Skeletal muscle oxygen dynamics and peak aerobic capacity

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Abstract Skeletal muscle O2 dynamics can be measured during whole body dynamic exercise noninvasively by near-infrared spectroscopy (NIRS), and muscle O2 dynamics can allow us to estimate muscle O2 extraction. Muscle O2 extraction is one of the determinants of peak pulmonary O2 uptake (\(\dot{V}O_2\)), and blunted peak \(\dot{V}O_2\) potentially increases cardiovascular-associated morbidity and mortality. However, muscle O2 dynamics and their relation to reduced peak aerobic capacity have not been fully established. This review briefly outlines the relationship between change in muscle O2 dynamics and an improvement of peak \(\dot{V}O_2\). Our findings suggest that aerobic training enhances estimated muscle O2 extraction, and the enhancement is related to an improvement of peak aerobic capacity in elderly subjects, with and without heart disease. The relationship may be potentially affected, however, by some factors such as: the initial level of aerobic capacity and cardiac function (ability of convective O2 supply), and training volume, phase, or type. The number of elderly people who have a low peak aerobic capacity will most likely be increasing in Japan, as a consequence of the aging population and physical inactivity due to advanced technology. Although we recognize several limitations of the NIRS technique and the necessity for further investigation, assessing muscle O2 dynamics is valuable to understand the peripheral impairments and mechanisms of lowered peak \(\dot{V}O_2\).

Keywords: near-infrared spectroscopy, peak O2 uptake, muscle O2 extraction, blood volume

Introduction

Skeletal muscle O2 dynamics can be measured noninvasively with 1-2 Hz temporal resolution during whole body exercise by near-infrared spectroscopy (NIRS), and the data reflects the information in the arterioles, capillaries, and venules in exercising muscles. Measurements of muscle O2 dynamics are valuable to clarify physiological and pathophysiological adaptations in exercising muscle, and therefore, NIRS is widely used in the research areas of sports sciences and exercise physiology. There already exist some excellent reviews dealing with the principles, technical and methodological developments (including limitations), and application of NIRS technique. This article gives a brief overview of the relationship between changes in muscle O2 dynamics measured by NIRS and improvement of peak \(\dot{V}O_2\), based on recent data from our laboratory.

Skeletal muscle O2 dynamics during cycling exercise

In specific terms, the near-infrared spatial resolved spectroscopy technique measures relative change from rest in oxygenated hemoglobin (Hb)/myoglobin (Mb) (Oxy-Hb/Mb: an indicator of the balance between O2 supply and utilization), deoxygenated-Hb/Mb (Deoxy-Hb/Mb: an indicator of the balance between O2 unloading in the muscle and blood outflow from the muscle), and total-Hb (Oxy-Hb/Mb plus Deoxy-Hb/Mb: indicator of blood volume) concentration and muscle O2 saturation (SmO2: oxy-Hb/Mb per total-Hb: an indicator of the balance between O2 supply and utilization, which is less sensitive to changes in blood volume than oxy-Hb/Mb). Muscle O2 extraction can be estimated by deoxy-Hb/Mb or SmO2 when total-Hb/Mb is stable. However, every variable has not always been represented in previous studies using NIRS.

Anterior thigh muscles, especially the vastus lateralis (VL), mainly contribute during cycling exercise. Therefore, muscle O2 dynamics in VL muscle are usually viewed as the representative response of the whole leg muscle in many studies, even though regional differences have been observed among several leg muscles and also within a single muscle. As exercise intensity increases during ramp cycling exercise, oxy-Hb/Mb is relatively maintained or reduced, especially in high intensity exercise, because muscle O2 supply either matches or is lower than O2 utilization in exercising muscle. In contrast, deoxy-Hb/Mb increases proportionally or in an S-shaped curve, and total-Hb also increases, partly due to vasodilation responses (i.e. increasing blood volume). As a result, SmO2 gradually decreases while exercise intensity is increasing.

Based on Fick’s Principle (mass conservation), muscle
O₂ uptake (\(\bar{V}O_2\)) is a product of muscle blood flow and muscle O₂ extraction\(^6\), and therefore, muscle O₂ extraction is one of the determinants of peak pulmonary \(\bar{V}O_2\). Lower peak aerobic capacity potentially increases cardiovascular-associated morbidity and mortality\(^7\). In Japan, the number of elderly people who have a low peak aerobic capacity will most likely be increasing as a consequence of the aging population and physical inactivity due to advanced technology, therefore, assessing muscle O₂ dynamics is potentially helpful to clarify an impairment of muscle circulation/metabolism and the mechanisms that cause low aerobic capacity. However, muscle O₂ dynamics and their relationship to reduced peak aerobic capacity have not been fully established.

**Relationship between muscle O₂ dynamics and peak \(\bar{V}O_2\)**

Some cross-sectional studies have demonstrated muscle deoxygenation (and estimated muscle O₂ extraction) during exercise measured by NIRS, related to peak \(\bar{V}O_2\) in healthy young subjects\(^8\), university athletes\(^9\), elderly subjects\(^10\), and ischemic heart disease patients (myocardial infarction\(^11\) and angina pectoris\(^12\) patients). These data suggest that muscle O₂ extraction may be enhanced in subjects with higher peak \(\bar{V}O_2\). Fig. 1 displays the relationship between \(\Delta SmO_2\) (SmO₂ at peak exercise minus SmO₂ at rest) and deoxy-Hb/Mb at peak exercise and peak \(\bar{V}O_2\) in elderly subjects with and without heart disease. Although a longitudinal approach is helpful to evaluate the direct relationship between increasing muscle O₂ extraction and an improvement of peak \(\bar{V}O_2\), the amount of longitudinal research is still limited.

Kime et al.\(^13\) reported that, in healthy untrained subjects, SmO₂ at peak exercise was decreased after 3-weeks’ aerobic training (cycling exercise at 60% of peak \(\bar{V}O_2\), for 30 min, 3 times/week), and the decrease in SmO₂ at peak exercise by training was significantly related to an improvement of peak \(\bar{V}O_2\) (pre: 42.7 ± 9.9 ml/kg/min, post: 51.7 ± 11.3 ml/kg/min). Changes in total-Hb after training were not presented in the paper, nevertheless, a decrease in SmO₂ may be interpreted to mean that muscle O₂ extraction was increased by aerobic training, and the increase in peak \(\bar{V}O_2\) can be partly explained by the enhancement of muscle O₂ extraction in the untrained young subjects of the study. Neary et al. studied short-term endurance training (60 minutes cycling at 80-90% of peak \(\bar{V}O_2\), 5 times/week for 3 weeks) in experienced cyclists, and they also found that the reduction in oxy-Hb/Mb during the 20-km time trial was related to improvement of peak \(\bar{V}O_2\)\(^14\). However, the change in total-Hb was not shown.

We investigated whether or not aerobic training reinforces muscle deoxygenation response, and if the reinforcement is related to improvement of peak \(\bar{V}O_2\) in healthy untrained elderly subjects (62 ± 4 years)\(^15\), as it had been seen in young subjects. The results of this study showed that, probably due to low volume of aerobic training (30 min cycling at around lactate threshold, 15 ± 6 sessions over 12 weeks), peak \(\bar{V}O_2\) (before: 20.1 ± 6.0 ml/kg/min, after: 21.1 ± 4.1 ml/L/kg/min) and muscle O₂ dynamics were not significantly changed. However, a reduction in SmO₂ at peak exercise after training was significantly associated with improvement of peak \(\bar{V}O_2\), in untrained elderly subjects. Because aging attenuates muscle blood flow, a compensatory increase in muscle O₂ extraction is commonly seen in elderly subjects, com-

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**Fig. 1** Cross-sectional relationship between \(\Delta SmO_2\) (A) and deoxy-Hb/Mb at peak exercise (B) and peak \(\bar{V}O_2\) in elderly subjects with and without heart disease.

Closed circles show the results in myocardial infarction patients (n = 16, 61 ± 9 years); closed triangles show the results in elderly subjects (n = 18, 60 ± 10 years) without heart disease; open triangles show angina pectoris patients (n = 7, 72 ± 6 years). \(\Delta SmO_2\): SmO₂ at peak exercise minus SmO₂ at rest. The effects of light scattering in fat layers on NIRS data were optically corrected\(^19\). (Data from references 11, 12)
Aerobic training enhances estimated muscle O$_2$ extraction during exercise compared to young subjects\textsuperscript{10}. Our findings potentially suggest that muscle O$_2$ extraction is additively enhanced by aerobic training in elderly subjects, if peak VO$_2$ is largely (significantly) increased. We presume that accelerating muscle O$_2$ extraction is likely to contribute to an improvement of peak VO$_2$ in elderly subjects.

In heart disease patients, there has been an investigation into the relationship between change in muscle O$_2$ dynamics and an improvement of peak VO$_2$ during aerobic training, which is common exercise for cardiac rehabilitation. Heart disease patients present not only reduced cardiac output, but also reduced skeletal muscle blood flow and reduced aerobic enzyme activity. We found that muscle O$_2$ extraction was already blunted (i.e. a blunted increase in deoxy-Hb/Mb and a minor decrease in SmO$_2$ with similar response in total-Hb) in early after onset of myocardial infarction (MI) patients, compared to age-matched elderly subjects without MI\textsuperscript{11}. Therefore, we recruited patients in early post-MI (n = 16, 60 ± 10 years) and divided them into aerobic training (30 min cycling at approximately lactate threshold, 20 ± 3 sessions over 12 weeks) or non-training groups\textsuperscript{16}. After 12 weeks, the training group showed a reduction in oxy-Hb/Mb (but the difference did not reach significance), an increase in deoxy-Hb/Mb, and a decrease in SmO$_2$ during ramp cycling exercise, while total-Hb was not significantly changed between before and after training. Peak VO$_2$ increased after 12-weeks’ training (18.1 ± 3.0 vs. 22.9 ± 2.8 mL/kg/min), while no variables were changed in non-training group. Change in ΔSmO$_2$ and deoxy-Hb/Mb was strongly related to an improvement of peak VO$_2$. In addition, the abnormalities of muscle O$_2$ dynamics and trainability are not particular to MI patients; In patients of angina pectoris (AP), which is one of the ischemic heart diseases, the abnormalities in muscle O$_2$ dynamics were also found, compared to age-matched controls without AP\textsuperscript{12}. Moreover, with aerobic training (30 min cycling at estimated lactate threshold, 15 ± 5 sessions over 12 weeks), SmO$_2$ and oxy-Hb/Mb were reduced and deoxy-Hb/Mb was increased during ramp cycling exercise, while total-Hb response was similar between before and after training. In AP patients, the change in ΔSmO$_2$ tended to be related to an improvement of peak VO$_2$ (before: 15.0 ± 3.9 mL/kg/min, after: 19.2 ± 5.1 mL/kg/min)\textsuperscript{12}. Change in deoxy-Hb/Mb at peak exercise was not significantly related to change in peak VO$_2$, probably due to the low number of subjects (n = 7, r = 0.56, p = 0.19, unpublished data). In these longitudinal studies, total-Hb response was not significantly changed between before and after training, whereas total-Hb was increased as exercise intensity increased. Hence, these results lead us to speculate that aerobic training enhances muscle O$_2$ extraction, and the enhancement is likely to cause an improvement of peak aerobic capacity. Because early after onset of ischemic heart disease patients already have impaired peak aerobic capacity and lowered muscle O$_2$ extraction, aerobic training is important for these patients to improve peak VO$_2$ via the increase in muscle O$_2$ extraction.

To summarize our findings, aerobic training potentially enhances estimated muscle O$_2$ extraction, and that enhancement contributes to improvement of peak VO$_2$. Fig. 2 represents the relationship between changes in ΔSmO$_2$ and deoxy-Hb/Mb at peak exercise during 12 weeks.

**Fig. 2** Longitudinal relationship between change in ΔSmO$_2$ (A) and change in deoxy-Hb/Mb at peak exercise (B) and improvement of peak VO$_2$ in elderly subjects with and without heart disease.

Closed circles show the results in myocardial infarction patients (n = 10, 59 ± 10 years) with aerobic training for 12 weeks (30 min cycling at estimated lactate threshold (LT), 2 times/week for 12 weeks); open circles show the results in myocardial infarction patients (n = 6, 61 ± 9 years) over a natural time course for 12 weeks without training; closed triangles shows the results in elderly subjects (n = 10, 62 ± 4 years) with 12 weeks’ aerobic training (30 min cycling at estimated LT, 15 ± 6 sessions/12 weeks); open triangles show angina pectoris patients (n = 7, 72 ± 6 years) with 12 weeks’ aerobic training (30 min cycling at estimated LT, 20 ± 3 sessions/12 weeks). ΔSmO$_2$: SmO$_2$ at peak exercise minus SmO$_2$ at rest. The effects of light scattering in fat layers on NIRS data were optically corrected\textsuperscript{19}. (Data from references 15-17.)
weeks of aerobic training and improvements of peak VO2 in elderly subjects and heart disease patients. However, the effects of exercise training on muscle O2 dynamics and its relationship to peak aerobic capacity may be influenced by some factors such as: initial level of aerobic capacity and cardiac function (ability of convective O2 supply), and training volume or phase. Additionally, we found both an increase in ΔSmO2 and reduction in deoxy-Hb/Mb at peak exercise without a change in total-Hb (i.e., decreasing muscle O2 extraction after training) were related to an improvement of peak VO2 after 8-weeks’ rugby training (including strength and aerobic training) in trained university rugby players (unpublished data). These findings lead us to speculate that increased muscle blood flow, rather than muscle O2 extraction, improves peak VO2 in trained rugby players with this type of training, though further investigation is needed in these areas.

Conclusions

Our findings suggest that aerobic training potentially enhances muscle O2 extraction during ramp cycling exercise, and the enhancements are related to improvement of peak aerobic capacity in elderly subjects with and without heart disease. Though we recognize several limitations in the NIRS technique and the necessity of further investigations, assessing muscle O2 dynamics is valuable in understanding the peripheral impairments and mechanisms of lowered peak VO2.

Conflict of Interests

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

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