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Original Article

Effect of aerobic exercise training frequency on arterial stiffness in middle-aged and elderly females

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Abstract. [Purpose] This study aimed to determine the effects of aerobic exercise training frequency on arterial stiffness in postmenopausal females. [Participants and Methods] This study included 45 postmenopausal females randomly assigned to one of the following three groups: 1) low-frequency training group (aerobic exercise training twice per week); 2) high-frequency training group (aerobic exercise training four times per week); and 3) control group (no training). Each group was subjected to an 8-week intervention period. Both traditional and newer indexes were measured immediately before and after the 8-week intervention period. [Results] In the low-frequency training group, carotid-femoral pulse wave velocity and arterial velocity pulse index decreased post 8 weeks compared with those at baseline. In the high-frequency training group, carotid-femoral, brachial-ankle, and heart-brachial pulse wave velocities and arterial velocity pulse and arterial pressure-volume indexes decreased post 8 weeks compared to those at baseline. In the control group, no change in any indices post 8 weeks compared to those at baseline was observed. [Conclusion] Carotid-femoral pulse wave velocity was lower after aerobic training than before training in both the exercise groups. Thus, aerobic exercise training might have a beneficial effect on aortic stiffness, regardless of the training frequency in this population.

Key words: Aerobic exercise training, Exercise frequency, New index of arterial stiffness

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INTRODUCTION

In 2020 alone, the number of deaths from cardiovascular diseases in Japan was approximately 340,000, accounting for approximately 25% of all deaths[1, 2)]. Mitchell et al.[3)] demonstrate increased rates of cardiovascular disease are linked to increased arterial stiffness. Since Japan is a super-aged society where the degree of arterial stiffness is higher in females than in males[4)], controlling the progression of arterial stiffness in elderly females is a social need[5)]. Aerobic exercise training, such as medium-intensity regular walking and running, has been shown to reduce arterial stiffness in middle-aged and older people[6)]. For example, in people undertaking 4 weeks of aerobic exercise (three times a week; 65% peak aerobic capacity [VO_{2peak}]), aortic stiffness was lower after the intervention than before the intervention[7)]. Our previous study also showed that 8 weeks of aerobic exercise training (three times a week; 65% reserve heart rate [HR]) improved brachial-ankle pulse wave velocity (baPWV, index of systemic arterial stiffness) and heart-brachial PWV (hbPWV, index of includes proximal

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aorta and peripheral arteries) in middle-aged and older adults[8]. Therefore, aerobic exercise training has a positive effect on reducing arterial stiffness.

However, the very same study also found that arterial stiffness decreased regardless of the intensity or duration of aerobic exercise training. This finding emphasized the need to examine the effect of exercise frequency[8]. Shibata et al.[9] found that carotid-femoral PWV (cfPWV), an index of aortic stiffness, was more sensitive to exercise frequency, but femoral-ankle PWV, an index of peripheral arterial stiffness, was less sensitive to exercise frequency. Although Miura et al.[10] have already investigated the effect of training frequency on arterial stiffness longitudinally, the index of arterial stiffness measured in that study was only in terms of baPWV; this posed a limited discussion for site-specific arterial adaptation. Furthermore, the training program of Miura et al.[10] was different from that of the present study. In our previous study, we also found that aerobic exercise training (jogging, running) three days a week reduced heart-brachial PWV (an index that includes proximal aorta and peripheral arteries)[7]. Therefore, in order to establish a prescription or guideline for aerobic exercise training for atherosclerosis, it is necessary to determine the frequency of training. Although changes in cfPWV and baPWV may differ depending on the frequency of aerobic training, the effect of the frequency of aerobic training on different sites of arterial stiffness has not been fully investigated.

This study evaluated the effects of different training frequencies on arterial stiffness in elderly females who participated in 8 weeks of aerobic exercise training and to identify the frequency per week required to improve arterial stiffness. We hypothesized that arterial stiffness would be affected by the frequency of regular aerobic training and that aortic stiffness would be more sensitive than peripheral arterial stiffness.

PARTICIPANTS AND METHODS

Forty-five healthy middle-aged and elderly females were randomly assigned to either a low-frequency training group [LF group, twice a week, 30 minutes per session, 65% reserve heart rate, n=15; age, 62.5 ± 2.8 years; height, 158.9 ± 1.7 cm; weight, 56.4 ± 3.8 kg; Body Mass Index (BMI), 22.4 ± 1.6 kg/m^2], a high-frequency training group (HF group, four times a week, n=15; age, 62.9 ± 1.9 years; height, 158.8 + 2.5 cm; weight, 57.5 ± 2.2 kg; BMI, 22.8 ± 1.1 kg/m^2), or a control group (CON group, no training, n=15; age, 60.9 ± 3.9 years; height, 158.6 ± 2.7 cm; weight, 57.0 ± 3.6 kg; BMI, 22.7 ± 1.4 kg/m^2). The 45 participants met the following inclusion criteria: normotensive (Japanese standard: less than 140/90 mmHg), non-smokers, no obvious disease on electrocardiography or other diagnostic tests, and no exercise habit before the study according to the questionnaire on physical activity (Table 1).

To determine the appropriate sample size, a power analysis was performed using G* Power 3[11]. The magnitude of the effect of exercise on arterial stiffness was assumed to be 0.5. Using an analysis of variance, we determined that in order to detect a difference with 80% power and 5% two-sided alpha, each group should include 7 participants. To account for dropouts, we included 15 participants in each group. This study was conducted in compliance with the Declaration of Helsinki in terms of ethics, human rights, and protection of the participants' personal information. Ethical approval for this study was obtained from the Ethics Committee of Teikyo University of Science (Approval No. 21A014). The study was conducted in accordance with the guidelines for human experimentation published by the Institutional Review Board. Informed consent was provided by all study participants. All research participants were informed orally and in writing about the study before the start of the experiment and their consent was obtained.

Exercise training consisted of 35 min of jogging or running under supervision for 8 weeks. Participants wore an exercise HR monitor (ForeAthlete 45S, GARMIN Ltd., Schaffhausen, Switzerland) on their left hand. They were asked to jog or run at a speed that would bring their HR to 65% of their estimated maximum HR. Throughout the study, participants were instructed to maintain a normal diet and activities of daily living, except for exercise training. To control for acute effects as much as possible, exercise, caffeine, and alcohol intake were prohibited for 24 h prior to each measurement. Brachial-ankle

Table 1. Participant characteristics (n=45)

Variable	LF group (n=15)		HF group (n=15)		CON group (n=15)	
	Baseline	8-week	Baseline	8-week	Baseline	8-week
Age (years)	62.5 ± 2.8		62.9 ± 1.9		60.9 ± 3.9	
Gender	15 females		15 females		15 females	
Height (cm)	158.9 ± 1.7		158.8 ± 2.5		158.6 ± 2.7	
Weight (kg)	56.4 ± 3.8	56.0 ± 3.5	57.5 ± 2.2	58.0 ± 2.2	57.0 ± 3.6	57.3 ± 3.6
BMI (kg/m^2)	22.4 ± 1.6	22.2 ± 1.5	22.8 ± 1.1	23.0 ± 0.8	22.7 ± 1.4	22.8 ± 1.4
VO_{2peak} (mL/kg/min)	21 ± 3	25 ± 4**†	22 ± 2	30 ± 4**	22 ± 2	22 ± 2††

Values are mean ± SD.
LF group: Low frequency exercise group; HF group: High frequency exercise group; CON group: non-exercise control group; BMI: body mass index; VO_{2peak}: peak aerobic capacity.
**p<0.01 and *p<0.05 vs. pre, †p<0.01 and ††p<0.05 vs. T4 group.

pulse wave velocity (baPWV), heart-brachial PWV (hbPWV), carotid-femoral PWV (cfPWV), brachial and ankle blood pressure (BP), HR, double product (DP), and VO_{2peak} were measured at baseline and after 8 weeks of training. Pulse waves were recorded at two measurable sites (carotid-to-femoral artery, heart-to-brachial artery, and brachial artery-to-ankle artery) from the body surface using oscillometric and tonometric sensors, and calculated from the distance between the two points and the time difference between the pulsations. The baPWV (a measure of systemic arterial stiffness), hbPWV (a measure including proximal aortic and brachial arterial stiffness), brachial and ankle BP, and HR were measured using a PWV/ABI vascular testing device (Omron-Colin Co. Ltd., Kyoto, Japan)[12, 13]. The cfPWV (a measure of aortic stiffness) was measured using a sphygmocor XCEL TM-2805V vascular testing device (AtCor Medical, Sydney, Australia)[14], and arterial velocity pulse index (AVI, a measure of systemic arterial stiffness) and arterial pressure volume index (API, a peripheral arterial stiffness) were measured using a PASESA AVE-1500 vascular testing device (Shisei Datum Co. Ltd., Tokyo, Japan)[15–17]. AVI measurement, the peak amplitude ratio of the amplitude of differential waveform, was evaluated according to the cuff pressure. In the API measurement, the arterial volume was evaluated according to the short-axis direction of the blood vessel. The principles and formulas for AVI and API were previously reported by Komine et al.[15] and Sasaki-Nakashima et al.[16] To assess peak aerobic capacity (VO_{2peak}), a measure of aerobic capacity, the participants performed an incremental exercise test using a bicycle ergometer (Medergo EM-400, OG Wellness Technologies Co. Ltd., Okayama, Japan). VO_{2peak} was assessed via an incremental test to exhaustion (1 min warm-up at 15 Watt, cycling at 15 Watt, followed by a 15 Watt/min increase)[8]. VO_{2peak} was monitored breath-by-breath using a VO2Master MW-1100 device (VO2 Master Health Sensors Inc., Vernon, BC, Canada).

The IBM SPSS Statistics for Windows/Macintosh, Version 25.0 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. Data were presented as means + standard deviations. Parametric analysis was performed using a two-way analysis of variance with repeated measures (time ×group) for the measures taken. The bonferroni method was used with post hoc tests for identifying changes in each intervention. Statistical significance was set at $p<0.05$, and all p values were two-sided.

RESULTS

Participants weight and BMI did not differ after 8 weeks compared to baseline or between groups ($p>0.05$, Table 1). VO_{2peak} was higher after 8 weeks compared to that at baseline in the LF and HF groups ($p<0.01$), but did not change in the CON group ($p>0.05$, Table 1). VO_{2peak} after 8 weeks was lower in the LF and CON groups than in the HF group ($p<0.05$, Table 1). cfPWV decreased after 8 weeks compared with that at baseline in the LF and HF groups ($p<0.01$), but did not change in the CON group ($p>0.05$, Table 2). After 8 weeks, cfPWV decreased in the LF and HF groups compared with the CON group ($p<0.05$, Table 2). baPWV, hbPWV, AVI, and API in the HF group decreased after 8 weeks compared with those at baseline ($p<0.01$), but did not change in the LF and CON groups, and there was no difference between the groups ($p>0.05$, Table 2). HF group brachial SBP, MBP, ankle SBP, and MBP decreased after 8 weeks compared to those at baseline ($p<0.05$), but there was no change in the LF and CON groups and no difference between the groups ($p>0.05$, Table 3). Upper arm diastolic BP (DBP), pulse pressure (PP), and ankle PP did not change after 8 weeks compared to baseline in all groups, and there was no difference between groups ($p>0.05$, Table 3). DP in the LF and HF groups decreased after 8 weeks compared to baseline ($p<0.05$), but there was no change in the CON group and no difference between groups ($p>0.05$, Table 3).

DISCUSSION

This study examined the effects of the frequency of regular aerobic exercise on arterial stiffness. An important new finding of the study was that cfPWV in the LF and HF groups was significantly lower after the intervention than before the 8 week intervention. In addition, API, AVI, baPWV and hbPWV in the HF group were significantly lower after the intervention than

Table 2. Changes in arterial stiffness between the baseline and post (8-week) values in all group

Variable	LF group (n=15)		HF group (n=15)		CON group (n=15)	
	Baseline	8-week	Baseline	8-week	Baseline	8-week
cfPWV (cm/sec)	919 ± 22	766 ± 47**†	926 ± 28	768 ± 30**†	912 ± 26	906 ± 35
baPWV (cm/sec)	1,514 ± 157	1,490 ± 165	1,515 ± 84	1,396 ± 91**	1,511 ± 150	1,530 ± 181
hbPWV (cm/sec)	545 ± 34	531 ± 31	566 ± 31	518 ± 67**	581 ± 44	582 ± 53
AVI (unit)	26 ± 4	19 ± 3	25 ± 9	17 ± 3*	25 ± 4	25 ± 4
API (unit)	33 ± 4	27 ± 3	32 ± 4	24 ± 2*	32 ± 6	30 ± 4

Values are mean ± SD.
LF group: Low frequency exercise group; HF group: High frequency exercise group; CON group: non-exercise control group; cfPWV: carotidfemoral pulse wave velocity; baPWV: brachialankle pulse wave velocity; hbPWV: heartbrachial pulse wave velocity; AVI: arterial velocity pulse index; API: arterial pressure volume index.
**p<0.01 and *p<0.05 vs. pre. †p<0.05 vs. CON group.

Table 3. Changes in blood pressure, heart rate, and double product between the baseline and post (8-week) values in all group

Variable	LF group (n=15)		HF group (n=15)		CON group (n=15)	
	Baseline	8-week	Baseline	8-week	Baseline	8-week
Brachial SBP (mmHg)	126 ± 5	122 ± 5	128 ± 7	120 ± 5**	127 ± 5	128 ± 4
Brachial DBP (mmHg)	73 ± 3	71 ± 3	71 ± 2	68 ± 2	75 ± 4	73 ± 5
Brachial MBP (mmHg)	90 ± 4	88 ± 3	90 ± 2	85 ± 5*	93 ± 6	91 ± 5
Brachial PP (mmHg)	53 ± 3	51 ± 2	57 ± 8	51 ± 6	51 ± 5	54 ± 4
Ankle SBP (mmHg)	149 ± 7	149 ± 8	151 ± 9	142 ± 8**	152 ± 10	150 ± 11
Ankle DBP (mmHg)	73 ± 3	71 ± 3	72 ± 5	69 ± 5*	75 ± 4	74 ± 4
Ankle MBP (mmHg)	98 ± 4	97 ± 5	99 ± 3	93 ± 2**	101 ± 6	99 ± 6
Ankle PP (mmHg)	75 ± 5	77 ± 5	78 ± 10	73 ± 9	77 ± 6	76 ± 7
Heart rate (beats/min)	66 ± 3	62 ± 3	64 ± 3	60 ± 2	65 ± 4	66 ± 5
DP ($\times 10^3$)	8,345 ± 548	7,674 ± 622*	8,288 ± 643	7,245 ± 466**	8,392 ± 493	8,496 ± 469

Values are mean ± SD.
LF group: Low frequency exercise group; HF group: High frequency exercise group; CON group: non-exercise control group; SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure; PP: pulse pressure; DP: double product.
**p<0.01 and *p<0.05 vs. pre.

before the 8 week intervention, but these did not change in the LF group. This clearly shows that aerobic exercise training has a beneficial effect on arterial stiffness and that more frequent exercise sessions may be effective in improving systemic arterial stiffness and BP.

Many previous studies have shown that aerobic exercise training can reduce arterial stiffness[18)]. For example, aortic stiffness improved after 12 weeks of cycling exercise 4–6 times a week in postmenopausal females[19)]. Similarly, in the present study, cfPWV was lower after aerobic training than before training in both the exercise groups. Thus, aerobic exercise training may have a beneficial effect on aortic stiffness regardless of the training frequency in this population. Previous studies have clearly shown that more frequent exercise improves cardiovascular disease morbidity and mortality[20)]. The older adults who performed 90 min of circuit training once a week showed no significant change in arterial stiffness, whereas older adults who performed exercise twice a week showed a significant decrease in systemic arterial stiffness[21)]. The ACSM guidelines for general exercise recommend that cardiorespiratory (i.e., aerobic) exercise should be performed three to five times a week)[20)]. Therefore, this study shows that short-term (8 weeks) aerobic exercise training is effective in reducing increases in arterial stiffness seen in healthy postmenopausal older females, but exercise frequency may influence the reduction in systemic arterial stiffness.

Hayashi et al.[21)] found that 30 min of aerobic exercise training per day (three times a week) reduced cfPWV but did not change faPWV in middle-aged males. In a cross-sectional study, Shibata et al.[9)] found that cfPWV was more sensitive to exercise frequency but faPWV was less sensitive to exercise frequency. In previous studies, 23% of the total variance in baPWV is explained by peripheral arterial stiffness as assessed by leg PWV[22)]. Moreover, Sugawara et al.[22)] suggest the following. much smaller changes in baPWV than in aortic PWV with exercise training may well be explained by the fact that baPWV contains some components that reflect peripheral arterial stiffness, which does not appear to change with exercise training[23, 24)]. Thus, although baPWV appears to primarily reflect the stiffness of central arteries, it may be influenced by the stiffness of peripheral arteries as well. Alternatively, these results may also indicate that baPWV may not be as sensitive as aortic PWV in detecting changes in short-term interventions. In the present study, cfPWV was decreased in the T2 group, and cfPWV, hbPWV, and baPWV were decreased in the T4 group. Therefore, peripheral arterial stiffness may be involved in the decrease in baPWV. As such, the interpretation of baPWV should be made carefully. The decrease in peripheral arterial stiffness caused by aerobic exercise training may be related to changes in blood flow. Blood changes associated with exercise produce shear stress in the arteries and promote vasodilation by producing nitric oxide and a downregulation in sympathetic nerve activity, which reduces smooth muscle tone[25)]. Increase in peripheral arterial vascular diameter and a decrease in peripheral vascular resistance are important in reducing peripheral arterial stiffness[26)], thereby indicating the need for frequent training. Thus, to reduce peripheral arterial stiffness in postmenopausal females, remodeling of the vascular structure through high frequent aerobic exercise training may be necessary. Changes in arterial stiffness are associated with BP[27)]. Previous studies have also reported reductions in arterial stiffness and SBP after aerobic exercise training[28)]. In the present study, API are indicators of peripheral arterial stiffness, were lower in the T4 group but remained unchanged in the T2 group. Thus, the decrease in arterial stiffness induced by aerobic exercise training can be explained by the decrease in BP. Changes in arterial stiffness and BP are related to the function of the vascular endothelium. Aerobic exercise training reduces arterial stiffness through the production of nitric oxide, a vasodilator, by vascular endothelial cells[6)]. Endurance training improves blood flow-mediated dilation of the brachial artery, a marker of vascular endothelial function, and increases the bioavailability of nitric oxide[6]. These data suggest that chronic aerobic exercise training not only prevents the adverse effects of arterial stiffness associated with transient vascular dysfunction and postmenopausal aging, but may also explain the differences in arterial stiffness effect sites with the frequency of aerobic exercise training. Therefore, in this study, the difference in the degree of stiffness of the aorta and peripheral arteries in the T4 and T2 groups may be influenced by the production of nitric oxide due to the shear stress associated with increased blood flow after each exercise training.

There are limitations to this study: first, the participants were healthy middle-aged and older females, and our results cannot be generalized to younger people or males; second, we did not design this study to investigate the possible mechanisms by which aerobic exercise training may reduce arterial stiffness. Third, we did not conduct this study to examine the mechanism of the effects of aerobic exercise training on arterial stiffness (autonomic nervous system, vascular endothelial function, oxidative stress, etc.). Fourth, differences in total physical activity between the training groups may have led to the current observations.

In conclusion, in the present study, cfPWV was lower after aerobic training than before training in both the exercise groups. Thus, aerobic exercise training may have a beneficial effect on aortic stiffness regardless of the training frequency in this population.

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Conflict of interest

None.

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