Chapter 7
Sex-Related Difference in Muscle Deoxygenation Responses Between Aerobic Capacity-Matched Elderly Men and Women

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Abstract Muscle O_2 dynamics during ramp cycling exercise were compared between aerobic capacity-matched elderly men ($n = 8$, age 65 ± 2 years) and women ($n = 8$, age 66 ± 3 years). Muscle O_2 saturation (SmO_2) and relative change in deoxygenated (Δdeoxy-Hb) and total hemoglobin concentration (Δtotal-Hb) were monitored continuously during exercise in the vastus lateralis (VL) and gastrocnemius medialis (GM) by near infrared spatial resolved spectroscopy. SmO_2 was significantly higher during exercise in women than in men in VL, but not in GM. In VL, Δdeoxy-Hb and Δtotal-Hb were significantly higher in men than in women, especially during high intensity exercise. However, no significant difference was observed in Δdeoxy-Hb or Δtotal-Hb in GM. Sex-related differences in muscle deoxygenation response may be heterogeneous among leg muscles in elderly subjects.

Keywords Aging • Cycling exercise • Muscle oxygen dynamics • Near infrared spectroscopy • Regional difference

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1 Introduction

Near infrared spectroscopy (NIRS) has been widely used in measuring muscle oxy-genation during dynamic exercise. A few previous studies evaluated sex-related differences in muscle deoxygenation response using NIRS during cycling exercise in young subjects [1–3]. However, sex-related differences in muscle deoxygenation responses have not been established in elderly subjects. It has been reported that the muscle deoxygenation responses are heterogeneous among leg muscles [4]. Ideally, peak aerobic capacity should be matched to evaluate the sex-related differences because peak aerobic capacity potentially affects the hemodynamic and vascular responses, regardless of age and sex [5]. Therefore, the aim of this study was to compare the muscle deoxygenation responses in thigh and lower leg muscles during cycling exercise in peak aerobic capacity-matched elderly men and women.

2 Methods

2.1 Subjects

Untrained elderly men ($n = 8$; age 65 ± 2 years; height 169.4 ± 6.1 cm; weight 67.3 ± 8.4 kg; body mass index (BMI) 23.5 ± 2.7 kg/m^2, mean $\pm$ SD) and women ($n = 8$; age 66 ± 3 years; height 154.0 ± 4.4 cm; weight 53.8 ± 8.1 kg; BMI 23.3 ± 2.8 kg/m^2) participated in the study, which was approved by the Tokyo Medical University Local Research Ethics Committee, Japan. Peak VO_2 was matched between groups (describe below). A statin was taken by one subject in the men's group and one subject in the women's group. All volunteers were informed of the purpose and nature of the study and written informed consent was obtained.

2.2 Experimental Design

The subjects performed 10 or 15 W/min ramp bicycle exercise, after a 3-min warm up at 10 W, until exhaustion (Strength Ergo 8, Fukuda-Denshi, Tokyo, Japan). Pulmonary O_2 uptake (VO_2) was measured continuously during the experiments to determine peak VO_2 by using an automated gas analysis system (AE300S, Minato Medical Science, Osaka, Japan).

Muscle O_2 saturation (SmO_2) and relative changes from rest in oxygenated hemoglobin concentration (Δoxy-Hb), deoxygenated hemoglobin concentration (Δdeoxy-Hb), and total hemoglobin concentration (Δtotal-Hb) were monitored at vastus lateralis (VL) and gastrocnemius medialis (GM) in the left leg by

multichannel near infrared spatial resolved spectroscopy (NIR_{SRS}). The NIR_{SRS} data were defined as the SmO_2 averaged over the last 10 s at rest, 20, 40, 60, 80, and 100 % of peak VO_2. In this study, peak workload was similar between groups (describe below), and therefore, we analyzed the muscle deoxygenation response as a function of percent of peak VO_2.

We used a two-wavelength (770 and 830 nm) light-emitting diode NIR_{SRS} (Astem Co., Japan). The probe consisted of one light source and two photodiode detectors, and the optode distances were 20 and 30 mm, respectively. The data sampling rate was 1 Hz. Even though fat layer thickness affects NIRS data because of light scattering, Niwayama et al. has recently reported that the effects of fat layer thickness can be corrected in relative changes in Hb and absolute value of SmO_2 by normalized measurement sensitivity [6]. In this study, we measured fat layer thickness at each measurement site in the muscles to correct these effects using an ultrasound device (LogiQ3, GE-Yokokawa Medical Systems, Japan). Even though an upper limit of fat layer thickness was designated as 10 mm to correct for the light-scattering effects in this study, fat layer thickness was within ~10 mm at each measurement site in all subjects.

2.3 Statistics

All data are given as means ± standard deviation (SD). To compare changes in NIRS variables during exercise between groups, a two-way repeated-measures analysis of variance was used with age and exercise intensity as factors. Where appropriate, the Bonferroni post hoc test was performed to determine specific significant differences. Differences in physical variables, peak VO_2, and peak workload were compared between groups using unpaired t-tests. For all statistical analyses, significance was accepted at $p < 0.05$.

3 Results

In VL, significantly lower SmO_2 was observed in men than women ($p < 0.05$), even though there was no significant sex × exercise intensity interaction for change in SmO_2 ($p = 0.96$). Moreover, there was a significant sex × exercise intensity interaction for change in Δdeoxy-Hb ($p < 0.05$) or Δtotal-Hb ($p < 0.05$), and a higher Δdeoxy-Hb or Δtotal-Hb was observed in men during high intensity exercise than women. In GM, no significant sex × exercise intensity interaction was observed in SmO_2 ($p = 0.64$), Δdeoxy-Hb ($p = 0.51$) or Δtotal-Hb ($p = 0.64$). In addition, no significant difference was observed in SmO_2 ($p = 0.45$), or in Δdeoxy-Hb ($p = 0.94$) or Δtotal-Hb ($p = 0.69$), in GM. No significant interaction or difference was observed in Δoxy-Hb at any measurement sites (Fig. 1).

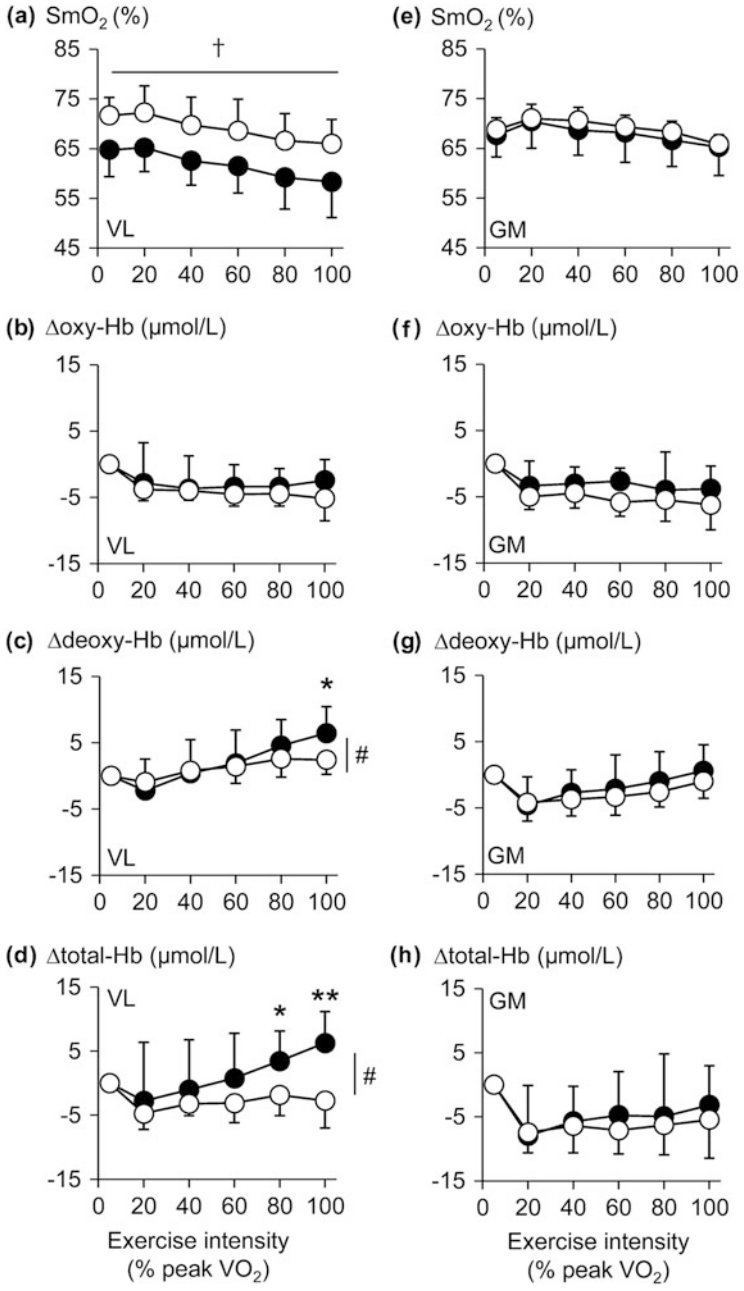

Fig. 1 Change in muscle O_2 saturation (SmO_2: **a**, **e**), oxygenated hemoglobin (oxy-Hb: **b**, **f**), deoxygenated hemoglobin (deoxy-Hb: **c**, **g**), and total hemoglobin (total-Hb: **d**, **h**) responses in VL (**a**, **b**, **c**, **d**) and GM (**e**, **f**, **g**, **h**) muscles during ramp cycling exercise. The *closed circles* show NIRS data in elderly men and the *open circles* show NIRS data in elderly women. There was a significant difference between groups (*$p < 0.05$, **$p < 0.01$). There was a significant sex × exercise intensity interaction (#$p < 0.05$). There was a main effect of sex (†$p < 0.05$)

Peak VO_2 per body weight was matched between groups (men: 21.3 ± 3.0 ml/kg/min, women: 22.2 ± 4.0 ml/kg/min, $p = 0.63$). As a result, there was no significant difference between groups in absolute peak VO_2 (1435 ± 261 vs. 1226 ± 245 ml/min, $p = 0.16$) or peak workload (men: 110 ± 18 W (ranged 75–127 W), women: 106 ± 19 W (ranged 72–124 W), $p = 0.69$). Even though BMI was matched between groups ($p = 0.89$), fat layer thickness was significantly higher in women than in men (VL: 4.05 ± 0.92 vs. 6.78 ± 2.37 mm, $p < 0.05$; GM: 3.51 ± 0.82 vs. 5.35 ± 1.34 mm, $p < 0.01$).

4 Discussion

In the present study, both Δdeoxy-Hb and Δtotal-Hb response in VL was more blunted in woman than men, and SmO_2 was higher throughout exercise in woman than in men. In addition, aerobic capacity and peak workload were matched between groups, and therefore, the effects of peak aerobic capacity and workloads on muscle O_2 dynamics may be negligible. A possible explanation of higher SmO_2 in women may be both higher arterial O_2 saturation and higher venous O_2 saturation than men [7]. Unfortunately, we did not measure these variables directly, and detailed mechanisms for the difference in SmO_2 are unclear. Even though the number of subjects is low, there was no significant relationship between fat layer thickness in the VL and corrected SmO_2 at resting ($r = 0.29$, $p = 0.27$) in all subjects ($n = 16$). Thus, the corrected SmO_2 is not critically affected by the fat layer thickness, and we believe that the correction algorithm is suitable for elderly people in this study. Additionally, in this study, Δdeoxy-Hb and Δtotal-Hb were lower in women than men, especially during high intensity exercise. Reduced estrogen level impairs leg blood flow and vasodilation response in elderly women [8, 9], and the age-related reduction in leg blood flow and vasodilation response tends to be larger in women than men [5]. In fact, mitochondrial content was also found to be reduced in ovariectomized rats [10]. Hence, the percentage of sex hormone may partly explain the difference in Δdeoxy-Hb and Δtotal-Hb. From our findings, we presume that elderly women have lower blood flow, lower vasodilation response, or lower mitochondrial content than peak aerobic capacity- and workloads-matched elderly men. In addition, lactate concentration after exercise may be still higher in elderly men than women, even though the difference in lactate concentrations is reduced as age advances [11]. Therefore, increased Δdeoxy-Hb via lactic acidosis (Bohr effects) may also be more blunted in women than men. However, there is a possibility that lower absolute VO_2 in women may be related to the lower Δdeoxy-Hb response in VL of women, even though the difference in absolute VO_2 between groups did not reach significance. Again, because of the low number of subjects, this area warrants further investigation.

There was some inconsistency of sex-related difference in muscle deoxygenation responses in VL among several previous studies. The disparities may be partly explained by the methods of normalized NIRS data. Peltonen et al. [2] reported that

young women displayed lower SmO_2, Δdeoxy-Hb, and Δtotal-Hb response in VL than young men, as a function of % of peak VO_2. However, in their study, the effect of fat layer thickness on NIRS data was not corrected. In contrast, in the other previous study using a cuff ischemia method, there was no sex-related difference in muscle deoxygenation response in young subjects as a function of percent of peak VO_2 [1, 3]. In the present study of elderly subjects, there was also a lower deoxygenation response in women than men, using the method of the fat layer thickness correction to normalize NIRS data. Although it is difficult to compare the muscle deoxygenation response directly with previous results, to our knowledge, this is the first study to compare deoxygenation response between elderly subjects.

In GM, muscle deoxygenation response was not different between the groups, in contrast to VL. This means that sex-related difference in muscle deoxygenation response may be regional. In line with our findings, a previous study indicated that mitochondrial content and respiration were similar between middle-aged men and women in GM [12], while Green et al. reported that 16.4–18.9 % difference in the activities of Krebs cycle and glycolytic enzyme between untrained young men and women in VL [13]. Moreover, Takagi et al. reported that muscle deoxygenation response was similar between young men and elderly men in GM [4]. The balance between circulation and metabolism in GM muscle may not be affected by aging in both men and women. In addition, an alternative explanation for similar muscle deoxygenation in GM may be that GM muscle does not mainly contribute during cycling exercise, in contrast to VL muscle.

In conclusion, sex-related differences in muscle deoxygenation response were observed between elderly men and women, even though peak aerobic capacity was matched. Moreover, the sex-related differences in muscle deoxygenation responses may be heterogeneous among leg muscles.

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References

1. Murias JM, Keir DA, Spencer MD et al (2013) Sex-related differences in muscle deoxygenation during ramp incremental exercise. Respir Physiol Neurobiol 189:530–536
2. Peltonen JE, Hägglund H, Koskela-Koivisto T et al (2013) Alveolar gas exchange, oxygen delivery and tissue deoxygenation in men and women during incremental exercise. Respir Physiol Neurobiol 188:102–112
3. Bhambhani Y, Maikala R, Buckley S (1998) Muscle oxygenation during incremental arm and leg exercise in men and women. Eur J Appl Physiol Occup Physiol 78:422–431
4. Takagi S, Kime R, Murase N et al (2013) Aging affects spatial distribution of leg muscle oxygen saturation during ramp cycling exercise. Adv Exp Med Biol 789:157–162
5. Martin WH 3rd, Ogawa T, Kohrt WM et al (1991) Effects of aging, gender, and physical training on peripheral vascular function. Circulation 84:654–664

6. Niwayama M, Suzuki H, Yamashita T et al (2012) Error factors in oxygenation measurement using continuous wave and spatially resolved near-infrared spectroscopy. J Jpn Coll Angiol 52:211–215
7. Reybrouck T, Fagard R (1999) Gender differences in the oxygen transport system during maximal exercise in hypertensive subjects. Chest 115:788–792
8. Hickner RC, Kemeny G, McIver K et al (2003) Lower skeletal muscle nutritive blood flow in older women is related to eNOS protein content. J Gerontol A Biol Sci Med Sci 58:20–25
9. Moreau KL, Donato AJ, Tanaka H et al (2003) Basal leg blood flow in healthy women is related to age and hormone replacement therapy status. J Physiol 547(Pt 1):309–316
10. Cavalcanti-de-Albuquerque JP, Salvador ID, Martins EG et al (2014) Role of estrogen on skeletal muscle mitochondrial function in ovariectomized rats: a time course study in different fiber types. J Appl Physiol 116:779–789
11. Benelli P, Ditroilo M, Forte R et al (2007) Assessment of post-competition peak blood lactate in male and female master swimmers aged 40–79 years and its relationship with swimming performance. Eur J Appl Physiol 99:685–693
12. Thompson JR, Swanson SA, Casale GP et al (2013) Gastrocnemius mitochondrial respiration: are there any differences between men and women? J Surg Res 185:206–211
13. Green HJ, Fraser IG, Ranney DA (1984) Male and female differences in enzyme activities of energy metabolism in vastus lateralis muscle. J Neurol Sci 65:323–331