Effect of resistance training combined with aerobic exercise on aortic arterial stiffness in older adults: a secondary analysis of randomized controlled trial

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Abstract Aerobic exercise prior to resistance training is likely to have a preventive effect on arterial stiffening caused by resistance training alone. The purpose of this study was to examine, as secondary analysis, the effect of aerobic exercise before resistance training on aortic arterial stiffness in older adults. A total of 56 participants were randomized to resistance training (RT) group (n = 28) or aerobic exercise (AE) + RT group (n = 28). All participants attended a supervised exercise training program (RT or AE + RT) twice a week for 12 weeks and were given fortified milk. Arterial stiffness was evaluated by pulse wave velocity (PWV) between carotid and femoral regions (e.g., aorta) and between femoral and ankle regions (e.g., leg). There was no significant difference between the two groups at all baseline measurements. After the intervention, although there was no significant interaction, carotid-femoral PWV was significantly increased only in the RT group (1032 ± 35 vs. 1072 ± 33 cm/sec, \(P < 0.05\)). Femoral-ankle PWV was not significantly changed in either group. Our findings reveal that resistance training significantly increases aortic arterial stiffness (carotid-femoral PWV); however, aerobic exercise before resistance training attenuates the aortic arterial stiffening in older adults. These results suggest that aerobic exercise before resistance training is likely to prevent the unfavorable effects of resistance training on vascular health in older adults.

Keywords: secondary analysis, exercise training modality, pulse wave velocity

Introduction

Resistance training combined with protein intake (e.g., by fortified milk) is the primary countermeasure for increasing muscle mass and strength and to prevent sarcopenia\textsuperscript{4-9}. In marked contrast to the favorable effects of resistance training on muscle mass and strength, however, the unfavorable effects on vascular health have been revealed. Several previous studies have demonstrated that resistance training reduces central arterial compliance and increases central arterial stiffness\textsuperscript{6-9}. Stiffening of the central arteries, including the aorta, is strongly associated with the development of cardiovascular disease. Therefore, a comprehensive training strategy for the prevention of sarcopenia that increases muscle mass and strength, but doesn’t increase aortic arterial stiffness is needed to sustain a better quality of life in older adults.

Aerobic exercise is widely known to be efficacious in preventing and improving arterial stiffening\textsuperscript{10}. Hence, the increase in aortic arterial stiffening from resistance training is theoretically preventable by including aerobic exercise. Indeed, several previous studies have already reported that resistance training combined with aerobic exercise can prevent arterial stiffening caused by resistance training\textsuperscript{11,12}. However, the beneficial effects of aerobic exercise on arterial stiffening caused by resistance training is verified by the non-randomized and short-term interventional approach. Furthermore, most previous studies have examined healthy young adults who have relatively higher reactivity. To our knowledge, there are no studies that have investigated the effect of resistance training combined with aerobic exercise on aortic arterial stiffness in older adults by a randomized controlled trial.

We recently reported the favorable effects of aerobic exercise before resistance training combined with fortified milk consumption on muscle mass, muscle strength, and physical performance in older adults\textsuperscript{13}. As secondary analysis, therefore, the purpose of this study was to further examine the effect of aerobic exercise before resistance training on aortic arterial stiffness in older adults.

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Methods

Study design and participants. This study was a pre-specified sub-study (secondary analysis) of an open, randomized controlled trial between September and December 2015 (UMIN000018972)[13]. This interventional study protocol received approval from the Ethics Committee of the University of Tsukuba, Japan (Tai27-9: 07/01/2015). Participants were eligible for inclusion if they (1) were aged 65 to 79 years, (2) were not restricted from exercise by a physician, (3) did not habitually conduct moderate intensity aerobic or resistance training, (4) had not participated in another clinical trial within one year, (5) did not have hypolactasia or milk allergy, (6) did not use diabetic medications, and (7) agreed to participate in the present study. We excluded participants who (1) had severe heart disease, cerebrovascular disease, or renal dysfunction, (2) had a habit of drinking too much milk (more than 2 cups/day), (3) participated in walking or strength exercise at light intensity. Finally, a total of 56 older adults participated in this study as previously reported[13]. All the participants provided written informed consent, and this study complied with the Declaration of Helsinki.

Study procedure. After the baseline measurements, a computer-generated random number allocated the participants to either the resistance training (RT) group or the aerobic exercise (AE) + RT group in a ratio of 1:1. All measurements were performed in the morning after a 12-h overnight fast at a quiet, temperature-controlled room (range 24-26°C).

Intervention. All participants attended a supervised exercise training program (RT or AE + RT) twice a week for 12 weeks and they were given 250 mL fortified milk (SAVAS milk; Meiji Holdings Co., Ltd, Tokyo, Japan) that contained as follows: 10.5 g of protein, 3.9 g of fat, 9.3 g of carbohydrates, 87 mg of sodium, and 337 mg of calcium. We instructed the participants to ingest the fortified milk every day after each exercise training program, or as a snack between meals on non-training days.

Participants in both groups underwent resistance training comprised of four kinds of movement (chest press, leg extension, leg curl, and leg press), all of which were performed with decided training machines (Technogym Japan Ltd, Tokyo, Japan). The 1-repetition maximums (RMs) were measured in each 4-week period and the training intensity was gradually increased according to their 1-RMs (1-4 weeks: 30-50% of 1-RM, 5-8 weeks: 50-70% of 1-RM, 9-12 weeks: ≥ 70% of 1-RM) and their rated perceived exertion. Participants performed 3 sets of 10 repetitions per set for the first 4 weeks, and then performed 3 sets of 12 repetitions per set during the following 5-12 weeks. The rest periods were set as one minute between sets and two minutes between movements.

In the AE + RT group, participants performed aerobic training using a cycling ergometer (828E; Monark, Exercise AB, Sweden) before resistance training. The intensity of aerobic exercise was set as light (40-50% of \( VO_{2peak} \)) and training volume was gradually increased (weeks 1-4: 20 minutes, weeks 5-8: 25 minutes, weeks 9-12: 30 minutes).

Measurements. Body weight was measured to the nearest 0.1 kg with a digital scale. Height was measured to the nearest 0.1 cm using a wall-mounted stadiometer. Body mass index was calculated as participant weight (kg) divided by height (m²). Brachial and ankle blood pressure, heart rate, and pulse wave velocity (PWV) were simultaneously measured by a semi-automated vascular testing device equipped with an electrocardiogram, phonocardiogram, oscillometric extremity cuffs, and optional applanation tonometry sensor unit (Form PWV/ABI: Model BP-203RPEII and TU-100; Colin Medical Technology, Aichi, Japan), as previously described[10]. Carotid and femoral arterial pressure waveforms were simultaneously recorded by two applanation tonometry sensors incorporating an array of 15 micropiezoresistive transducers. To evaluate aortic and leg arterial stiffness, PWV (arterial path length/pulse transit time) was obtained between carotid and femoral regions (e.g., aorta) and between femoral and ankle regions (e.g., leg).

Statistical analysis. Data were reported as means ± SE and frequency and percentage for categorical data. In the present study, intent-to-treat analysis was performed to maintain homogeneous characteristics except intervention exposure and to generalize results of the study. Therefore, missing data were replaced by the baseline (last) observation carried forward (LOCF). Baseline characteristics were compared between groups using Student’s t-tests and chi-square tests as appropriate. The effects of the intervention on all outcome measures were evaluated using two-way repeated-measures ANOVA with a post hoc test. Statistical significance was set a-priori at \( P < 0.05 \) for all comparisons. Statistical analysis was performed using the SPSS software (version 25.0).

Results

Study flow is depicted in Fig. 1. A total of 167 persons were assessed for eligibility to participate, and 111 of them were excluded for not meeting the inclusion criteria. A full description of the screening results was published previously[13]. Although a total of 56 participants were enrolled at the baseline, two participants dropped out of the study during the intervention periods because of medical reasons.

Baseline and changes in anthropometry, heart rate, blood pressure for each group are summarized in Table 1. There was no significant difference between the two groups at all baseline measurements. After the interven-
**JPFSM**: Resistance training, aerobic exercise, and arterial stiffness

![ Consort diagram of study flow. ]

Fig. 1 Consort diagram of study flow.

**Table 1.** Baseline and changes in anthropometry, heart rate, and blood pressure in each group

<table>
<thead>
<tr>
<th>Variables</th>
<th>RT (n = 28) Before</th>
<th>RT (n = 28) After</th>
<th>AE + RT (n = 28) Before</th>
<th>AE + RT (n = 28) After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of women, n (%)</td>
<td>18 (64)</td>
<td>-</td>
<td>20 (71)</td>
<td>-</td>
</tr>
<tr>
<td>Age, yr</td>
<td>71 ± 1</td>
<td>-</td>
<td>70 ± 1</td>
<td>-</td>
</tr>
<tr>
<td>Height, cm</td>
<td>156 ± 2</td>
<td>-</td>
<td>157 ± 1</td>
<td>-</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>55.7 ± 1.9</td>
<td>56.1 ± 1.9</td>
<td>56.3 ± 1.8</td>
<td>56.7 ± 1.8</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>22.9 ± 0.6</td>
<td>23.0 ± 0.6</td>
<td>22.7 ± 0.5</td>
<td>22.8 ± 0.5</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>68 ± 2</td>
<td>68 ± 2</td>
<td>64 ± 2</td>
<td>66 ± 2</td>
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<tr>
<td>Mean arterial pressure, mmHg</td>
<td>94 ± 2</td>
<td>94 ± 2</td>
<td>92 ± 2</td>
<td>91 ± 2</td>
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<tr>
<td>Brachial SBP, mmHg</td>
<td>127 ± 2</td>
<td>128 ± 3</td>
<td>125 ± 3</td>
<td>123 ± 3</td>
</tr>
<tr>
<td>Brachial DBP, mmHg</td>
<td>77 ± 1</td>
<td>77 ± 2</td>
<td>76 ± 2</td>
<td>75 ± 2</td>
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<tr>
<td>Brachial PP, mmHg</td>
<td>49 ± 2</td>
<td>51 ± 2</td>
<td>49 ± 2</td>
<td>48 ± 1</td>
</tr>
<tr>
<td>Ankle SBP, mmHg</td>
<td>144 ± 4</td>
<td>144 ± 4</td>
<td>145 ± 4</td>
<td>143 ± 3</td>
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<td>Ankle DBP, mmHg</td>
<td>75 ± 2</td>
<td>74 ± 2</td>
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<td>74 ± 1</td>
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<td>Ankle PP, mmHg</td>
<td>69 ± 3</td>
<td>70 ± 3</td>
<td>71 ± 3</td>
<td>68 ± 2</td>
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<tr>
<td>Ankle-brachial index</td>
<td>0.89 ± 0.02</td>
<td>0.90 ± 0.02</td>
<td>0.86 ± 0.01</td>
<td>0.86 ± 0.01</td>
</tr>
</tbody>
</table>

Data are shown as the means ± SE. RT, resistance training + fortified milk group; AE + RT, aerobic and resistance training + fortified milk group; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure.
tion, weight, body mass index, heart rate, brachial and ankle blood pressure, and ankle-brachial index were not significantly changed in each group. However, it was previously reported\(^1\) that muscle strength and physical performance were significantly improved in both groups (data not shown).

Fig. 2 shows the effects of each intervention on carotid-femoral PWV and femoral-ankle PWV. Carotid-femoral PWV was not significantly different between the groups before the intervention and did not have significant interaction after the intervention. However, carotid-femoral PWV had a significant main effect and was significantly increased only in the RT group \((1032 \pm 35 \text{ vs. } 1072 \pm 33 \text{ cm/sec, } P < 0.05)\). On the other hand, femoral-ankle PWV was not significantly different between the groups before the intervention and was not significantly changed in both groups.

Discussion

The main finding of this study was as follows. Although there was no significant interaction after each intervention, resistance training significantly increased aortic arterial stiffness (carotid-femoral PWV); whereas aerobic exercise before resistance training did not significantly increase the aortic arterial stiffness. These results indicate that aerobic exercise before resistance training is likely to attenuate the aortic arterial stiffening caused by resistance training alone in older adults.

Regarding the effects of resistance training on vascular function remains highly controversial. Although many previous studies have revealed that resistance training might have unfavorable effects on vascular health\(^6,8,9,15\), it has also been reported that resistance training doesn’t have unfavorable effects on vascular health\(^16,17\). In the present study, the randomized controlled trial demonstrated that the 12 weeks of resistance training intervention significantly increased aortic arterial stiffness (carotid-femoral PWV), but not leg arterial stiffness (femoral-ankle PWV) in older adults. Although the detailed mechanisms involved in the change in arterial stiffness in each region with resistance training remain obscure, it is thought that the unfavorable effects of resistance training are likely to be more manifested in the central arteries than in the peripheral arteries\(^7\). Therefore, the results of this study support the results of previous studies showing that resistance training leads to poor vascular health, especially in the central arteries. However, further investigation is needed with different conditions in exercise intensity and frequency.

The timing of aerobic exercise (e.g., before or after resistance training) is important in considering the combined aerobic exercise and resistance training effect. From the viewpoint of the promotion of muscle mass and strength, aerobic exercise before resistance training may be more effective because it is likely to stimulate muscle protein synthesis-dependent on vasodilation\(^18,19\). The beneficial effects of aerobic exercise before resistance training on muscle mass, muscle strength, and physical performance in older adults has been previously reported\(^13\). However, previous studies regarding vascular health have demonstrated that aerobic exercise after resistance training might have more effect on arterial stiffness\(^11,12\). Furthermore, it has been suggested that aerobic exercise before resistance training might not promote arterial flexibility since the beneficial effects of aerobic exercise might be neutralized by resistance training\(^11\). Consistent with previous results, this study demonstrated that aortic arterial stiffness was not reduced by aerobic exercise before resistance training. Meanwhile, in the case of only resistance training, aortic arterial stiffness was significantly increased after the intervention. Furthermore, the relative changes in aortic arterial stiffness tended to vary between the two groups \((4.5 \pm 8.8 \text{ vs. } 1.8 \pm 7.4\%); \text{ however, this difference was not significant (}\(P = 0.231\)). Considering these results, it was concluded that aerobic exercise before resistance training did not cause a reduction in arterial stiffness, but it was likely to be effective for attenuating arterial stiffening caused by the resistance training. Therefore, aerobic exercise before resistance training...
training may be a useful strategy from both viewpoints of muscle and vascular health in older adults.

Aortic arterial stiffening has been recognized as a major determinant of aortic blood pressure and known to be associated with hypertension. The present study was showed that both brachial and ankle (i.e., peripheral) blood pressure were not significantly changed in each group after the intervention; however, aortic blood pressure might be increased with aortic arterial stiffening after the resistance training. Although all we can do is just speculate, the attenuation of aortic arterial stiffening by aerobic exercise before resistance training may have a preventive implication for hypertension.

Milk proteins have been reported to have positive effects in improving and/or maintaining vascular health. Moreover, a recent clinical study has reported that milk protein supplementation and combined moderate-intensity aerobic and resistance training reduced arterial stiffness in young obese women. In the present study, all participants ingested fortified milk every day after each exercise training program, or as a snack between meals on non-training days. Accordingly, the milk proteins included in fortified milk are likely to have influenced the change in arterial stiffness after each intervention. However, in this study, aortic arterial stiffness was significantly increased after resistance training even if combined with fortified milk consumption. This result suggests the possibility that only milk proteins included in fortified milk might be insufficient to prevent the unfavorable effects of resistance training on aortic arterial stiffness in older adults.

The current study has several critical limitations. First, this study was secondary analysis for the combined effect of aerobic exercise and resistance training, and only investigated the effect of aerobic exercise before resistance training. Investigation of the effects of aerobic exercise after resistance training on vascular and muscle health are also needed. Second, the evaluation of arterial stiffness was only performed by PWV analysis; therefore, comprehensive evaluations for arterial stiffness are needed. Third, the effect of milk proteins included in fortified milk on the results of this study cannot be excluded. Fourth, the precise mechanisms responsible for the changes in arterial stiffness induced by each intervention remains unclear. Finally, there was the possibility of several biases, including selection and arbitrary bias, because all participants who were interested in the present study and blinding could not be incorporated in the study design.

In conclusion, although there was no significant interaction after each intervention, the 12 weeks of resistance training intervention significantly increased aortic arterial stiffness, whereas aerobic exercise before resistance training did not significantly increase the aortic arterial stiffening in older adults. These results suggest that aerobic exercise before resistance training may attenuate the unfavorable effects of resistance training on vascular health in older adults.

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Conflict of Interests

All other authors declare no conflict of interests.

References


