot{V}_{E} \) as the common logarithm. Actually, in another article Baba\(^{2} \) showed the same equation as Eq. (1) with \( \log_{e} \dot{V}_{E} \). In the literature following the works of Baba et al.\(^{2,3} \), both \( \log \dot{V}_{E} \) and \( \log_{e} \dot{V}_{E} \) were used as the common logarithm. Fu et al.\(^{9} \) only used the natural logarithm. There is a relation between the common logarithm (log base 10) and the natural logarithm (log base \( e \)) that \( \log_{10} \dot{V}_{E} = \frac{\log \dot{V}_{E}}{\log 10} \). The absolute value of OUES differs by 1/\( \log 10 \) between the regression lines with \( \log \dot{V}_{E} \) and with \( \log_{e} \dot{V}_{E} \), but the unit of OUES is unrelated to the base of the logarithm.

Heine et al.\(^{23} \) showed the equation \( \dot{V}_{O2} \) (mL/min/kg) = \( a \log \dot{V}_{E} \) (L/min) + \( b \), and described that the slope \( a \) is a dimensionless measure of the efficiency of oxygen uptake with increasing \( \dot{V}_{E} \). If \( a \) is a dimensionless measure, the first term of their equation \( a \log \dot{V}_{E} \) is dimensionless because \( \log \dot{V}_{E} \) is a numerical value without the unit. Their equation is contrary to the principle that each term of an equation has the same unit.

Dougherty et al.\(^{24} \) wrote that because the OUES value is calculated as a regression slope, the unit is arbitrary. An arbitrary unit is a relative unit used to compare a quantity shown as a ratio. The authors\(^{24} \) might use an arbitrary unit from the ratio \( \dot{V}_{O2}/\log \dot{V}_{E} \) in Eq. (1). However, the unit of OUES is not arbitrary, but L/min as shown by Eq. (2).

The units L/min/\( \log(\text{L/min}) \)\(^{25-31} \), L/min/log\( L \)\(^{32-35} \) and L/min/\( \log \dot{V}_{E} \)\(^{36} \) are not logical, because logarithm is not included in the unit.

The unit (L/min \( O2 \))/(L/min \( \dot{V}_{E} \))\(^{37-39} \) is equivalent to dimensionless, and thus an incorrect unit for OUES.

The \( y \)-intercept of the regression line

In contrast to the wide acceptance of the slope \( a \) (OUES), little attention has been paid to the \( y \)-intercept \( b \) in Eq. (1). It is obvious from Eq. (3) that \( b \) also has the same unit as \( \dot{V}_{O2} \). Equation (2) is useful not only to clarify the unit of OUES, but also to identify the \( y \)-intercept \( b \).

Generally, for an upward sloping straight line like Eqs. (1) and (2), the steeper the slope, the smaller the \( y \)-intercept. In Eq. (3) the absolute value of the \( y \)-intercept \( b \) is large with a large slope \( a \). Baba et al.\(^{31} \) showed a strong positive correlation between the slope \( a \) (OUES) and \( \dot{V}_{O2\text{rest}} \) in mL/min = -1.43 +1.03OUES. That is, the larger the OUES, the higher the exercise tolerance. Similarly, the \( y \)-intercept \( b \) may be used as an index of exercise tolerance.

Conclusions

A new equation \( \dot{V}_{O2} = a \log_{10}(\dot{V}/\dot{V}_{E\text{rest}}) + \dot{V}_{O2\text{rest}} \) shows that the oxygen uptake efficiency slope \( a \) (OUES) has the same unit as \( \dot{V}_{O2} \). Besides the clarification of the unit of OUES, the new equation is useful to identify the \( y \)-intercept \( b \) as \( \dot{V}_{O2\text{rest}} - a \log_{10}\dot{V}_{E\text{rest}} \).

Conflict of Interests

The author declares that there is no conflict of interests regarding the publication of this article.

References

1) Baba R, Nagashima M, Goto M, Nagano Y, Yokota M, Tauchi N and Nishibata K. 1996. Oxygen uptake efficiency slope: a new index of cardiorespiratory functional reserve derived from the relation between oxygen uptake and minute ventilation during incremental exercise. J Am Coll Cardiol 28: 1567-1572. doi: 10.1016/S0735-1097(96)00412-3.
2) Baba R. 2000. The oxygen uptake efficiency slope and its value in the assessment of cardiorespiratory functional reserve. Congest Heart Fail 6: 256-258. doi: 10.1111/j.1527-5299.2000.80164.x.
3) Mollard P, Woorons X, Antoine-Jonville S, Jutand L, Richalet JP, Favret F and Pichon A. 2008. 'Oxygen uptake efficiency slope' in trained and untrained subjects exposed to hypoxia. Respir Physiol Neurobiol 161: 167-173, doi: 10.1016/j.resp.2008.01.006.
4) Giardini A, Specchia S, Gargiulo G, Sangiorgi D and Picchio FM. 2009. Accuracy of oxygen uptake efficiency slope in adults with congenital heart disease. Int J Cardiol 133: 74-79, doi: 10.1016/j.ijcard.2007.11.092.
5) Tordi N, Mourot L, Maire J, Parratte B and Regnard J. 2010. Evaluation of cardiorespiratory functional reserve from arm exercise in the elderly. Ann Phys Rehabil Med 53: 474-482, doi: 10.1016/j.rehab.2010.07.006.
6) Woods PR, Bailey KR, Wood CM and Johnson BD. 2011. Submaximal exercise gas exchange is an important prognostic tool to predict adverse outcomes in heart failure. Eur J Heart Fail 13: 303-310. doi: 10.1093/eurjhf/hfq187.
7) Phypers BJ, Robiony-Rogers D, Pickering RM and Garden AL. 2011. Test-retest reliability of the oxygen uptake efficiency slope in surgical patients. Anaesthesia 66: 659-666, doi: 10.1111/j.1365-2044.2011.07614.x.
8) Toste A, Soares R, Feliciano J, Andreozzi V, Silva S, Abreu
A, Ramos R, Santos N, Ferreira L and Ferreira RC. 2011. Prognostic value of a new cardiopulmonary exercise testing parameter in chronic heart failure: oxygen uptake efficiency at peak exercise - comparison with oxygen uptake efficiency slope. *Rev Port Cardiol* 30: 781-787. doi: 10.1016/S0870-2551(11)70026-9.

9) Fu T, Wang C, Hsu C, Cherng W, Huang S and Wang J. 2011. Suppression of cerebral hemodynamics is associated with reduced functional capacity in patients with heart failure. *Am J Physiol Heart Circ Physiol* 300: H1545-H1555. doi: 10.1152/ajpheart.00867.2010.

10) Yabumoto T, Baba R, Watanabe T, Sakakibara N, Ukai T, Fukutomi O and Matsuoka T. 2012. Oxygen uptake efficiency slope calculations based on heart rate reserve endpoints in young, intellectually disabled individuals. *J Phys Fitness Sports Med* 1: 703-707. doi: 10.7600/jpfsm.1.703.

11) Ramos PS, Ricardo DR and Araújo CG. 2012. Cardiorespiratory optimal point: a submaximal variable of the cardiopulmonary exercise testing. *Arq Bras Cardiol* 99: 988-996. doi: 10.1590/S0066-782X2012000500009.

12) Dufay-Bougon C, Belin A, Dahdouh ZS, Barthelemy S, Maribre J, Sabatier R, Mililie P and Grollier G. 2013. The prognostic value of the cardiopulmonary exercise test in patients with heart failure who have been treated with beta-blockers. *Turk Kardiyol Dern Arş* 41: 105-112. doi: 10.5543/tkda.2013.87404.

13) Cardozo GG, Oliveira RB and Farinatti PTV. 2015. Effects of high intensity interval versus moderate continuous training on markers of ventilatory and cardiac efficiency in coronary heart disease patients. *Sci World J* 2015: 192479. doi: 10.1155/2015/192479.

14) Coeckelberghs E, Buys R, Goetschalckx K, Cornelissen VA and Vanhees L. 2016. Prognostic value of the oxygen uptake efficiency slope and other exercise variables in patients with coronary artery disease. *Eur J Prev Cardiol* 23: 237-244. doi: 10.1177/2047487315694140.

15) Barron A, Francis DP, Mayet J, Ewert R, Obst A, Mason M, Elkin S, Hughes AD and Wensel R. 2016. Oxygen uptake efficiency slope and breathing reserve, not anaerobic threshold, discriminate between patients with cardiovascular disease over chronic obstructive pulmonary disease. *JACC Heart Fail* 4: 252-261. doi: 10.1016/j.jchf.2015.11.003.

16) Kosmala W, Rojek A, Przewlocka-Kosmala M, Wright L, Straburzyńska-Migaj E. 2017. Comparison of prognostic values of cardiopulmonary and heart rate parameters in exercise testing in men with heart failure. *Cardiol J* [Epub ahead of print]. doi: 10.5603/CJ.2017.0070.

17) Zhao Q, Wang L, Pudasaini B, Jiang R, Yuan P, Gong S, Guo J, Xiao Q, Liu H, Wu C, Jing Z and Liu J. 2017. Cardiopulmonary exercise testing improves diagnostic specificity in patients with echocardiography-suspected pulmonary hypertension. *Clin Cardiol* 40: 95-101. doi: 10.1002/clc.22635.

18) Tang Y, Luo Q, Liu Z, Ma X, Zhao Z, Huang Z, Gao L, Jin Q, Xiong C and Ni X. 2017. Oxygen uptake efficiency slope predicts poor outcome in patients with idiopathic pulmonary arterial hypertension. *J Am Heart Assoc* 6: e005037. doi: 10.1161/JAHA.116.005037.

19) Canada JM, Trankle CR, Buckley LF, Carbone S, Abouzaki NA, Kadariya D, Shah K, Cooke R, Kontos MC, Patel J, Mankad P, Schatz A, Bhatnagar A, Arena R, Van Tassell BW and Abbate A. 2017. Severely impaired cardiopulmonary fitness in patients with recently decompensated systolic heart failure. *Am J Cardiol* 120: 1854-1857. doi: 10.1016/j.amjcard.2017.07.099.

20) Yabumoto T, Baba R, Watanabe T, Sakakibara N, Ukai T, Fukutomi O and Matsuoka T. 2012. Oxygen uptake efficiency slope calculations based on heart rate reserve endpoints in young, intellectually disabled individuals. *J Phys Fitness Sports Med* 1: 703-707. doi: 10.7600/jpfsm.1.703.

21) Ramos PS, Ricardo DR and Araújo CG. 2012. Cardiorespiratory optimal point: a submaximal variable of the cardiopulmonary exercise testing. *Arq Bras Cardiol* 99: 988-996. doi: 10.1590/S0066-782X2012000500009.

22) Dufay-Bougon C, Belin A, Dahdouh ZS, Barthelemy S, Maribre J, Sabatier R, Mililie P and Grollier G. 2013. The prognostic value of the cardiopulmonary exercise test in patients with heart failure who have been treated with beta-blockers. *Turk Kardiyol Dern Arş* 41: 105-112. doi: 10.5543/tkda.2013.87404.

23) Cardozo GG, Oliveira RB and Farinatti PTV. 2015. Effects of high intensity interval versus moderate continuous training on markers of ventilatory and cardiac efficiency in coronary heart disease patients. *Sci World J* 2015: 192479. doi: 10.1155/2015/192479.

24) Coeckelberghs E, Buys R, Goetschalckx K, Cornelissen VA and Vanhees L. 2016. Prognostic value of the oxygen uptake efficiency slope and other exercise variables in patients with coronary artery disease. *Eur J Prev Cardiol* 23: 237-244. doi: 10.1177/2047487315694140.

25) Barron A, Francis DP, Mayet J, Ewert R, Obst A, Mason M, Elkin S, Hughes AD and Wensel R. 2016. Oxygen uptake efficiency slope and breathing reserve, not anaerobic threshold, discriminate between patients with cardiovascular disease over chronic obstructive pulmonary disease. *JACC Heart Fail* 4: 252-261. doi: 10.1016/j.jchf.2015.11.003.

26) Kosmala W, Rojek A, Przewlocka-Kosmala M, Wright L, Mysiak A and Marwick TH. 2016. Effect of aldosterone antagonism on exercise tolerance in heart failure with preserved ejection fraction. *J Am Coll Cardiol* 68: 1823-1834. doi: 10.1016/j.jacc.2016.07.763.

27) Edwards T, Klaren RE, Motl RW and Pilutti LA. 2017. Further characterization and validation of the oxygen uptake efficiency slope for persons with multiple sclerosis. *J Rehabil Med* 49: 234-240. doi: 10.2340/16501977-2204.

28) Czubaszewski L, Straburzyńska-Lupa A, Migaj J and Straburzyńska-Migaj E. 2017. Comparison of prognostic values of cardiopulmonary and heart rate parameters in exercise testing in men with heart failure. *Cardiol J* [Epub ahead of print]. doi: 10.5603/CJJa.2017.0070.

29) Zhao Q, Wang L, Pudasaini B, Jiang R, Yuan P, Gong S, Guo J, Xiao Q, Liu H, Wu C, Jing Z and Liu J. 2017. Cardiopulmonary exercise testing improves diagnostic specificity in patients with echocardiography-suspected pulmonary hypertension. *Clin Cardiol* 40: 95-101. doi: 10.1002/clc.22635.
33) Terziyski KV, Marinov BI, Aliman OI and St Kostianev S. 2009. Oxygen uptake efficiency slope and chronotropic incompetence in chronic heart failure and chronic obstructive pulmonary disease. Folia Med 51: 18-24.

34) Gruet M, Brisswalter J, Mely L and Vallier JM. 2010. Clinical utility of the oxygen uptake efficiency slope in cystic fibrosis patients. J Cyst Fibros 9: 307-313. doi: 10.1016/j.jcf.2010.03.003.

35) Williams CA, Tomlinson OW, Chubbock LV, Stevens D, Saynor ZL, Oades PJ and Barker AR. 2018. The oxygen uptake efficiency slope is not a valid surrogate of aerobic fitness in cystic fibrosis. Pediatr Pulmonol 53: 36-42. doi: 10.1002/ppul.23896.

36) Ramos RP, Ota-Arakaki JS, Alencar MC, Ferreira EV, Nery LE and Neder JA. 2014. Exercise oxygen uptake efficiency slope independently predicts poor outcome in pulmonary arterial hypertension. Eur Respir J 43: 1510-1512. doi: 10.1183/09031936.0017713.

37) Hollenberg M and Tager IB. 2000. Oxygen uptake efficiency slope: an index of exercise performance and cardiopulmonary reserve requiring only submaximal exercise. J Am Coll Cardiol 36: 194-201. doi: 10.1016/S0735-1097(00)00691-4.

38) Stein R, Chiappa GR, Güths H, Dall’Ago P and Ribeiro JP. 2009. Inspiratory muscle training improves oxygen uptake efficiency slope independently predicts poor outcome in chronic heart failure. J Cardiopulm Rehabil Prev 29: 392-395. doi: 10.1097/HCR.0b013e3181b4e41.

39) Riksfjord SM, Brendvik SM, Raksund OD and Aamot IL. 2017. Ventilatory efficiency and aerobic capacity in people with multiple sclerosis: a randomized study. SAGE Open Med 5: 1-8. doi: 10.1177/2050312117743672.

40) Davies LC, Wensel R, Georgiadou P, Cicoira M, Coats AJ, Piepoli MF and Francis DP. 2006. Enhanced prognostic value from cardiopulmonary exercise testing in chronic heart failure by non-linear analysis: oxygen uptake efficiency slope. Eur Heart J 27: 684-690. doi: 10.1093/eurheartj/ehi672.

41) Van Laethem C, Van de Veire N, De Backer G, Bihija S, Seghers T, Cambier D, Vanderheyden M and De Sutter J. 2007. Response of the oxygen uptake efficiency slope to exercise training in patients with chronic heart failure. Eur J Heart Fail 9: 625-629. doi: 10.1016/j.ejheart.2007.01.007.

42) Arena R, Myers J, Abella J, Peberdy MA, Bensimhon D, Chase P and Guazzi M. 2008. The influence of body mass index on the oxygen uptake efficiency slope in patients with heart failure. Int J Cardiol 125: 270-272. doi: 10.1016/j.ijcard.2007.11.013.

43) Barron AJ, Medlow KJ, Giannoni A, Unsworth B, Coats AJ, Mayet J, Howard LS and Francis DP. 2010. Reduced confounding by impaired ventilatory function with oxygen uptake efficiency slope and $\dot{V}O_2/\dot{V}CO_2$ slope rather than peak oxygen consumption to assess exercise physiology in suspected heart failure. Congest Heart Fail 16: 259-264. doi: 10.1111/j.1751-7133.2010.00183.x.

44) Kunz VC, Serra KB, Bogers ÉN, Serra PE and Silva E. 2012. Cardiopulmonary exercise testing in the early-phase of myocardial infarction. Rev Bras Fisioter 16: 396-405. doi: 10.1590/S1413-355520120005000047.

45) Teopompi E, Tzani P, Aiello M, Ramponi S, Andrani F, Marangio E, Clini E and Chetta A. 2014. Fat-free mass depletion is associated with poor exercise capacity irrespective of dynamic hyperinflation in COPD patients. Respir Care 59: 718-725. doi: 10.4187/respcare.02709.

46) Prado DML, Rocco EA, Silva AG, Rocco DF, Pacheco MT, Silva PF and Furlan V. 2016. Effects of continuous vs interval exercise training on oxygen uptake efficiency slope in patients with coronary artery disease. Braz J Med Biol Res 49: e4890. doi: 10.1590/1414-431X20154890.

47) Koch AL. 1966. The logarithm in Biology 1. Mechanisms generating the log-normal distribution exactly. J Theoret Biol 12: 276-290.