ISSN 2377-1658

PULMONARY RESEARCH AND RESPIRATORY MEDICINE
Open Journal

Openventio PUBLISHERS

Editorial

New Ideas on Limitations to $\dot{V}O_{2max}$: Five Major Determinants for $\dot{V}O_{2max}$

Masahiro Kohzuki, MD, PhD

Department of Internal Medicine and Rehabilitation Science, Tohoku University Graduate School of Medicine, Sendai, Japan

**Corresponding author*
Masahiro Kohzuki, MD, PhD
Department of Internal Medicine and Rehabilitation Science, Tohoku University Graduate School of Medicine, 1-1, Seiryo-cho, Aoba-ku, Sendai, Japan;
Tel. 022-717-7351; Fax. 022-717-7355; E-mail: kohzuki@med.tohoku.ac.jp

Article information

Received: August 5th, 2018; **Accepted:** August 8th, 2018; **Published:** August 8th, 2018

Cite this article

Kohzuki M. New ideas on limitations to $\dot{V}O_{2max}$: Five major determinants for $\dot{V}O_{2max}$. *Pulm Res Respir Med Open J.* 2018; 5(1): e1-e2. doi: 10.17140/PRRMOJ-5-e010

Chronic obstructive pulmonary disease (COPD) is an important and a growing cause of morbidity and mortality worldwide. Cardiovascular, musculoskeletal, metabolic, and mental comorbidities are considered to be part of the frequently prevalent non-pulmonary sequelae of the disease.[1,2] Increasing evidence suggests that extra-pulmonary effects of COPD and airflow limitation are only poorly correlated.[3] Waschki, et al. found that objectively measured physical activity is the strongest predictor of all-cause mortality in patients with COPD.[4]

The association between physical inactivity and poor outcomes are well established for patients with pulmonary disease, cardiac disease, chronic kidney disease.[4-6] Patients with pulmonary disease, cardiac disease, or renal disease typically engage in a lower level of physical activity than do the general population, which can induce a catabolic state including reduced neuromuscular functioning, reduced exercise tolerance and reduced cardiorespiratory fitness (CRF).

CRF is an important consideration, in addition to physical activity, as it is a strong predictor of mortality; low CRF presents a particularly high risk of death compared to other common risk factors, such as diabetes, high cholesterol or hypertension.[7] CR fitness is defined as the ability of the circulatory and respiratory systems to supply oxygen during sustained physical activity and is usually expressed as maximal oxygen uptake ($\dot{V}O_{2max}$) during maximal exercise testing.[8] In 2016, the American Heart Association published a scientific statement[9] recommending that CRF, quantifiable as $\dot{V}O_{2max}$, be regularly assessed and utilized as a clinical vital sign. This statement was based on mounting evidence that lower CRF levels are associated with high risk of cardiovascular disease, all-cause mortality, and mortality rates stemming from various types of cancers.

$\dot{V}O_{2max}$ is expressed either as an absolute rate in (for example) liters of oxygen per minute (L/min) or as a relative rate in (for example) milliliters of oxygen per kilogram of body mass per minute (e.g., mL/(kg•min)). The latter expression is often used to compare the performance of endurance athletes and patients.

Figure shows gas transport mechanisms for coupling cellular (internal) to pulmonary (external) respiration. The gears represent the functional interdependence of the physiological components of the system. Cardiac output, pulmonary diffusion capacity, oxygen carrying capacity, renal function and other peripheral limitations like muscle diffusion capacity, mitochondrial enzymes, and capillary density are all examples of $\dot{V}O_{2max}$ determinants.

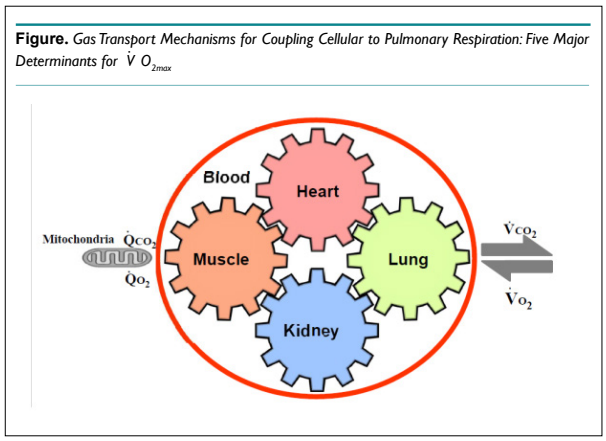

Figure. *Gas Transport Mechanisms for Coupling Cellular to Pulmonary Respiration: Five Major Determinants for* $\dot{V}O_{2max}$

The large increase in O_2 utilization by the muscles (QO_2) is achieved by increased extraction of O_2 from the blood perfusing the muscles, the dilatation of selected peripheral vascular beds, an increase in cardiac output (stroke volume and heart rate), an in-

© Copyright 2018 by Kohzuki M. This is an open-access article distributed under Creative Commons Attribution 4.0 International License (CC BY 4.0), which allows to copy, redistribute, remix, transform, and reproduce in any medium or format, even commercially, provided the original work is properly cited.

crease in pulmonary blood flow by recruitment and vasodilatation of pulmonary blood vessels, and finally, an increase in ventilation. O_2 is taken up ($\dot{V}O_2$) from the alveoli in proportion to the pulmonary blood flow and degree of O_2 desaturation of hemoglobin in the pulmonary capillary blood. Metabolic acidosis in chronic kidney disease (CKD) patients promote muscle protein wasting and protein-energy wasting (PEW) by increasing protein degradation[10] and reducing protein synthesis.[11] As a result, maintenance of muscle mass is impaired in CKD patients with altered protein turnover rates.[12] Adding to sarcopenia, metabolic acidosis, protein-energy wasting, angiotensin II, myostatin overexpression in uremia contribute the etiology for muscle wasting in CKD.[13] Moreover, the drug erythropoietin (EPO) can boost $\dot{V}O_{2max}$ by a significant amount in both humans and other mammals.[14]

COPD often coexists with other diseases (comorbidities such as heart disease, CKD, osteoporosis) that may have a significant impact on prognosis. Thirty-three percent of elderly patients with heart failure had COPD and 25% of elderly patients with COPD also had heart failure.[15] This risk of comorbid disease can be increased by the sequelae of COPD; e.g., reduced physical activity. As super-aged society has come, the number of persons with multimorbidity and multiple disabilities (MMD)[16] and their needs of rehabilitation have increased rapidly more than we have expected.[16] $\dot{V}O_{2max}$ offers the investigator the unique opportunity to study simultaneously the cellular, cardiovascular, ventilatory and metabolic systems' responses under conditions of precisely controlled stress. This is of significant practical importance because $\dot{V}O_{2max}$ measured by cardiopulmonary exercise testing, provides what is probably the most sensitive assessment of the effect of new therapy on function of any diseased organ system whose major function is to couple pulmonary gas exchange to cellular respiration. For example, it is important to determine whether new medical, surgical, and rehabilitative procedures can effectively intervene to improve the gas transport capability of a diseased organ system.

REFERENCES

1. Barnes PJ, Celli BR. Systemic manifestations and comorbidities of COPD. *Eur Respir J.* 2009; 33: 1165-1185. doi: 10.1183/09031936.00128008

2. Magnussen H, Watz H. Systemic inflammation in chronic obstructive pulmonary disease and asthma: relation with comorbidities. *Proc Am Thorac Soc.* 2009; 6: 648-651. doi: 10.1513/pats.200906-053DP

3. Fabbri LM, Rabe KF. From COPD to chronic systemic inflammatory syndrome? *Lancet.* 2007; 370 (9589): 797-799. doi: 10.1016/S0140-6736(07)61383-X

4. Waschki B, Kirsten A, Holz O, et al. Physical activity is the strongest predictor of all-cause mortality in patients with COPD. *Chest* 2011; 140: 331-342. doi: 10.1378/chest.10-2521

5. Cacciatore F, Amarelli C, Ferrara N, et al. Protective effect of physical activity on mortality in older adults with advanced chronic heart failure: A prospective observational study. *Eur J Prev Cardiol.* 2018: 2047487318790822. doi: 10.1177/2047487318790822

6. Beddhu S, Baird BC, Zitterkoph J, Neilson J, Greene T. Physical activity and mortality in chronic kidney disease (NHANES III). *Clin J Am Soc Nephrol.* 2009; 4, 1901-1906. doi: 10.2215/CJN.01970309

7. Blair SN, Sallis RE, Hutber A, Archer E. Exercise therapy the public health message. *Scand J Med Sci Sports.* 2012; 22, 24-28. doi: 10.1111/j.1600-0838

8. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: Definitions and distinctions for health-related research. *Public Health Rep.* 1985; 100, 126-131.

9. Ross R, Blair SN, Arena R, et al. Importance of assessing cardiorespiratory fitness in clinical practice: A case for fitness as a clinical vital sign: A Scientific Statement from the American Heart Association. *Circulation.* doi: 10.1161/CIR.0000000000000461

10. Caso G, Garlick PJ. Control of muscle protein kinetics by acid-base balance. *Curr Opin Clin Nutr Metab Care.* 2005 ; 8: 73-76.

11. Bailey JL, Wang X, England BK. The acidosis of chronic renal failure activates muscle proteolysis in rats by augmenting transcription of genes encoding proteins of the ATP-dependent Ubiquitin-proteasome pathway. *J Clin Invest.* 1996; 97: 1447-1453. doi: 10.1172/JCI118566

12. Mitch WE. Influence of metabolic acidosis on nutrition. *Am J Kidney Dis.* 1997; 29: 16-18.

13. Fahal IH. Uraemic sarcopenia: Aetiology and implications. Nephrology Dialysis. *Nephrol Dial Transplant.* 2014; 29: 1655-1665. doi: 10.1093/ndt/gft070

14. Kolb EM. Erythropoietin elevates VO_{2max} but not voluntary wheel running in mice. *J Exp Biol.* 2010; 213: 510-519. doi: 10.1242/jeb.029074

15. Incalzi RA, Corsonello A, Pedone C, et al. Construct validity of activities of daily living scale: A clue to distinguish the disabling effect of COPD and congestive heart failure. *Chest.* 2005; 127: 830-838. doi: 10.1378/chest.127.3.830

16. Kohzuki M. Paradigm shift in rehabilitation medicine in the era of multimorbidity and multiple disabilities (MMD). *Physical Medicine and Rehabilitation International.* 2014; 1(2): id1006.