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Vascular adaptations to hypobaric hypoxic training in postmenopausal women

Masato Nishiwaki · Ryoko Kawakami ·
Kazuto Saito · Hiroyuki Tamaki ·
Hiroaki Takekura · Futoshi Ogita

Abstract The objective of this study was to examine the effects of exercise training in hypoxia on arterial stiffness and flow-mediated vasodilation (FMD) in postmenopausal women. Sixteen postmenopausal women (56 ± 1 years) were assigned to a normoxic exercise group (Normoxic group, $n = 8$) or a hypoxic exercise group (Hypoxic group, $n = 8$). The Hypoxic group performed exercise under hypobaric hypoxic conditions corresponding to 2000 m above sea level, and was exposed to these conditions for 2 h per session. Aquatic exercise was performed at an intensity of around 50% peak oxygen uptake for 30 min, 4 days per week, for 8 weeks. Arterial stiffness was assessed by brachial–ankle pulse wave velocity (baPWV), and FMD was evaluated by peak diameter of the popliteal artery during reactive hyperemia. After the 8 weeks of training, the Normoxic group showed no significant changes. In contrast, baPWV ($P < 0.05$) was significantly reduced and peak diameter ($P < 0.05$) and %FMD ($P < 0.01$) were significantly increased in the Hypoxic group after training. These results suggest that exercise training under mild intermittent hypoxic conditions could more effectively reduce arterial stiffness in postmenopausal women, compared with exercise training performed at the same relative intensity under normoxic conditions. Our data also indicate that hypoxic exercise training may induce vascular functional adaptation, for example an increase in FMD response. These findings therefore could have important implications for the development of a new effective exercise prescription program.

Keywords Aquatic exercise · Arterial stiffness · Flow-mediated vasodilation · Hypobaric hypoxia · Pulse wave velocity · Postmenopausal women

M. Nishiwaki
Graduate School of Physical Education,
National Institute of Fitness and Sports in Kanoya,
Kanoya, Japan

M. Nishiwaki
Faculty of Environmental and Symbiotic Sciences,
Prefectural University of Kumamoto, Kumamoto, Japan

R. Kawakami
Project for Physical Activity, National Institute of Health and Nutrition, Tokyo, Japan

K. Saito · H. Takekura · F. Ogita (✉)
Department of Physiological Sciences,
National Institute of Fitness and Sports in Kanoya,
Shiromizu-cho 1, Kanoya, Kagoshima 891-2393, Japan
e-mail: ogita@nifs-k.ac.jp

H. Tamaki
Faculty of Medical Technology,
Niigata University of Health and Welfare,
Niigata, Japan

Introduction

Pulse wave velocity (PWV) is an index of arterial stiffness, and is well known to increase with age [1]. When looking at gender differences in changes to arterial stiffness with age, arterial stiffness is significantly lower in premenopausal women than in age-matched men, whereas the difference disappears upon reaching menopause [2, 3]. In general, estrogen secretion is dramatically reduced in postmenopausal women compared with premenopausal women [4]. Because estrogen has potent vasodilatory and antiatherosclerotic effects in vascular tissue [5], estrogen deficiency after menopause brings a rapid increase in arterial stiffness [3, 6]. In recent years, increased arterial stiffness has been considered to increase the risk of

cardiovascular disease [6–8]. To reduce this risk in women, the importance of preventing and/or ameliorating increases in arterial stiffness among postmenopausal women has been emphasized.

Systemic hypoxia per se is known to induce acute vasodilation [9–11]. In addition, Thomson et al. and Vedam et al. have shown a significant reduction in augmentation index, used to assess arterial stiffness, in healthy men breathing hypoxic gas [12, 13]. Similarly, regular aerobic exercise training is widely accepted to induce a decrease in arterial stiffness and/or enhancement of flow-mediated vasodilation (FMD) [14–19]. Exercise under hypoxic conditions would thus seem likely to more effectively induce vascular adaptations (i.e., a decrease in arterial stiffness).

In contrast, Calbet and Lundby et al. have demonstrated that chronic hypoxia (approximately 4500–5000 m above sea level) elicits a significant increase in systemic blood pressure (BP) even in healthy humans [20, 21]. Moreover, it is possible that acute mountain sickness could result from high-intensity physical activity under hypoxic conditions ($\geq$2500 m above sea level, $\geq$4 h) [22, 23]. However, such physiological responses are altered by the level of hypoxia, exposure duration, and the intensity or type of physical activity under hypoxic conditions [22–24]. In fact, at mild altitude (approximately 2000 m above sea level), it has often been observed that systemic BP either does not change, or decreases [25–29]. In addition, Beidleman et al. [30] found that BP does not change significantly during intermittent hypoxic exposure (4300 m above sea level).

In general, BP during neck-level immersion in cold-water (14°C) significantly increases compared to pre-immersion control values (i.e., BP on land) because cold stimulus and hydrostatic pressure induce peripheral vasoconstriction [31, 32]. However, several investigations have revealed that BP does not change, or decreases slightly, during water immersion up to xiphisternal-level immersion when the water temperature is in the range 24–32°C [32–34]. Furthermore, recent studies have reported interesting observations that aquatic exercise training elicits a reduction of BP and/or an increase in arterial distensibility (a decrease in arterial stiffness) in humans and animals [35–40]. Also, weight-bearing force on the skeletal joints during aquatic exercise is reduced by the buoyancy effect [41]. Because water resistance is proportional to the square of body movement velocity, the force on exercising limbs can be easily and voluntarily adjusted by varying the body movement velocity [41]. Therefore, aquatic exercise is often used as a safer and easier type of exercise for the elderly, arthralgic patients, and obese individuals.

Based on these characteristics of hypoxic and aquatic environments on the human body, the purpose of this study was to examine the effects of low-intensity aquatic exercise under mild intermittent hypoxic conditions on vascular response in postmenopausal women. Our hypothesis was that aquatic exercise under mild hypoxic conditions would induce a decrease in arterial stiffness in postmenopausal women more effectively than exercise under normoxic conditions.

Materials and methods

Subjects

Sixteen Japanese postmenopausal women with a mean age of 56 $\pm$ 1 years (mean $\pm$ standard error of the mean (SEM)) were studied. Mean height and body mass were 151.9 $\pm$ 1.6 cm and 55.7 $\pm$ 1.5 kg, respectively. Subjects were either sedentary or recreationally active. All the subjects were at least a few years past menopause, and mean duration since menopause was 6 $\pm$ 1 years. None of the women were receiving hormone-replacement therapy or had a history of smoking or took any medications, at least during this experimental period. Subjects were divided by matching for age and physical fitness level into two groups: a normobaric normoxic exercise group (Normoxic group, $n = 8$); and a hypobaric hypoxic exercise group (Hypoxic group, $n = 8$). All subjects were informed about the procedures and risks of the study before providing written informed consent to participate. All study protocols were approved by the Ethics Committee for Human and Animal Experiments of the National Institute of Fitness and Sports.

Experimental procedures

Before and after the training period, peak oxygen uptake ($\dot{V}O_{2peak}$), arterial stiffness and flow-mediated vasodilation were assessed in both groups. To avoid potential diurnal variations, subjects were tested at the same time of day and the same number of hours after the last meal in both test periods. Also, subjects were required to abstain from caffeine and to fast for $\geq$4 h before each test (an 8-h overnight abstention from caffeine and fast for determination of FMD). Subjects were studied 3 days after their last exercise training session to avoid the acute effects of exercise or hypobaric hypoxia. All tests were performed on different days, and were conducted in a quiet air-conditioned room (22–24°C) under normobaric normoxic (normal) conditions.

Exercise training

Exercise training was performed in a specific swimming pool located in a chamber in which atmospheric pressure

could be regulated [42]. Aquatic exercise was performed for 30 min per training session, 4 days per week, for 8 weeks. The aquatic exercise program was done with expert instructors who demonstrated this program for the subjects throughout the exercise period. Heart rate (HR) was monitored (Accurex Plus; Polar, USA) and constantly displayed to both subjects and instructors, and subjects were required to perform exercise maintaining approximately the target HR, which was predetermined from cycling exercise at an intensity of 50% $\dot{V}O_{2peak}$. To achieve the target HR, instructors also gave movement instructions to individual subjects. Water level was set at around the xiphisternal level (water temperature 27–29°C). The Normoxic group performed exercise training under normobaric normoxic conditions (749.3–750.0 mmHg). In contrast, the Hypoxic group performed exercise training under hypobaric hypoxic conditions corresponding to 2000 m above sea level (600.1–603.8 mmHg), and was exposed to this condition for 2 h per session. Subjects were instructed to maintain their normal diet and to refrain from any other specific exercise training throughout the study period. All subjects completed 100% of all training sessions as scheduled (32 total training sessions in 8 weeks).

Pre test and assessment of $\dot{V}O_{2peak}$

To establish a relationship between submaximal exercise intensity (work rate) and steady-state oxygen uptake ($\dot{V}O_2$) for each subject, $\dot{V}O_2$ during a 6-min bout at constant exercise intensity was determined intermittently at ≥ 3 different submaximal exercise intensities in cycling ergometer exercise (75XL II; Combi, Japan). Pedaling rate was kept constant at 60 rpm for all volunteers. $\dot{V}O_2$ was measured during the last 2 min of the 6-min bout at each intensity. The mean coefficient of correlation (r value) calculated individually from the linear relationship between $\dot{V}O_2$ and exercise intensity was 0.998 ± 0.001. After this linear relationship was determined, $\dot{V}O_{2peak}$ was also measured during an incremental cycle ergometer exercise. Exercise intensity was first set at 40 W, then increased by 15 W every 1 min until exhaustion. Exhaustion was defined by subjects being unable to maintain the pedaling rate or asking to discontinue the exercise. $\dot{V}O_2$ was measured during the last 2–3 min, and $\dot{V}O_{2peak}$ was determined as the highest value during incremental exercise. In this study, $\dot{V}O_2$ was measured using the Douglas bag method. O_2 and CO_2 fractions in expired gas were determined using an automatic gas analyzer (Vmax29c; Sensormedics, USA). Gas volume was measured using a dry gas meter (NDS-2A-T; Shinagawa, Japan).

Submaximal exercise test

Exercise intensity at 50% of $\dot{V}O_{2peak}$ was estimated individually by interpolating the linear relationship between $\dot{V}O_2$ and submaximal exercise intensity. To determine the target HR during aquatic exercise program, subjects were required to perform cycling ergometer exercise at an intensity of 50% $\dot{V}O_{2peak}$ for 10 min, and HR was measured during the final 1 min of exercise. HR during exercise was measured continuously using a HR monitor (above apparatus), and the mean was calculated. In this study, the submaximal exercise intensity used in the Normoxic and Hypoxic groups was 36 ± 4 and 38 ± 6 W, respectively.

Assessment of arterial stiffness

After subjects had rested in a supine position for ≥ 15 min, brachial–ankle pulse wave velocity (baPWV) was measured in accordance with previously reported methods [2, 43–46]. PWV, arterial BP, electrocardiography (ECG), heart sounds, and HR were measured using a semiautomated device (form PWV/ABI; Colin Medical Technology, Japan). ECG electrodes were placed on both wrists, and a heart sound microphone was placed at the left edge of the sternum. HR at rest was also automatically calculated from the R–R intervals of ECG. Cuffs to measure baPWV were wrapped around both upper arms and ankles. These cuffs were connected to a volume-plethysmographic sensor that determines volume pulse form and an oscillometric pressure sensor that measures blood pressure. PWV was calculated by dividing the distance between the two arterial recording sites by the transit time. These times were determined from the time delay between the brachial and ankle waveforms. Pass lengths between the arm and ankle were calculated automatically according to the height of the subject [46]. The mean of left and right baPWV in each subject was used for subsequent analyses [44]. In our laboratory, the day-to-day coefficient of variation was $2.7 \pm 0.3\%$ for baPWV.

Assessment of FMD

Measurements were conducted, following a standardized procedure and guidelines [47–50]. Subjects rested for ≥ 15 min in a prone position before the study. After 1 min of acquisition to measure diameter of the popliteal artery (DPA) at rest [19], an arterial occlusion cuff placed at the thigh (SC10; D.E. Hokanson, USA) was inflated for 5 min at 300 mmHg, then deflated to induce reactive hyperemia. Image acquisition was continued for 2 min after cuff deflation. Artery diameter was determined using an ultrasound imaging system (SSH-140A; Toshiba, Japan) by the same

experienced observer throughout the experimental period. A B-mode scan of the left popliteal artery was obtained in longitudinal section between 1 and 2 cm below the popliteal fossa, using a 7.5-MHz transducer. All images showed the same point of the popliteal artery, 1–2 cm above the bifurcation into anterior and posterior tibial arteries, and this bifurcation was used as an anatomical marker to identify the same artery and the same position in every measurement [51]. All the images were recorded on an S-VHS videocassette for later off-line manual analysis using image-analysis software (Image J; National Institutes of Health, USA) [52]. Each frame was measured three times, and means were calculated. Artery diameters were determined by measuring the distance between the anterior and posterior walls of the intima [48]. Time points corresponding to maximum systolic expansion of the popliteal artery and basal (minimum) diastolic relaxation were selected [17, 53]. In accordance with previously reported methods [51], DPA was represented as the mean diameter corresponding to the relative time periods of the systolic (1/3) and diastolic (2/3) blood pressure phases (diameter = systolic 1/3 + diastolic 2/3). Diameter at rest was analyzed for 3 consecutive cycles, and these values were averaged. Diameter during reactive hyperemia was analyzed every 10 s, and peak arterial diameter of each subject was adopted as the maximum value during reactive hyperemia (after cuff release). In addition, %FMD was calculated as the percentage rise of this peak diameter from the preceding diameter at rest. The same single investigator who was unaware of group assignment or time points (pre, post) performed all image analyses. The coefficients of variation from the intraobserver measured on two separate days were 0.9 ± 0.3, 1.0 ± 0.4, and $9.1 \pm 3.0\%$ for diameter at rest, peak diameter during reactive hyperemia, and %FMD, respectively.

Statistical analysis

Results are reported as means $\pm$ SEM. Student's t test was used to compare values before training and target HR during aquatic exercise between two groups. Changes in values were analyzed by two-way (group $\times$ period) repeated-measures analysis of variance (ANOVA). In the case of a significant F value, the Tukey method was used for post-hoc multiple comparisons. Results were regarded as statistically significant if $P < 0.05$.

Results

Baseline

Before training, no significant differences in any values were identified between groups. In addition, target HR

during aquatic exercise in Normoxic and Hypoxic groups was 89 ± 3 and 96 ± 4 beats min^{-1}, respectively. No significant difference was observed in target HR between Normoxic and Hypoxic groups.

Effects of aquatic exercise training

After 8 weeks of aquatic exercise, $\dot{V}O_{2peak}$ was not significantly changed in either absolute values or relative values as per body weight in either group (Table 1). Similarly, neither BP nor HR at rest differed significantly after training in either group (Table 1). Mean baPWV was significantly reduced in the Hypoxic group ($P < 0.05$), but not in the Normoxic group (Fig. 1). DPA at rest was not significantly changed in either group after training, and peak diameter during reactive hyperemia ($P < 0.05$) and %FMD ($P < 0.01$) were significantly increased in the Hypoxic group only (Fig. 2).

Discussion

This is the first study to investigate the effects of exercise training in hypoxia on arterial stiffness in postmenopausal women. The main new finding of this study was that exercise training in hypoxia significantly reduced baPWV, whereas exercise training performed at the same relative intensity under normoxic conditions did not. Furthermore, significant increases in peak diameter during reactive hyperemia and %FMD were observed in the Hypoxic group only.

A recent study has reported that regular physical activity is an important component in the prevention and treatment of an increase in arterial stiffness in postmenopausal women [6]. Previous studies have demonstrated that vascular adaptations (i.e., arterial compliance, FMD, etc.) and/ or an increase in $\dot{V}O_{2max}$ occurred within approximately 8 weeks of aerobic exercise training [19, 54–56]. Therefore, the 8-week period seems to be adequate to induce cardiovascular and/or respiratory adaptations. This is the reason why this training study was conducted for an 8-week period. However, baPWV in the Normoxic group, which trained at a low-intensity level for 30 min, for 8 weeks, did not change significantly. Sugawara et al. [57] demonstrated that even low-intensity exercise training (total 900 kcal week^{-1}) could improve central arterial compliance (i.e., an increase in arterial distensibility), and they implied that the total energy expenditure of the training is more important than exercise intensity for improvement of arterial distensibility. In contrast, because our training protocol was composed of exercise with low intensity for a short time (30 min), total energy expenditure

Table 1 $\dot{V}O_{2peak}$ and cardiovascular data before and after exercise training

Variables	Normoxic group		Hypoxic group	
	Pre	Post	Pre	Post
MV (l min^{-1})	43.4 ± 1.9	43.3 ± 2.0	42.4 ± 3.4	44.7 ± 3.6
$\dot{V}O_{2peak}$ (l min^{-1})	1.41 ± 0.11	1.39 ± 0.11	1.49 ± 0.16	1.41 ± 0.12
$\dot{V}O_{2peak}$ (ml kg^{-1} min^{-1})	25.0 ± 1.9	25.5 ± 1.8	27.2 ± 2.6	26.0 ± 1.9
HR (beats min^{-1})	59 ± 3	55 ± 2	59 ± 2	55 ± 2
Systolic BP (mmHg)	130 ± 6	128 ± 8	135 ± 8	126 ± 7
Diastolic BP (mmHg)	72 ± 3	72 ± 4	76 ± 4	71 ± 3
Mean BP (mmHg)	97 ± 4	98 ± 7	101 ± 6	96 ± 5

Data are mean $\pm$ standard error of the mean

MV, minute ventilation at exhaustion; $\dot{V}O_{2peak}$, peak oxygen uptake; HR, heart rate; BP, blood pressure; Pre, before training; Post, after training

Fig. 1 Changes in brachial–ankle pulse wave velocity (*baPWV*) before and after exercise training. *Closed circles* represent change in baPWV for each individual value in Normoxic and Hypoxic groups. *Open circles* represent change in baPWV for mean values before and after exercise training. *Vertical bars* indicate standard error of the mean
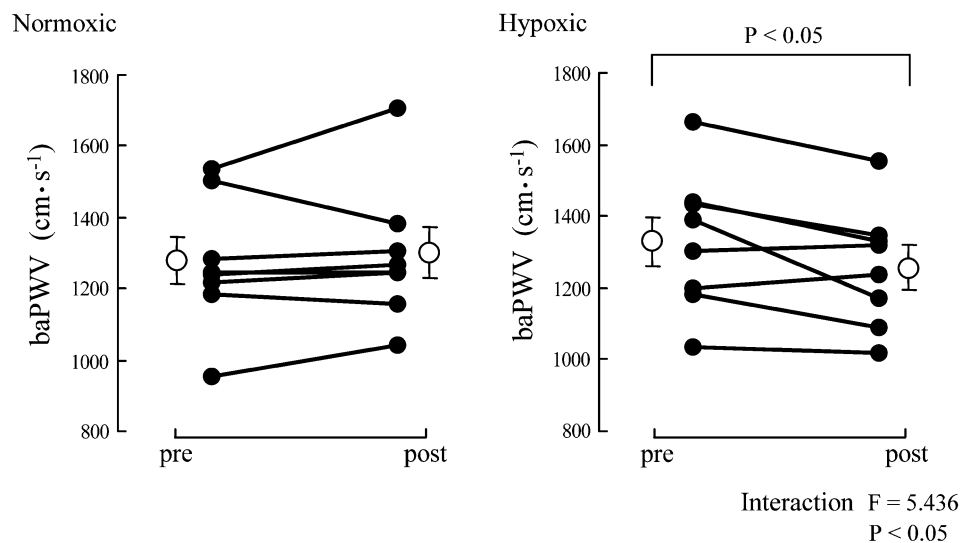
of this training (estimated value approximately 400 kcal week^{-1}) may be insufficient to induce a decrease in arterial stiffness. Therefore, these results, which showed that exercise training in normoxia did not reduce arterial stiffness, are thought to result from insufficient total energy expenditure of the training.

In this experiment, aquatic exercise training was performed at the same training frequency and with the same training period in both groups. Also, HR level during exercise training in this study did not differ significantly between groups. Although $\dot{V}O_{2peak}$ and maximum HR were not determined under hypoxic conditions in this study, Haufe et al. [58] demonstrated that training HR in a Normoxia group did not differ significantly from that in a Hypoxia group when exercise training was conducted at the same relative intensity under normoxic and hypoxic conditions, respectively. Therefore, exercise stimulus for the cardiovascular system would be considered comparable between groups. Conversely, the absolute intensity of

training might be lower in the Hypoxic group than in the Normoxic group [58, 59]. Nevertheless, reduced baPWV was found only in the Hypoxic group. It has been reported that baPWV provides information qualitatively similar to that derived from central arterial stiffness and that the validity and reproducibility of baPWV measurements are high [46, 60, 61]. Our result thus suggests that exercise training under mild intermittent hypoxic conditions could more effectively reduce arterial stiffness in postmenopausal women, compared with exercise training under normoxic conditions. These results also imply that hypoxia per se could be an even better stimulus to induce a decrease in arterial stiffness compared with normoxia.

Vascular adaptations are generally thought to result from structural changes, functional changes, or a combination of the two [62, 63]. The results of this study demonstrated that peak diameter during reactive hyperemia after training was significantly increased in the Hypoxic group only, although no significant change was observed in
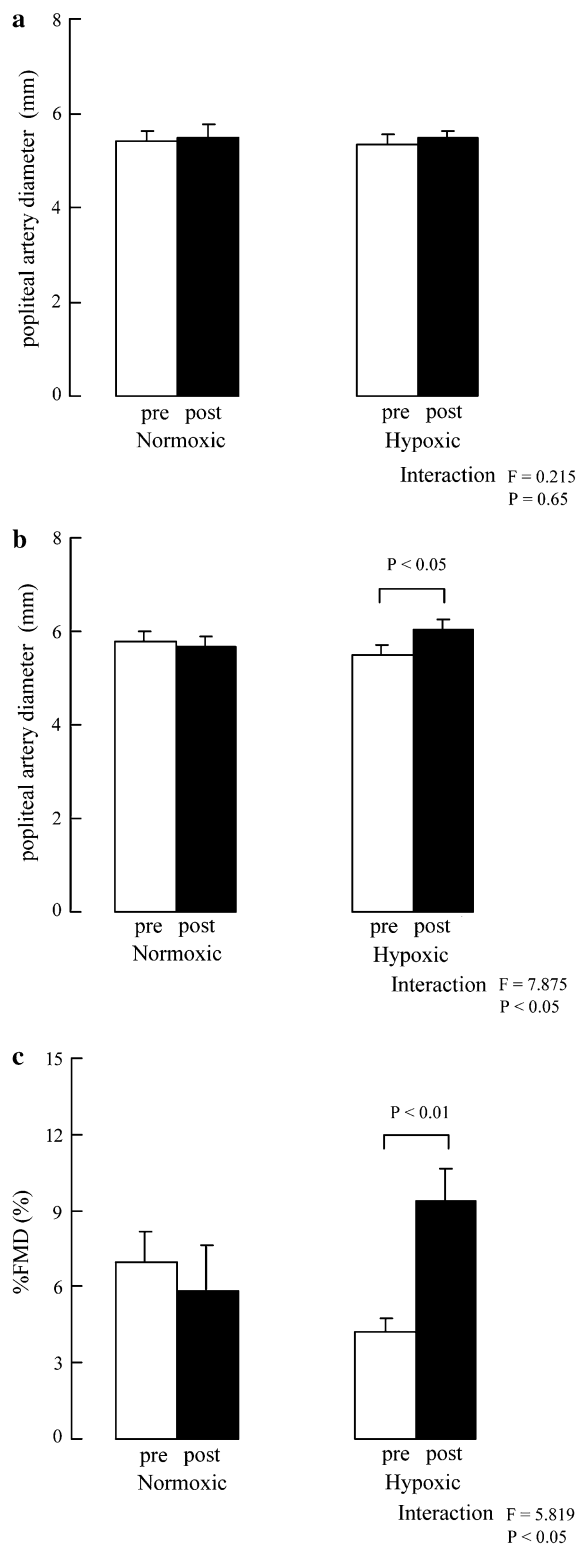
Fig. 2 Changes in diameter of popliteal artery and %FMD before and after exercise training. **a** Diameter of popliteal artery at rest. **b** Peak diameter during reactive hyperemia. **c** %FMD (%FMD was calculated as the percentage rise of the peak diameter from the preceding diameter at rest). *Vertical bars* indicate standard error of the mean

diameter at rest. This increased peak diameter means an enhanced FMD response, which would be related to functional changes of conduit artery [14, 18, 19]. Therefore, our results also raise the possibility that hypoxic exercise training may elicit vascular functional adaptation such as an increase in FMD response.

The physiological mechanisms underlying vascular adaptations to hypoxic exercise training have not yet been elucidated. However, several studies have indicated that hypoxia is one of the most potent inducers of vasodilators [9, 10, 13, 64, 65]. Hypoxic exposure is also known to induce a decrease in arterial stiffness [12, 13]. Meanwhile, aerobic exercise increases shear stress, which triggers a release of vasodilators [66], and repetitive increases in blood flow or shear stress with exercise may enhance vasodilator release in the vascular endothelium [14, 18, 67]. Therefore, it seems that these combined effects of hypoxic exposure and aerobic exercise lead to reduced arterial stiffness. Further investigations are thus needed to determine the physiological mechanisms which explain the reduced arterial stiffness with hypoxic exercise training.

Changes in BP per se are well known to affect changes in PWV [60, 68]. Because of increased sympathetic activity, prolonged exposure to moderate or severe hypoxia generally causes strong vasoconstriction and, consequently, elicits an increase in BP [20, 21, 59]. At mild altitude (approximately 2000 m above sea level), however, it has often been observed that systemic BP does not change, or decreases [25–29]. Because our results indicated no significant changes in BP at rest, BP per se is unlikely to have affected a reduction in baPWV. Therefore, the reduction in baPWV observed in the Hypoxic group after training primarily results from a decrease in arterial stiffness.

The results of this study showed similar or somewhat smaller changes in arterial stiffness compared with previous studies [15, 45, 56, 57, 60, 69, 70]. This reduced arterial stiffness may thus seem unlikely to be clinically meaningful. However, a decrease in arterial stiffness helps to increase cardiac output and thereby inhibits excessive BP rise, especially during acute exercise [16, 71]. Therefore, the decreased arterial stiffness per se seems to have advantages at least for reduction of cardiovascular risks. To clarify whether or not exercise in hypoxia is efficacious for treatment or prevention of enhanced arterial stiffness, further experiments targeting high-risk populations (i.e., cardiovascular patients) are required.

Although our results showed that the vascular adaptations were induced by hypoxic training, FMD reportedly decreased significantly after 3 weeks of physical activities at mild altitude (1700 m above sea level) [72], or endothelium-dependent vasodilation did not change significantly with only intermittent hypoxic exposure (15% O_2,

1 h per session, 5 times per week, for 4 weeks) [24]. Furthermore, animal studies indicated that hypoxic exposure (2800 m above sea level) with exercise training depressed endothelium-dependent vasorelaxation [73, 74]. At the moment, causes of the conflicting findings between this investigation and previous studies [24, 72] are hard to explain. However, our protocol was composed of low-intensity exercise and intermittent exposure to a mild hypoxic environment. Our results thus imply that the effects of exercise at a low-intensity and a mild intermittent hypoxic stimulus act synergistically to induce favorable adaptations for vascular function. However, because we cannot suggest any mechanisms of this adaptation, further studies are needed to elucidate it.

These findings have clinically and physiologically important implications. Chronic hypoxia (approximately 4500–5000 m above sea level) is widely accepted to elicit a significant increase in BP even in healthy humans [20, 21]. Moreover, acute mountain sickness can occur as a result of high-intensity physical activity under hypoxic conditions (≥ 2500 m above sea level, ≥ 4 h) [22, 23]. However, our results showed that low-intensity exercise training under mild intermittent hypoxic conditions resulted in a decrease in arterial stiffness for postmenopausal women without inducing excessive increase in BP and acute mountain sickness. Furthermore, it should be emphasized that exercise training performed at low intensity under mild intermittent hypoxic conditions can induce a significant decrease in arterial stiffness even though exercise training at the same relative intensity conducted under normoxic conditions does not induce any vascular adaptation. These findings therefore could have important implications for the development of a new effective exercise prescription program in order to prevent and/or ameliorate an increase in arterial stiffness.

Limitations of this study

This study has several important limitations. First, the subjects were postmenopausal women, and the number of subjects was small ($n = 16$). Therefore, to generalize our results, further studies are needed. Second, this study did not include determination of plasma female hormone levels (i.e., estrogen). Although the subjects were at least a few years past menopause, the effects of estrogen on vascular tissue are unclear. Third, in this study, the maximum obtainable vasodilator response using an exogenous nitric oxide donor was not assessed. In addition, blood flow was not measured during FMD. Thus, the authors could not express the FMD data normalized to the shear rate stimulus responsible for endothelium-dependent FMD [18, 50, 75]. Fourth, this study did not provide measurements of arterial oxygen saturation (SpO_2). Although our unpublished data

indicate that SpO_2, which was recorded with a finger pulse oximeter (Pulsox-Me300; Teijin Pharma, Japan) during aquatic exercise (50% $\dot{V}O_{2peak}$ level) under hypobaric hypoxic conditions corresponding to 2000 m above sea level, was $92 \pm 4\%$ in seven healthy men (23 ± 1 years), the effect of this hypoxic aquatic exercise on SpO_2 in postmenopausal women is not clear. Accordingly, we failed to demonstrate whether subjects in the Hypoxic group were even hypoxic during the aquatic exercise. Fifth, this training study was conducted only for 8 weeks. Such short-term study gives no information about whether reduced arterial stiffness and enhanced FMD will persist long-term. Finally, because no significant changes in $\dot{V}O_{2peak}$ were observed in either group, aquatic exercise in this study was not intense enough to induce an increase in $\dot{V}O_{2peak}$. Investigations using different exercise stimuli in hypoxia (i.e., type and intensity) may thus reveal important new insights into vascular adaptation to hypoxic exercise training.

Conclusions

This study examined the effects of hypoxic exercise training on arterial stiffness and FMD in postmenopausal women. The results suggest that low-intensity exercise training under mild intermittent hypoxic conditions could more effectively reduce arterial stiffness in postmenopausal women than exercise training performed at the same relative intensity under normoxic conditions. In addition, our results indicate that hypoxic exercise training may induce vascular functional adaptation such as an increase in FMD response. These findings therefore could have important implications for the development of a new effective exercise prescription program.

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