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Review article

Anti-aging effects for arteriosclerosis by exercise and nutrition.

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Abstract

Cardiovascular disease is one of the leading causes of annual deaths in Japan and overseas. Arterial stiffness, which is associated with the risk of cardiovascular disease, increases with age. Chronic aerobic exercise training (jogging or cycling, *etc*.) in old age is known to improve the aging-induced decrease in vascular endothelial function and furthermore, reduce arterial stiffness through vasodilatory effect. Also, in addition to aerobic exercise, increasing physical activity or decreasing physical inactivity in daily living has an effect of reducing arterial stiffness. Furthermore, the possibility of reducing arterial stiffness by stretching exercises has also been reported. In recent years, combination therapies that further reduce arterial stiffness effectively, not only by exercise but also through the combined effect of exercise and nutrition intake, have been studied. It will become clear in the future based on scientific evidence that exercise and nutrient intake are effective in reducing arterial stiffness of the elderly.

***KEY WORDS*:** arterial stiffness, aging, exercise, nutrition

1. Background

Currently, with the progression of an aging society, heart disease (the second leading cause of death) and cerebrovascular disease (fourth leading cause of death) are the causes for about 25% of annual deaths in Japan, and heart disease is first of the leading causes of death worldwide. As said by William Osler, "man is as old as his arteries" arterial stiffness, which is associated with the risk of cardiovascular disease, increases with advancing of age. Furthermore, lifestyle-related diseases have increased the risk factors of arteriosclerosis. Therefore, a prevention and improvement in arterial stiffness in the elderly is an important issue. From the results of previous studies, it has become clear that regular aerobic exercise in the elderly improves the aging-induced reduction of vascular endothelial function, and reduces arteriosclerosis through vasodilation by suppressing the proliferation and tonus of smooth muscle cells. In recent years, the effect on arterial stiffness has also been studied by not only training intervention using aerobic exercises in the elderly but also increasing low-intensity stretching exercises and physical activity, and reducing physical inactivity. Moreover, studies are being conducted regarding improvement of arterial stiffness by nutrient intake and the combined effect of nutrient intake and exercise. Therefore, this section outlines the anti-aging effect that reduces arterial stiffness in the elderly by exercise and nutrient intake by including the latest findings.

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2. Changes in Arteriosclerosis Risk with Aging

The main reasons for the increase in arterial stiffness associated with aging are stiffening of elastic arterial blood vessels such as those of the aorta and reduction in the vascular endothelial function. Arterial blood vessels have the role of buffering a sudden increase in blood pressure by temporarily storing the ejected blood from the heart and maintaining the internal pressure by the elasticity of the dilated arterial blood vessels after ejection. This action is called the Windkessel effect, which contributes to the reduction of afterload on the left ventricle and protection of the peripheral blood vessels. The decline in the Windkessel function increases the pulse pressure due to the increase in systolic blood pressure and decrease in diastolic blood pressure. The Windkessel function of the central artery is influenced by the vascular smooth muscle tonus, along with elastin, collagen, and calcium, which are the structural components of the arterial wall. Changes in the arterial vascular structure such as decreased elastin and increased collagen along with decreased vasodilation through decreased vascular endothelial function are observed with aging, and functional and phenotypic changes such as vascular wall hardening and vascular wall thickening are factors causing arteriosclerosis. Therefore, maintenance and improvement of arterial endothelial function and arterial distensibility lead to a reduction in the risk of developing arteriosclerosis associated with aging.

Carotid-femoral pulse wave velocity (cfPWV), brachial-ankle pulse wave velocity (baPWV) and carotid β-stiffness that evaluate the stiffness of the arteries are used as indices for arterial stiffness. Carotid arterial compliance is an evaluation method used to evaluate the arterial distensibility. Arterial stiffness is an independent risk factor for cardiovascular diseases and furthermore, increased arterial stiffness, and decreased arterial compliance affect increase in incidence of cardiovascular events. It is reported that these indices change with aging, cfPWV and carotid β-stiffness increase with aging, and arterial compliance decreases with aging (*Fig. 1*) [1-3].

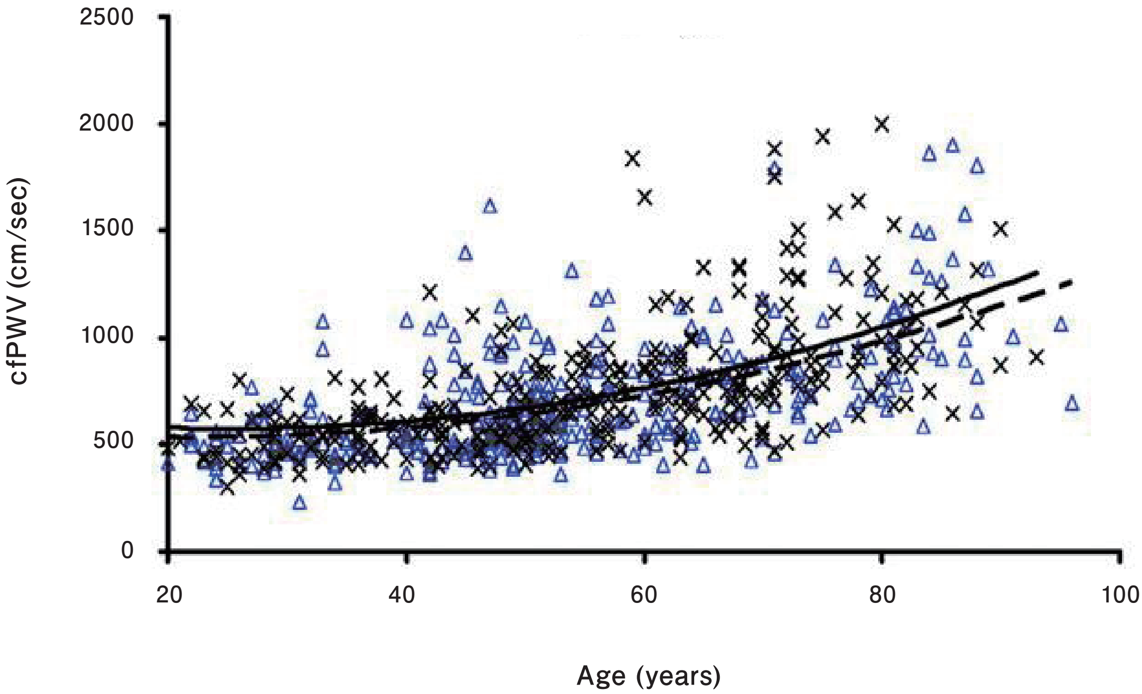

Fig. 1. **Aging and arterial stiffness.**

cfPWV, carotid-femoral pulse wave velocity. The figure is quoted from Reference 1).

3. Effects of Aerobic Exercise Training

It has been elucidated that aerobic exercise training of moderate intensity such as jogging, walking, and cycling over a long duration reduces arteriosclerosis [4]. It has been reported that there was mitigation of age-related changes such as increased carotid β-stiffness and decreased arterial compliance due to aging in the elderly who underwent aerobic training for five days or more a week [3]. Further, when elderly persons without exercise habits were made to undergo twelve weeks of aerobic exercise training for four to six days a week and 40 to 45 minutes per day, with an exercise intensity of 70 to 75% maximum heart rate, carotid β-stiffness decreased and arterial compliance increased [3]. Also, the authors had reported that when middle-aged and older adults without exercise habits were made to undergo eight weeks of aerobic exercise training for three days a week and 45 minutes per day, with exercise intensity of 60 to 70% peak oxygen uptake, carotid β-stiffness, cfPWV and baPWV decreased [5-7]. Furthermore, as a result of examining the effects of exercise on arterial stiffness over time, it was elucidated that arterial stiffness gradually decreased after starting the exercise training, and also that a statistically significant decrease was observed from the sixth week onward (*Fig. 2*) [8]. Thus, from the results of previous studies, it is considered that the increase in arterial stiffness associated with aging can be prevented and improved with aerobic exercise training of 30 minutes per day for three or more days a week over eight weeks.

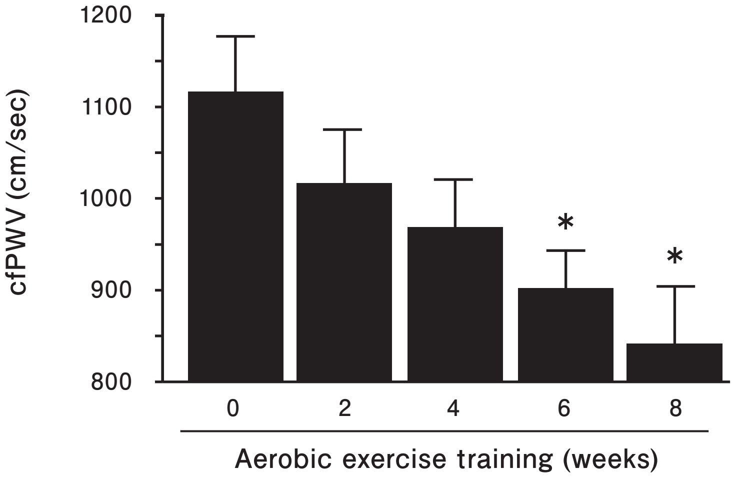

Fig. 2. **Time course of change in cfPWV during eight-week exercise intervention.**

Results are expressed as means ± SE, n = 16, *p < 0.01 vs. zero week. cfPWV, carotid-femoral pulse wave velocity; SE, standard error. The figure is quoted from Reference 8).

4. Stretching Exercises and Arteriosclerosis

Flexibility, which is one of the factors of physical fitness, decreases with aging. To examine the relationship between flexibility and arterial stiffness, after dividing the subjects as having poor-flexibility or having high flexibility, the authors reported that baPWV and cfPWV in the elderly having poor-flexibility had increased compared to the elderly having high-flexibility [9]. This result suggests that arterial stiffness may increase in the elderly with reduced flexibility. On the other hand, it was reported that carotid arterial compliance significantly increased in middle-age and older men and women as a result of a 13-week whole-body stretching exercise, three days a week and 30-45 minutes per session [10]. Furthermore, it has been reported that baPWV was also significantly reduced due to stretching exercise intervention by four weeks of stretching exercise for middle-aged men (whole-body stretching exercise for five days a week and 30 minutes per session) and six months stretching exercise for middle-aged women (whole-body stretching exercise for seven days a week and 15 minutes per session) (*Fig. 3*) [11, 12]. Since these results show that not only aerobic exercise training but also stretching exercises that increase flexibility have the effect of attenuating the increase in age-associated arterial stiffness, it may be useful to incorporate stretching exercises as an exercise therapy when introducing exercise for persons with low physical fitness such as the elderly.

The authors conducted a single session of whole-body stretching exercise (40 minutes) in young adults which significantly decreased baPWV and femoral-ankle pulse wave velocity (faPWV) at 15 and 30 minutes after exercise compared to before exercise [13]. Also, with a stretching exercise of the triceps surae muscles of one leg (six sets of a 30-second stretching exercise with ten seconds of rest after each set), only the faPWV of the leg subjected to the stretching exercise reduced immediately and at 15 minutes after exercise compared to before the exercise (*Fig. 4*) [14]. This finding suggests that the effect of reducing arterial stiffness due to a stretching exercise may only occur at the site where the stretching exercise is performed, and caution may be required when introducing stretching exercises to reduce arterial stiffness.

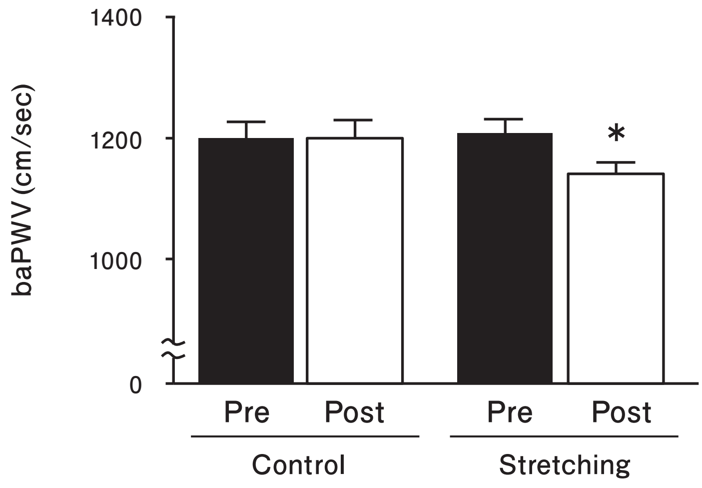

Fig. 3. **Effect of regular stretching on baPWV.**

Results are expressed as means ± SE, n = 16, *p < 0.05 vs. Pre in Stretching. Control, sedentary-control group, n = 8; Stretching, regular stretching group, n = 8. baPWV, brachial-ankle pulse wave velocity; SE, standard error. The figure is quoted from Reference 11).

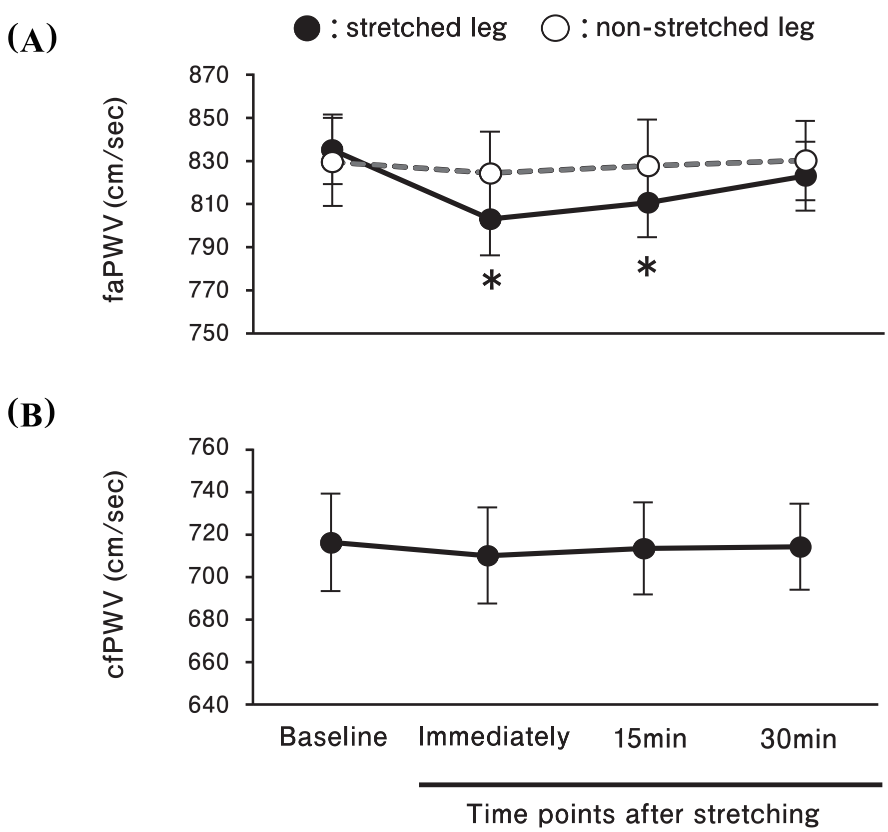

Fig. 4. **Arterial stiffness (faPWV, baPWV) before and after passive one-legged static stretching.**

A, faPWV; **B**, baPWV. Results are expressed as means ± SE, *p < 0.01 vs. Baseline. Control, sedentary-control group, n = 25; Stretching, regular stretching group, n = 25; faPWV, femoral-ankle pulse wave velocity; cfPWV, carotid-femoral pulse wave velocity; SE, standard error. The figure is quoted from Reference 14).

5. Resistance Training and

Resistance training is an effective exercise for mitigating the loss of muscle mass and strength due to aging and is also necessary from the perspective of care prevention. Miyachi *et al.*[15] reports that although arterial compliance decreases with age, the decline associated with age is further accelerated in the elderly who have been performing high-intensity resistance training for more than two years (***Fig. 5***). However, it has been reported that there was no effect on arterial stiffness in older men who underwent 12-week moderate-intensity resistance training (three sets a day, twice a week)[16]. Thus, though the effect of resistance training on arterial stiffness varies depending on the exercise intensity, it is considered that high-intensity resistance training does not have a favorable impact. However, it has been reported that combined training with aerobic exercise training after high-intensity resistance training, the effects of the resistance training can be eliminated[17] and an increase in arterial stiffness can be prevented even if low intensity resistance training is implemented after high-intensity resistance training[18]. However, these results are based on studies conducted on young individuals, and whether the same effect can be achieved in the middle-aged and older adults is a topic for future study.

Since baPWV has also been reported to decrease when leg exercises that include low-intensity resistance exercise and recreational activities are performed two days a week with approximately 90-minute sessions for 12 weeks (***Fig. 6***)[19], it is considered necessary to take into account not only resistance training but also combinations with other exercises and intensities.

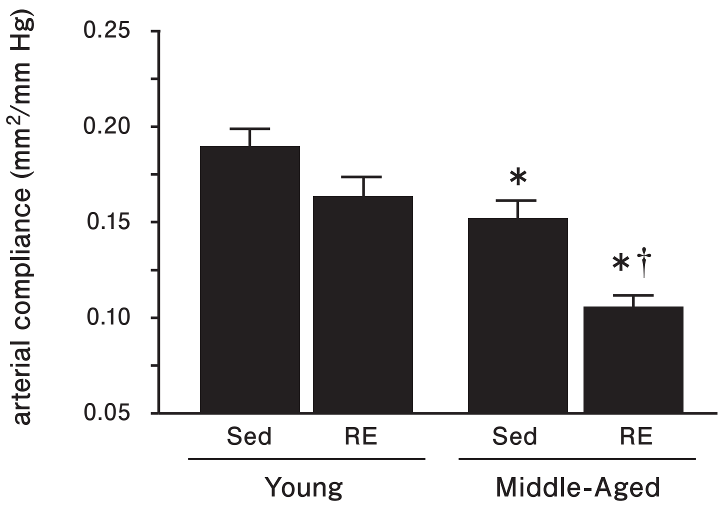

Fig. 5. **Carotid arterial compliance of sedentary and resistance-trained men.**

Results are expressed as means ± SE, *p < 0.05 vs young of same activity group, †p < 0.01 vs sedentary of same age group. Young-Sed, young sedentary-control group, n = 17; Young-RE, young resistance-trained group, n = 16, Middle-aged-Sed, middle-aged sedentary-control group, n = 15; Middle-aged-RE, middle-aged resistance-trained group n = 14; SE, standard error. The figure is quoted from Reference 15).

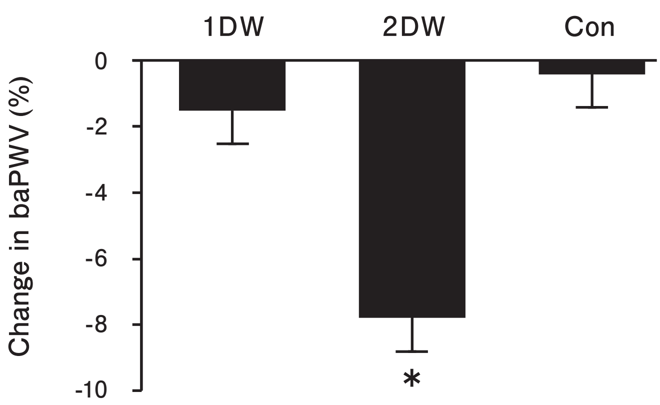

Fig. 6. **Effect of low intensity resistance-training on baPWV.**

Results are expressed as means ± SD, *p < 0.05 vs Con and 1DW groups; 1DW, low intensity resistance-trained one day per week group, n = 29; 2DW, low intensity resistance-trained two days per week group, n = 25; Con, sedentary-control group, n = 23; SD, standard deviation. The figure is quoted from Reference 19).

6. Physical Activity and Arteriosclerosis

The amount of physical activity includes both activities of daily living and exercise, and an increase in physical activity is considered to be linked to reducing the risk of lifestyle-related diseases. The authors measured the amount of physical activity in the middle-aged and older adults, and divided them into persons with high physical activity and persons with low physical activity, and reported that persons with physical activity of 186 to 216 kcal or more per day have lower baPWV than persons with physical activity of 186 to 216 kcal or less per day (***Fig. 7***)[20, 21]. It has been reported that in the elderly, a negative correlation was observed between cfPWV and a low-intensity physical activity time of 1.1-2.9 Mets or a moderate-intensity physical activity time of 3.0-5.9 Mets, and a positive correlation was observed between the physical inactivity time and cfPWV, while these relationships were not observed in young individuals[22]. From these results, it can be considered that for older adults, the increase in arteriosclerosis associated with aging can be prevented and improved by increasing low- and moderate-intensity physical activity time and decreasing physical inactivity time. Also, it has been reported that when men and women between the ages of 35 and 75 were instructed to increase their daily walking time from 1.6 hours to two hours, cfPWV significantly decreased after one year[23]. In other words, arterial stiffness can be expected to reduce not only by exercise patterns such as aerobic and stretching exercises but also by increasing activities of daily living. Even if there are no special facilities or times to exercise, an effect may also be expected with guidance such as increasing physical activity time and reducing physical inactivity time.

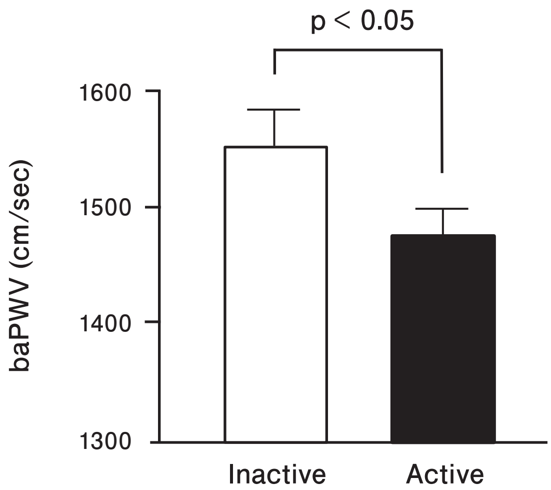

Fig. 7. **Effects of physical activity and physical inactivity on baPWV.**

Results are expressed as means ± SE. Inactive: Physical inactive group, n = 87; Active: Physical active group, n = 104; baPWV, brachial-ankle pulse wave velocity; SE, standard error. The figure is quoted from Reference 21).

7. Nutritional Intake, Exercise and Arteriosclerosis

In recent years, combination therapies that further reduce arterial stiffness effectively, not only by exercise but also through the combined effect of exercise and nutrient intake, have also been reported. Lactotripeptides is a generic name that has been separated and identified as two types of milk-derived tripeptides (valine-proline-proline, isoleucine-proline-proline), and has been confirmed to have angiotensin-converting enzyme (ACE) inhibitory activity[24], and are now being developed as a supplement. In a study conducted on postmenopausal women, it has been reported that a combination of aerobic exercise training for eight weeks (three to five days a week, 30 to 45 minutes per day, exercise intensity of 70 to 75% maximum heart rate) and intake of lactotripeptides (2.8 g casein hydrolyzed powder containing valine-proline-proline 2.4 mg and isoleucine-proline-proline 4.3 mg) increased arterial compliance more effectively than each method individually (***Fig. 8***)[25]. Thus, in addition to exercise, the possibility of effectively reducing arterial stiffness by combining exercise and nutrition has also been observed, and results of combined effects with various nutrients are expected in the future.

8. Summary

To summarize the evidence to date, for prevention and improvement of increase in arterial stiffness due to aging, therapies such as (1) Aerobic exercise training: Aerobic exercise of moderate intensity for 30 minutes per day, three days or more per week for about eight weeks, (2) Stretching exercises: Whole body stretching exercises, 30 to 45 minutes per day, three days or more per week for four weeks or more, (3) Resistance training: Advisable to implement at moderate

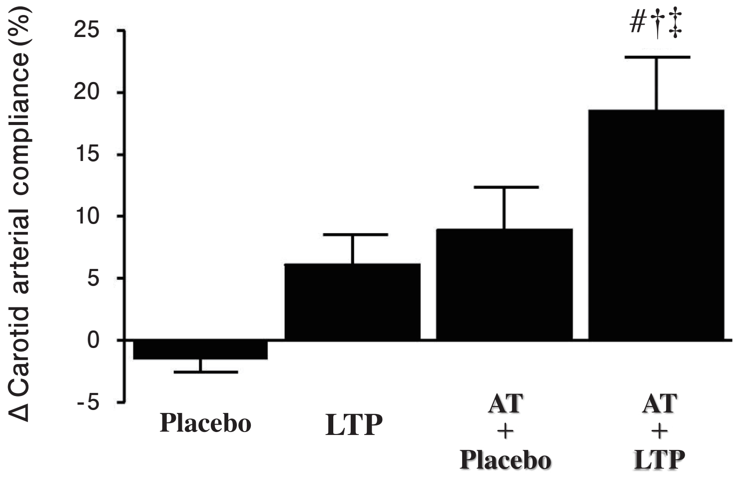

Fig. 8. **Effects of exercise and/or LTP intake interventions on arterial compliance.**

Results are expressed as means ± SE, #p < 0.01 vs. Placebo, †p < 0.05 vs. LTP, ‡p < 0.05 vs. AT + Placebo. Placebo, Placebo intake group, n = 13; LTP, lactotripeptides intake group, n = 15; AT + Placebo, Placebo intake with aerobic exercise training group, n = 15; LTP + Placebo, lactotripeptides intake with aerobic exercise training group, n = 12. The figure is quoted from Reference 25).

or low intensity or in combination with aerobic exercise, (4) Physical activity: Increasing the time of low- to moderate-intensity physical activity and decreasing the time of physical inactivity, (5) Combined use of exercise and nutrient intake (such as lactotripeptides) rather than using them individually, can be considered to be effective. Thus, in the future, it is necessary to verify the benefits of more effective and sustainable exercise and nutrient intake programs based on scientific evidence for the improvement of aging-induced increase in arterial stiffness.

Conflict of interest statement

The authors claim no conflict of interest in this study.

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