J Physiol Sci (2009) 59:457–464
DOI 10.1007/s12576-009-0057-3

ORIGINAL PAPER

Effect of combined resistance and aerobic training on reactive hyperemia in men

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Received: 20 February 2009 / Accepted: 24 July 2009 / Published online: 18 August 2009

Abstract Reduced response to reactive hyperemia (RH) in the extremities reflects impaired endothelium-dependent vasodilation of the microvasculature. The aims of the present study were to determine whether resistance training and a combination of aerobic and resistance training increase the endothelial vasodilation of the forearm assessed by RH. A total of 39 young men were assigned to either high-intensity resistance training (HIR; six types of exercises, 80% 1RM × 10 repetitions × 3 sets, $n = 14$) or moderate-intensity resistance training (MIR; six types of exercises, 50% 1RM × 16 repetitions × 3 sets, $n = 14$) or a combination of high-intensity resistance training and moderate-intensity endurance training (COMBO; HIR and 60% maximal heart rate × 30 min, $n = 11$) groups. We measured forearm blood flow response to RH before and after 4 months of exercise intervention. All training groups increased maximal strength in all muscle groups tested (all $P < 0.05$). After 4 months of training, the forearm blood flow during RH increased significantly in the MIR and COMBO groups, from 57 ± 4 to 66 ± 7 ml/min per 100 ml tissue and from 59 ± 6 to 74 ± 8 ml/min per 100 ml tissue, respectively (both $P < 0.05$). There was no change in the response to RH in the HIR groups. In conclusion, the findings in this study demonstrate that combined resistance and aerobic training may affect the vasoreactivity response to RH in the forearm, but not resistance training alone.

Keywords Reactive hyperemia · Endothelial function · Blood flow · Resistance training · Exercise · Combined training

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Introduction

Reduced response to reactive hyperemia (RH) in the forearm or leg, reflecting impaired endothelium-dependent vasodilation of the microvasculature, is an independent predictor of cardiovascular morbidity [1, 2] or mortality [3]. Recently, it has been reported that daily aerobic exercise augments forearm blood flow response to RH, suggesting improved endothelial function of the microvasculature [4–6]. Therefore, aerobic training is being recommended as an effective way of preventing and improving endothelial dysfunction.

Resistance training has become a popular modality of exercise performed by most populations, and has become an integral component of exercise recommendations endorsed by a number of national health organizations [7, 8]. It is important to determine an effective exercise program incorporating resistance exercises on endothelium-dependent vasodilation in the microvasculature, an independent risk factor for cardiovascular disease [1, 2]. We and others have demonstrated that high- and moderate-intensity resistance training is associated with reduced arterial compliance by using longitudinal or cross-sectional studies [9–11], but not with a change of endothelial function in conduit arteries (carotid or brachium) [12, 13].

It remains unclear, however, whether the resistance training favorably affects endothelium-dependent vasodilation, in particular, the microvasculature. Furthermore, to gain and maintain cardiorespiratory fitness, muscle strength or healthy cardiovascular function, the importance of combined endurance and resistance exercise has been reported by some papers [10, 14–18], but the effects on endothelial function of the microvasculature evaluated by using RH is not known.

Accordingly, the aims of the present study were to determine whether resistance training and a combination of aerobic and resistance training increase the endothelial function of the forearm assessed by using RH. To investigate in detail the effects of resistance training, a total of 39 young men were randomly assigned to groups for either high-intensity resistance (HIR) or moderate-intensity resistance (MIR) training or a combination of high-intensity resistance training and moderate-intensity endurance (COMBO) training. We measured forearm blood flow response to RH, an index of endothelium-dependent vasodilation in the microvasculature, before and after the 4-month interventional study, and hypothesized that MIR training and combined resistance and aerobic training induce enhancement of the endothelial function of the forearm assessed by RH, if MIR as well as COMBO training have aerobic factors or components, including increased heart rate or blood flow during exercise.

Methods

Subjects

A total of 39 young healthy men 19 to 38 years old were studied. We excluded subjects who had participated in any resistance or endurance training on a regular basis (i.e., >3/week), but included subjects who had taken part in recreational activities. All subjects were normotensive (blood pressure <140/90 mmHg), nonobese (body mass index <30 kg/m^2) and free of overt chronic diseases as assessed by their medical history and a physical examination. Candidates who had smoked in the previous 4 years, who were taking medications or anabolic steroids, or who had significant intima-media thickening, plaque formation and/or other characteristics of atherosclerosis (e.g., ankle-brachial index <0.9) were excluded. All subjects gave their written informed consent to participate, and all procedures were approved by the Institutional Review Board. Subjects were randomly assigned into the HIR group ($n = 14$), the MIR group ($n = 14$) or the COMBO group ($n = 11$). Before the intervention period, there were no significant differences in any of the variables between the groups.

Measurements

Three groups were studied three times: before training, at 2 months and after 4 months of exercise training. To avoid potential diurnal variations, subjects were tested at the same time of day throughout the study period [9, 19]. Before each testing, subjects abstained from caffeine and fasted for at least 4 h; most subjects were studied after an overnight fast. Subjects were studied 20–24 h after their last exercise training session to avoid the acute effects of exercise, but they were still considered to be in their normal (i.e., habitually exercising) physiological state.

Incremental exercise

To demonstrate that participants had been sedentary, we measured the maximal oxygen consumption during incremental cycle ergometer exercise [20]. The oxygen consumption, heart rate and ratings of perceived exertion were measured throughout the protocol.

Strength testing

Maximal muscular strength was assessed before and after resistance training using the following exercises: half squat, bench press, leg extension, leg curls, lateral row and abdominal bend. After ten warm-up repetitions, one-repetition maximum (1RM) values were obtained according to established guidelines. The day-to-day coefficient of variation for 1RM strength in our laboratory is 4 ± 2%.

Body composition

The body composition was determined using the bioelectric impedance method (coefficient of variance 4 ± 2%).

Arterial blood pressure and heart rate at rest

Chronic levels of arterial blood pressure or heart rate at rest were measured with a semiautomated device (Form PWV/ABI, Colin Medical, Komaki, Aichi, Japan) [21]. Recordings were made in triplicate with participants in the supine position.

Forearm blood flow following RH

Forearm blood flow was measured by using a mercury-filled silastic strain-gauge plethysmograph (EC-5R, DE Hokanson Inc.), as previously described [5]. A cuff was placed around the right upper arm of the subject. A strain gauge around the widest part of the forearm on the same side was connected to the plethysmography device and supported above the level of the right atrium. The upper arm cuff was inflated to 40 mmHg for 5 s in each 15-s cycle to occlude venous outflow from the arm using a rapid cuff inflator (EC-20, DE Hokanson Inc.). The forearm blood flow output signal was recorded on a personal computer via an A/D converter (PowerLab, AD Instruments). Forearm blood flow was expressed in milliliters per minute per 100 ml of forearm tissue volume.

To obtain measures of flow-mediated vasodilation, arm blood flow was occluded for 5 min by inflating a blood pressure cuff over the upper arm to a pressure 100 mmHg above systolic blood pressure. Following rapid release of the inflation pressure, changes in forearm volume were measured for 3 min by strain-gauge plethysmography, following the above-mentioned 15-s cycle method [5, 22]. The day-to-day coefficient of variation for RH in our laboratory is 9 ± 5%.

Blood pressure following RH

Radial blood pressure waveforms were determined using arterial tonometry (JENTOW-7700; Colin Medical Technology). Arterial blood pressure waveforms were sampled at 1,000 samples per second by connecting each device to a computer using an A/D converter (PowerLab; AD Instruments). The principle of arterial tonometry is that blood pressure at the radial artery can be obtained by measuring the reaction forces produced by flattening the radial [artery]. A tonometric sensor was attached to the left wrist that was placed on a padded platform at the level of the heart. The oscillometric calibrations were carried out for accurate tonometric measurement before RH [23, 24].

Exercise training intervention

In the 4 months of the study period, all participants underwent three supervised resistance training sessions per week. During each training session, participants in the HIR and the COMBO groups completed three sets of 8–12 exercises at 80% of 1RM, and subjects in the MIR group completed three sets of 14–16 exercises at 50% of 1RM, in the following order: leg extension, seated chest press, leg curls, lateral row, squat and sit-ups. The resistance of each exercise was increased progressively throughout the resistance training period. The recovery time between exercise bouts was controlled at 2-min intervals. Each resistance training session lasted approximately 45 min. Subjects in the COMBO group performed a cycle exercise at 60% of the maximal heart rate for 30 min immediately after each resistance training session. Training assistants verbally encouraged the subjects and ensured proper form and technique at each exercise session. Participants were instructed to refrain from any other regular exercise during the entire study period.

Statistical analysis

Results are presented as the mean ± SE. Values of $P < 0.05$ were considered significant. One-way ANOVA was used to evaluate differences among HIR, MIR and COMBO groups concerning parameters before exercise training intervention. Comparisons of time course curves of forearm blood flow and blood pressure during RH were analyzed by two-way ANOVA (time point × period) with repeated measures for each group. Changes in other parameters were also assessed by two-way ANOVA (group × period) with repeated measures. In the case of significant F values, a post hoc test (Newman–Keuls method) was used to identify significant differences among mean values.

Results

Before exercise training, there were no significant differences in any of the characteristics of subjects among the three groups (Table 1). In all groups, there were no changes in height, weight or body mass index throughout this study period.

All groups increased 1RM strength significantly in all muscle groups tested ($P < 0.05$–$P < 0.0001$). Percentages of increases in 1RM strength for the HIR, MIR and COMBO groups were 47, 6 and 25% for leg extension; 26, 13 and 14% for leg curl; 30, 10 and 25% for squat; 25, 8 and 17% for lateral row; 20, 6 and 21% for bench press; and 32%, 12% and 21% for abdominal bend, respectively.

There were no significant differences in baseline brachial blood pressure and resting heart rate, although forearm blood flow was lower in the COMBO group compared to the MIR group in the pre-training period (Table 2). Brachial blood pressure, resting heart rate and forearm

Table 1 Characteristics of selected subjects at the baseline

Variables	HIR	MIR	COMBO
N	14	14	11
Age, years	22 ± 1	20 ± 1	21 ± 1
Height, cm	173 ± 2	170 ± 2	171 ± 2
Body weight, kg	66 ± 3	65 ± 3	66 ± 2
Body mass index, kg/m^2	22 ± 1	22 ± 1	23 ± 1
Body fat, %	18 ± 2	20 ± 2	21 ± 1
Peak oxygen consumption, ml/min per kg	51 ± 2	52 ± 2	49 ± 2

Data are mean ± SEM

HIR high-intensity resistance training group, *MIR* moderate-intensity resistance training group, *COMBO* combined high-intensity resistance training and moderate-intensity aerobic exercise training group

Table 2 Cardiovascular indices

Variables/group	0 month	2 month	4 month	Interaction
Brachial systolic BP, mmHg				
HIR	116 ± 3	118 ± 3	116 ± 3	$F = 1.986$
MIR	121 ± 3	117 ± 3	119 ± 3	$P = 0.1058$
COMBO	115 ± 2	115 ± 2	116 ± 3	
Brachial diastolic BP, mmHg				
HIR	68 ± 1	69 ± 2	66 ± 2	$F = 1.806$
MIR	71 ± 2	67 ± 2	67 ± 2	$P = 0.1371$
COMBO	67 ± 1	66 ± 2	67 ± 2	
Brachial pulse pressure, mmHg				
HIR	68 ± 1	69 ± 2	66 ± 2	$F = 0.208$
MIR	71 ± 2	67 ± 2	67 ± 2	$P = 0.9333$
COMBO	67 ± 1	66 ± 2	67 ± 2	
Heart rate at rest, bpm				
HIR	56 ± 2	56 ± 2	54 ± 1	$F = 0.472$
MIR	55 ± 3	53 ± 2	54 ± 2	$P = 0.6273$
COMBO	52 ± 3	50 ± 1	49 ± 1	
FBF at baseline, ml/min per 100 mL tissue				
HIR	12.7 ± 1.2	13.2 ± 1.2	13.6 ± 1.9	$F = 2.435$
MIR	15.2 ± 1.9	14.4 ± 0.4	15.8 ± 2.4	$P = 0.0517$
COMBO	9.1 ± 1.5*	18.2 ± 2.6	19.8 ± 2.9	

Data are mean ± SEM

HIR high-intensity resistance training group, *MIR* moderate-intensity resistance training group, *COMBO* combined high-intensity resistance training and moderate-intensity aerobic exercise training group. *BP* blood pressure, *FBF* forearm blood flow

* $P < 0.05$ vs. MIR

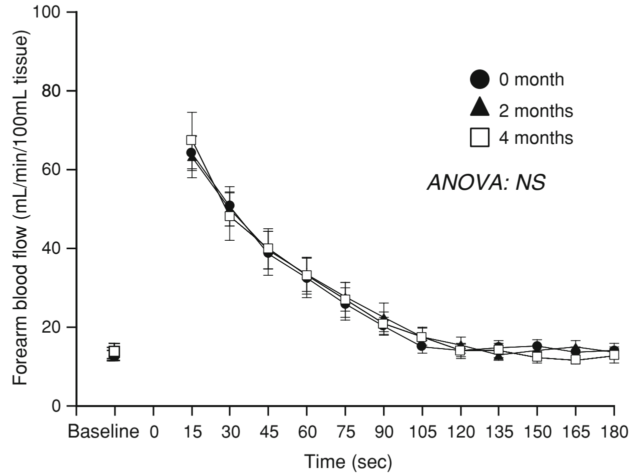

Fig. 1 Forearm blood flow during reactive hyperemia at before (*filled circle* 0 month), middle (*filled triangle* 2 months) and after (*open square* 4 months) resistance training at high intensity. Data presented as the mean ± SEM

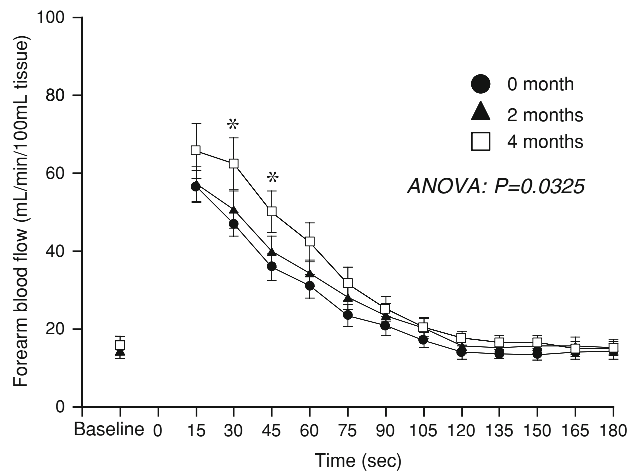

Fig. 2 Forearm blood flow during reactive hyperemia at before (*filled circle* 0 month), middle (*filled triangle* 2 months) and after (*open square* 4 months) resistance training at moderate intensity. Data presented as the mean ± SEM. *$P < 0.05$; 0 versus 4 months

blood flow in all groups did not change after exercise training intervention.

After 4 months of training, the forearm blood flow during RH did not change in the HIR groups (Fig. 1), but increased significantly in both the MIR and COMBO groups, from 57 ± 4 to 66 ± 7 ml/min per 100 ml tissue and from 59 ± 6 to 74 ± 8 ml/min per 100 ml tissue, respectively (Figs. 2, 3, both $P < 0.05$). In the COMBO group, baseline forearm blood flow increased at the 2-month and post-training periods compared with pre-training (Fig. 1), but not in the HIR and MIR groups. In the three groups, there was no change in blood pressure during RH after 4 months of training (Figs. 4, 5, 6).

Discussion

The primary findings of this study are twofold. First, resistance training performed at a moderate intensity increased changes in forearm blood flow response to RH, but not when performed at a high intensity. Second, the combined resistance and aerobic training augmented forearm blood flow response to RH for the 4-month intervention. These results suggest that although performing only moderate-intensity resistance training slightly improves vasoreactivity during RH in the microvasculature, regular combined resistance and endurance exercise training greatly and favorably impacts vasoreactivity to response to RH in the microvasculature.

It is necessary to perform habitual endurance exercise [7] for the enhancement and/or maintenance of aerobic capacity, leading to the prevention and reversal of cardiovascular disease [7] via improvements in arterial function [4, 19, 25], including endothelium-dependent dilation in the microvasculature [4]. Additionally, the current recommendation has demonstrated that resistance training should

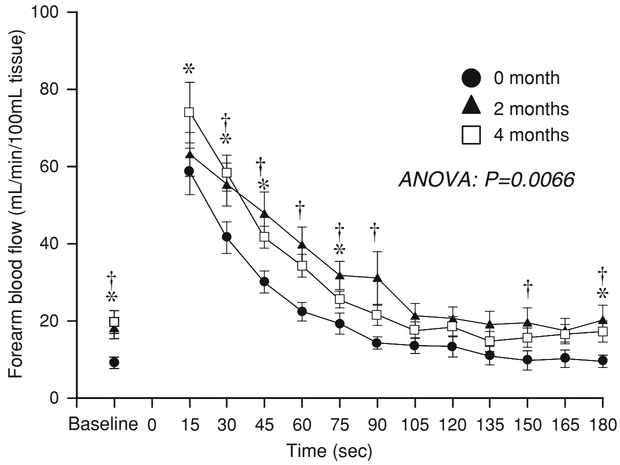

Fig. 3 Forearm blood flow during reactive hyperemia at before (*filled circle* 0 month), middle (*filled triangle* 2 months) and after (*open square* 4 months) combined resistance and aerobic training. Data presented as the mean ± SEM. †$P < 0.05$; 0 versus 2 months, *$P < 0.05$; 0 versus 4 months

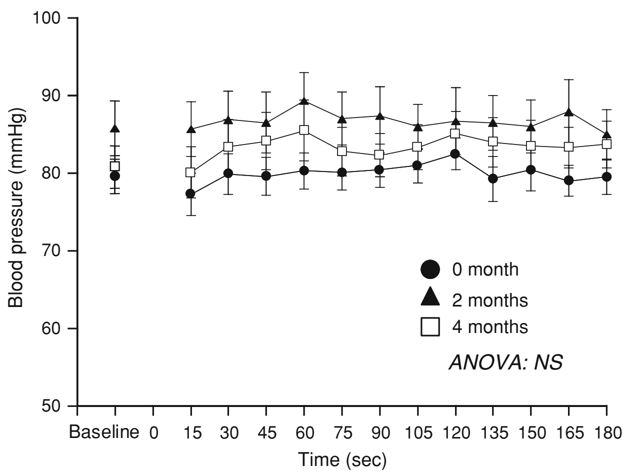

Fig. 4 Blood pressure during reactive hyperemia at before (*filled circle* 0 month), middle (*filled triangle* 2 months) and after (*open square* 4 months) resistance training at high intensity. Data presented as the mean ± SEM

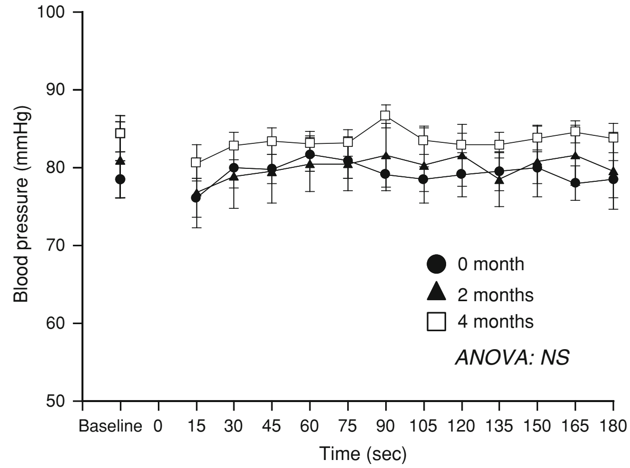

Fig. 5 Blood pressure during reactive hyperemia at before (*filled circle* 0 month), middle (*filled triangle* 2 months) and after (*open square* 4 months) resistance training at moderate intensity. Data presented as the mean ± SEM

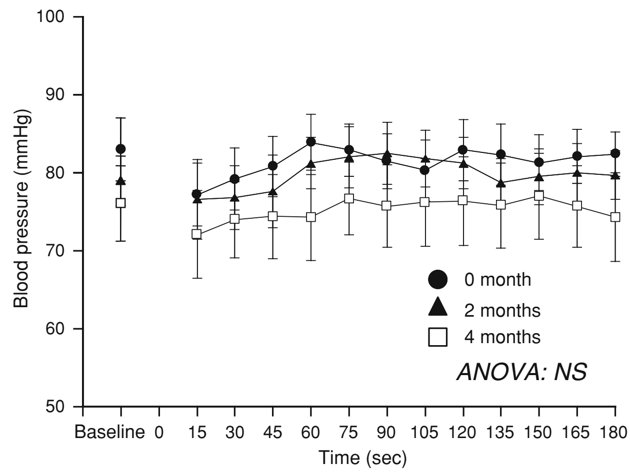

Fig. 6 Blood pressure during reactive hyperemia at before (*filled circle* 0 month), middle (*filled triangle* 2 months) and after (*open square* 4 months) combined resistance and aerobic training. Data presented as the mean ± SEM

be incorporated into exercise regimens for the prevention of sarcopenia or osteoporosis and the maintenance of functional capacity [7, 8]. Therefore, in the future, combined resistance and aerobic exercise may be endorsed as a treatment in clinical practice as well as prescribed exercise. It is, however, incompletely understood whether cardiovascular function is affected by resistance training, let alone by a combination of resistance and aerobic training. We have determined the effects of different intensities of resistance training as well as a combination of aerobic and resistance training on forearm blood flow during RH, resulting in enhanced endothelial function in the microvasculature with both moderate-intensity resistance training and combined aerobic and resistance training. Our findings may contribute to understanding the adaptation of microvascular function with exercise training, including resistance exercise, leading to the development of prescribed exercise.

In our results, moderate-intensity resistance training increased forearm blood flow response to RH, but high-intensity resistance training did not. Although the exercise volumes of the HIR and MIR groups in the present study were similar, the total time that tonic force was applied to the muscular function in the MIR group was longer compared with the HIR group in the present intervention study. Our results suggest that resistance exercise for a longer time and at a lower intensity in the MIR group might induce the enhancement of endothelial function in the microvasculature of the forearm assessed by RH. Previous studies have demonstrated that low-intensity resistance exercise with slow movement and the generation of tonic force on muscular function induces hypertrophy through the hypoxic intramuscular environment [26], and this may lead to the activation of angiogenesis. One possibility is therefore that intramuscular hypoxia induced by moderate-intensity resistance training in the present study increased the forearm blood flow during RH via angiogenesis. On the other hand, we previously demonstrated that performing resistance training not only at high-intensity but also at moderate-intensity decreased central arterial compliance [9, 10], suggesting an increase in the risk of cardiovascular disease. Previous and present findings indicate that resistance training has an unfavorable effect on the elastic properties of the central artery, but the reverse effect on the endothelial function in the peripheral microvasculature. We propose that, given these unfavorable and favorable effects on central and peripheral cardiovascular function, resistance training should be carefully prescribed, taking into account the clinical characteristics of the clients or patients.

In the present study, forearm blood flow during RH was increased by a combination of high-intensity resistance and moderate-intensity aerobic training, but not by high-intensity resistance training alone. These results suggest that aerobic training performed concurrently with resistance training may enhance the endothelial function in the microvasculature, even if high-intensity resistance training does not favorably affect the function. We have recently demonstrated that high- and moderate-intensity resistance training is associated with a reduction in arterial compliance, an independent risk factor for cardiovascular disease [9, 10], but a combination of resistance and aerobic training is not [10]. These results suggest the importance of performing aerobic training concurrently with resistance training. Results in the present study also support the hypothesis that a combination of resistance and aerobic exercise training maintains and enhances the vascular functions, including endothelium-dependent vasodilation in the microvasculature.

Chronic and repeated increases in blood flow exert their effects on endothelial vasodilatation by modulating the expression of nitric oxide synthase [27], and regular aerobic exercise thereby improves endothelium-dependent vasorelaxation in the microvasculature and peripheral conduit arteries through an increase in the release of nitric oxide in both normotensive and hypertensive men [4, 28]. Recently, we and others have demonstrated that resistance training is not associated with the endothelial function in the carotid and brachial arteries [12, 13]. It is speculated that the enhancement of endothelial vasodilatation during RH with a combination of resistance and aerobic training was engendered by the effects of aerobic factors in the combined training, such as increased blood flow, shear stress or nitric oxide bioavailability. Indeed, considering that forearm vasoreactivity to RH was not changed by high-intensity resistance training, our speculation may be reasonable. Nonetheless, because moderate-intensity resistance training in the present study enhanced endothelium-dependent vasodilation during RH, future studies are needed to confirm the effects of a combination of moderate-intensity resistance and aerobic training, and to determine the effective intensity of resistance training needed for the enhancement of endothelial function in the microvasculature.

There was a more pronounced trend toward an increase in forearm blood flow during RH after 2 months than after 4 months in the COMBO group, but the difference was not significant. We speculate that adaptation of forearm blood flow during RH response to combined training had already been completed during the training period (i.e., 2 months), and increased forearm blood flow during RH due to combined training was gradually beginning to return to baseline. On the other hand, in the MIR group, the increase in forearm blood flow lasted for as long as that in the COMBO groups. Although it seems that increases in forearm blood flow during RH in the MIR and COMBO groups are the same adaptations, we feel that there are different mechanisms in increased forearm blood flow during RH between the MIR and COMBO groups. We hypothesize that an increase in forearm blood flow during RH in the COMBO group may be induced by the aerobic training component in the combined training. On the other hand, subjects in the MIR group performed resistance training at moderate intensity without aerobic exercise training. Moderate intensity resistance training may induce an hypoxic intramuscular environment [26]. As previously described in this discussion, this may induce the activation of angiogenesis, resulting in increased forearm blood flow during RH with moderate intensity resistance training. Generally, improvements in endothelial function may be induced by a number of stimuli (i.e., aerobic training) rather than by angiogenesis. At 2 months in the present study, forearm blood flow during RH in the COMBO group increased, but was unchanged in the MIR group. These results suggest that there may be differences in mechanisms between the MIR and COMBO groups.

We continuously measured radial blood pressure using a tonometric sensor before and during RH. Radial blood pressure during RH was not affected by exercise training in the three groups. Therefore, this result supports the hypothesis that increased forearm blood flow in the MIR and COMBO groups may be induced by enhanced endothelial-dependent vasodilation.

Previous studies have demonstrated that a combination of resistance and aerobic training (including circuit training) improved endothelial dysfunction in patients with cardiovascular disease or type 2 diabetes [14, 18]. Although there are differences in subjects, and the intensity and duration of the combined training, the results of the present study—enhanced endothelial function with a combination of resistance and aerobic training—are consistent with previous studies. Overall, it is considered that aerobic training performed concurrently with resistance training may improve endothelial function, not only in patients with cardiovascular disease or type 2 diabetes mellitus, but in healthy young adults as well.

Using one-way ANOVA, baseline forearm blood flow in the COMBO group significantly increased at the middle- and end-point training period compared with pre-training (Fig. 3). Although previous studies, focused on blood flow response to RH, have not paid attention to baseline blood flow [5, 22, 29–34], we should emphasize that the increased RH in the COMBO group may be partly associated with an increase in baseline blood flow. The increase in baseline blood flow and RH may be induced by angiogenesis, muscular hypertrophy and improvements of endothelial and autonomic functions [5, 35, 36], but further study is warranted to clarify the mechanisms.

We have not examined the change in maximal oxygen consumption over the 4-month study period. Considering the effect of aerobic training on aerobic capacity, changes in maximal oxygen uptake induced by exercise training should have been determined, and the result would have provided supportive evidence that subjects performed exercise training properly during time of the intervention study. As an alternative to this approach, we monitored all training sessions performed by subjects.

Conclusion

The findings of this study demonstrate that a combination of resistance and aerobic training increases the blood flow response to RH and resting blood flow in the forearm, whereas resistance training alone does not. However, performing resistance training at moderate intensity may also induce increase of blood flow during RH. These results suggest that aerobic training performed concurrently with resistance training enhances the vasoreactivity response to RH via partly improvint the endothelial function in the forearm. In addition, future studies should determine the synergic effects of combining moderate intensity resistance with aerobic training on endothelial function in the microvasculature.

Acknowledgments We wish to thank Dr. Sho Onodera, Dr. Osamu Yuzuki, Dr. Izumi Tabata, Dr. Kenta Yamoto, Dr. Motoyuki Iemitsu and Dr. Michiya Tanimoto for supporting our study. This work was supported by grant-in-aid for Scientific Research 13780041 (to M. Miyachi) from the Japan Society for the Promotion of Science.

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