Short-Term Aerobic Exercise Reduces Arterial Stiffness in Older Adults With Type 2 Diabetes, Hypertension, and Hypercholesterolemia

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OBJECTIVE — The relationship between increased arterial stiffness and cardiovascular mortality is well established in type 2 diabetes. We examined whether aerobic exercise could reduce arterial stiffness in older adults with type 2 diabetes complicated by comorbid hypertension and hyperlipidemia.

RESEARCH DESIGN AND METHODS — A total of 36 older adults (mean age 71.4 ± 0.7 years) with diet-controlled or oral hypoglycemic–controlled type 2 diabetes, hypertension, and hypercholesterolemia were recruited. Subjects were randomly assigned to one of two groups: an aerobic group (3 months vigorous aerobic exercise) and a nonaerobic group (no aerobic exercise). Exercise sessions were supervised by a certified exercise trainer three times per week, and a combination of cycle ergometers and treadmills was used. Arterial stiffness was measured using the Complior device.

RESULTS — When the two groups were compared, aerobic training resulted in a decrease in measures of both radial (−0.7 ± 6.3 vs. +6.5 ± 6.6%, P = 0.005) and femoral (−13.9 ± 6.7 vs. +4.4 ± 3.3%, P = 0.015) pulse-wave velocity despite the fact that aerobic fitness as assessed by VO2max did not demonstrate an improvement with training (P = 0.026).

CONCLUSIONS — Our findings indicate that a relatively short aerobic exercise intervention in older adults can reduce multifactorial arterial stiffness (type 2 diabetes, aging, hypertension, and hypercholesterolemia).

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The normal aging process is associated with an increase in vascular stiffness (1), a process that is accelerated by the presence of type 2 diabetes (2), hypercholesterolemia (3), and hypertension (4). The relationship between increased arterial stiffness and cardiovascular mortality is well established (5). Exercise has successfully reduced vascular stiffness in young populations (6), suggesting that it could be used in older adults with type 2 diabetes complicated by other cardiovascular risk factors.

Previous cross-sectional studies have shown that older adults who engage in regular aerobic exercise training have lower arterial stiffness than sedentary older adults (7). Prospective examinations of a moderate aerobic exercise program in middle-aged subjects with type 2 diabetes (6) and normal older adults (7) have demonstrated a decrease in arterial stiffness. In fact, even brief aerobic interventions in healthy middle-aged men have demonstrated a direct impact on arterial compliance without any effect on cholesterol, blood pressure, body weight, or resting heart rate (7). It has been hypothesized that mechanical distension during aerobic exercise sessions results in pulsatile “stretching” of the collagen fibers that reverses the glycation-related collagen cross-linking that is responsible for reduced arterial compliance in diabetes (8). The impact of aerobic exercise on arterial stiffness in older adults with extensive vascular damage due to multiple etiologies (type 2 diabetes, hypercholesterolemia, and hypertension) has not been examined previously.

In the current study, we examined whether aerobic exercise can reverse arterial stiffness in adults at very high cardiovascular risk (long-standing diabetes, geriatric age-group, hypercholesterolemia, and hypertension). We hypothesized that despite these multifactorial reasons for reduced arterial compliance, aerobic exercise would be an effective nonpharmacological therapy for increased arterial stiffness.

RESEARCH DESIGN AND METHODS — Forty older adults (21 men and 19 women, mean age 71.4 ± 0.7 years, age range from 65 to 83 years) were recruited from the local community through advertisement in local publications (Table 1). All subjects had to be aged >65 years and were excluded if they had any history of angina, myocardial infarction, stroke, chronic pulmonary disease, were current smokers, or had exercise-limiting orthopedic impairment. All older subjects were required to have type 2 diabetes for at least 5 years, hypertension, and hyperlipidemia. Hypertension, diabetes, and hyperlipidemia were defined by current American Diabetes Association guidelines (9). Hypertension was defined as taking antihypertensive agents or having an average blood pressure (based on the mean of three measurements) with a systolic blood pressure >130 mmHg or a diastolic blood pressure >80 mmHg (9).
Subjects were excluded if they took β-blockers, calcium channel blockers, or any other agent that influenced autonomic function. Entry requirements included a normal resting electrocardiogram, a normal Bruce protocol treadmill maximal exercise stress test, a normal hematocrit, and a normal creatinine level. Subjects had to refrain from consumption of alcohol or caffeine for the preceding 24 h. To avoid the confounding acute effects of exercise, the aerobic training program was also halted for the preceding 24 h (12).

Arterial stiffness was measured using the Complior device (Artech Medical, Pantin, France), a semiautomated device that uses two pressure transducers (12). The pressure transducers are held in place by Velcro straps that allow them to be fixed over the skin. Each pressure transducer measures the pulse-wave form at each site, allowing one to measure transit time of the pulse wave between the two locations. A higher pulse-wave velocity (PWV) represents greater arterial stiffness. The transducers are placed over the carotid and femoral arteries for a measure of central arterial stiffness and over the carotid and radial arteries for a measure of peripheral arterial stiffness (12). PWV was calculated from these transducer measures, which are digitally recorded (sampling rate 500 Hz), resulting in measures of radial and femoral PWV. PWV was chosen as our measure of arterial stiffness because it is the most commonly used measure both in the literature and in consensus statements (13). Femoral PWV is also one of the only indexes of arterial stiffness directly linked with cardiovascular mortality and morbidity (14). Heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean (MAP) blood pressure were

### Table 1—Subject characteristics

|                          | All subjects | AT subjects | NA subjects | P     |
|--------------------------|--------------|-------------|-------------|-------|
| Age (years)              | 71.4 ± 0.7   | 71.7 ± 1.1  | 71.1 ± 0.9  | 0.417 |
| Weight (kg)              | 80.3 ± 2.1   | 81.9 ± 2.2  | 79.3 ± 3.1  | 0.554 |
| Height (cm)              | 167.6 ± 1.5  | 165 ± 2.1   | 169.0 ± 2.1 | 0.263 |
| BMI (kg/m²)              | 28.6 ± 0.64  | 30.1 ± 1.1  | 27.7 ± 1.0  | 0.064 |
| Waist-to-hip ratio       | 0.95 ± 0.01  | 0.96 ± 0.02 | 0.94 ± 0.02 | 0.315 |
| SBP (mmHg)               | 143 ± 3      | 150 ± 6     | 139 ± 4     | 0.149 |
| DBP (mmHg)               | 85 ± 2       | 83 ± 2      | 86 ± 2      | 0.329 |
| MAP (mmHg)               | 104 ± 2      | 105 ± 3     | 104 ± 3     | 0.723 |
| Heart rate (bpm)         | 66.0 ± 2.2   | 66.8 ± 4.1  | 65.3 ± 2.3  | 0.744 |
| Fasting blood glucose (mEq) | 7.5 ± 0.3 | 7.9 ± 0.6   | 7.1 ± 0.3   | 0.22  |
| A1C (%)                  | 6.5 ± 0.1    | 6.7 ± 0.2   | 6.4 ± 0.1   | 0.432 |
| Total cholesterol (mmol/l) | 4.7 ± 0.2 | 5.0 ± 0.2   | 4.6 ± 0.3   | 0.290 |
| LDL cholesterol (mmol/l) | 2.6 ± 0.2    | 2.6 ± 0.8   | 2.5 ± 0.2   | 0.592 |
| HDL cholesterol (mmol/l) | 1.5 ± 0.1    | 1.5 ± 0.1   | 1.5 ± 0.1   | 0.619 |
| Radial PWV (m/s)         | 10.08 ± 0.34 | 10.41 ± 0.58| 9.65 ± 0.60 | 0.368 |
| Femoral PWV (m/s)        | 11.97 ± 0.44 | 12.68 ± 0.76| 11.17 ± 0.75| 0.163 |

Data are means ± SEM. Demographic data for aerobically trained (AT), untrained (NA), and all subjects. P < 0.05 was considered significant.
measured using an automated blood pressure cuff (BpTRU Medical Devices, Coquitlam, BC, Canada). Each subject's weight was measured using a physician's balance scale. BMI, waist circumference, hip circumference, and waist-to-hip ratio were measured and calculated as per established guidelines (15). VO$_{2\text{max}}$ was determined using a maximal Bruce treadmill protocol exercise test. The change in VO$_{2\text{max}}$ was examined in all groups, including the untrained and strength-trained subjects.

**Statistical analysis**

All data analysis was done in a blinded fashion. Results are expressed as means ± SEM. Our sample size calculations for our three primary outcome measures (radial PWV, femoral PWV, and VO$_{2\text{max}}$) assumed a power of 90% and a 1.66% level of significance (after a Bonferroni correction for multiple comparisons). We found that we required a sample size of at least 15 subjects to detect a 15% difference in our primary outcome measures. The effects of training on all measures were calculated by a two-way ANOVA for repeated measures (time × group). The interaction of sex with training effects was examined by a three-way ANOVA for repeated measures (time × group × sex) (16). A value of P < 0.0166 was considered significant, because of a Bonferroni correction for multiple comparisons (16). Dropouts were handled on an intention-to-treat basis.

**RESULTS**

**Subject characteristics**

There were two dropouts from the study, one from each group (a total of 34 subjects completed the intervention). One dropout (aerobic group) was lost to follow-up. Other than the dropouts mentioned above, all of the remaining 34 subjects attended at least 90% of the training sessions. Therefore, 17 subjects from the aerobic group and 17 from the nonaerobic group completed the intervention. As shown in Table 1, at the time of entry into the study, there was no significant difference between aerobic and nonaerobic group subjects with respect to demographic data, resting heart rate, resting blood pressure, fasting blood glucose, A1C, or lipid profile.

**Effects of training on measures of arterial stiffness**

As shown in Fig. 1, aerobic training resulted in a decrease in both radial (P = 0.005) and femoral (P = 0.015) PWV that was not demonstrated in the nonaerobic group. In fact, aerobic training resulted in an $\sim$20.7 ± 6.3% decrease in radial PWV and a 13.9 ± 6.7% decrease in femoral PWV over 3 months. In comparison, the nonaerobic group demonstrated an 8.5 ± 6.6% increase in radial PWV and a 4.4 ± 3.3% increase in femoral PWV.

Male subjects in the aerobic group demonstrated a 25.5 ± 9.8% decrease in radial PWV and a 15.1 ± 7.7% decrease in femoral PWV, whereas female subjects in the aerobic training group demonstrated an 18.6 ± 8.3% decrease in radial PWV and a 12.6 ± 6.6% decrease in femoral PWV. In the nonaerobic group, male subjects demonstrated a 9.0 ± 11.0% increase in radial PWV and an 11.5 ± 11.0% increase in femoral PWV; female subjects in the nonaerobic group demonstrated an 4.1 ± 10.5% decrease in radial PWV and a 1.8 ± 2.3% increase in femoral PWV. There was no significant interaction of sex (time × group × sex) with the effects of training on radial (P = 0.731) and femoral (P = 0.260) PWV.

**Effects of training on measures of fitness**

The 3-month training program did not result in a significant increase in VO$_{2\text{max}}$ (Fig. 2) (P = 0.026). As shown in Table 2, there was no significant difference between the nonaerobic and aerobic groups with respect to changes in weight (P = 0.942), BMI (P = 0.396), waist-to-hip ratio (P = 0.786), or fasting blood glucose (P = 0.098). There was no significant difference between the two groups with respect to changes in SBP (P = 0.171), MAP (P = 0.078), DBP (P = 0.091), or resting heart rate (P = 0.073). There was also no significant interaction of sex (time × group × sex) with the effects of training on weight, BMI, blood pressure, baseline heart rate, and fasting blood glucose (Table 2).

**CONCLUSIONS** — Aerobic training reversed multifactorial (geriatric age, type 2 diabetes, hypertension, and hypercholesterolemia) arterial stiffness, as shown by significant decreases in both radial and femoral PWV. Improvements in arterial stiffness occurred with only 3 months of aerobic training despite the fact that this was in a population at quite high cardiovascular risk. Interestingly, this improvement occurred without any significant improvements in aerobic fitness, weight, BMI, waist-to-hip ratio, or blood pressure. This finding indicates that the effects of aerobic training on the vasculature may be independent of these other well-established benefits of exercise. Previous work on the effects of aerobic exercise on arterial compliance has consisted of cross-sectional data (7), pro-

![Figure 1](image-url)
Aerobic exercise and arterial stiffness

Figure 2—The 3-month training program did not result in a significant increase in $VO_{2\text{max}}$ ($P = 0.026$) in the aerobic group (AT, ■) or nonaerobic (NA, □) group.

Table 2—Change in fitness measures after intervention

| Measure            | Δ for AT subjects | Δ for NA subjects | $P$ (time × group) | $P$ (time × group × sex) |
|--------------------|-------------------|-------------------|--------------------|--------------------------|
| Weight (kg)        | +0.082 ± 0.732    | +0.140 ± 0.36+    | 0.942              | 0.103                    |
| BMI (kg/m²)        | −0.23 ± 0.28      | +0.05 ± 0.17      | 0.396              | 0.137                    |
| Waist-to-hip ratio | −0.002 ± 0.007    | 0.002 ± 0.011     | 0.786              | 0.854                    |
| SBP (mmHg)         | −10 ± 5           | −2 ± 3            | 0.171              | 0.567                    |
| DBP (mmHg)         | −5 ± 2            | −1 ± 2            | 0.091              | 0.396                    |
| MAP (mmHg)         | −7 ± 3            | −1 ± 3            | 0.078              | 0.906                    |
| Heart rate (bpm)   | −5.4 ± 2.7        | −0.4 ± 1.1        | 0.073              | 0.103                    |
| Fasting blood glucose (mEq) | −0.8 ± 0.3 | −0.1 ± 0.2 | 0.098              | 0.698                    |

Data are means ± SEM. Changes in measures of fitness for aerobically trained (AT) and untrained (NA) subjects are shown. None of these measures showed a significant training effect (time × group) because our study was only powered to find an effect for our three primary outcomes. There was also no significant interaction of gender (time × group × sex) with the effects of training.

Spective interventions in young athletes (6), and prospective interventions in middle-aged healthy persons (17). Cross-sectional studies of older healthy adults have shown that those who perform regular aerobic exercise have lower arterial stiffness than sedentary older adults (7). High-intensity exercise (running, 6 weeks) has been shown to reduce arterial stiffness prospectively in young athletes (6). More moderate training (daily walking, 3 months) has been shown prospectively to improve arterial compliance in middle-aged healthy women by ~40%, similar to the present study (17). Congruent with the results of the present study, brief (3 months of walking) aerobic interventions in healthy middle-aged men (mean age 52 years) have demonstrated reductions in arterial stiffness without any effect on cholesterol, blood pressure, body weight, or resting heart rate (7). A combined nutrition and walking program (18) as well as a pure walking intervention (6) have also demonstrated prospectively a decrease in arterial stiffness in the middle-aged type 2 diabetic population. To our knowledge, our study is the first to show that even in older adults at very high cardiovascular risk due to type 2 diabetes, age, hypertension, and hypercholesterolemia arterial stiffness can be reduced with regular aerobic exercise.

Clinical implications

In persons with diabetes, previous research has strongly established the relationship between vascular stiffness and cardiovascular mortality (5). Our study population consisted of older subjects with type 2 diabetes complicated by comorbid hypertension and hyperlipidemia, putting them at very high risk for arterial stiffness and the consequent cardiovascular risks associated with this condition. Despite having multiple cardiovascular risk factors, we were able to show a significant decrease in both radial and femoral PWV. This is especially important with respect to femoral PWV, one of the few measures directly linked with cardiovascular mortality and morbidity (14). Although there have been some proposed pharmacological treatments for arterial stiffness (23), the results of the current study indicate that aerobic exer-
cise should be the first-line treatment to reduce arterial stiffness in older adults with type 2 diabetes, even if the patient has additional cardiovascular risk factors such as hypertension and hypercholesterolemia.

**Limitations**

Further research is needed to determine the pathophysiologcal mechanism for the reduction in radial and femoral PWV with aerobic exercise in our population. We also do not know if the observed improvements in arterial stiffness with aerobic exercise persist over longer periods of time, because our subjects were only examined during the 3-month training period.

Our study was unable to detect any significant training effect on weight, BMI, waist circumference, and fasting blood glucose. The main reason is that our study was only powered to detect three primary outcome measures (radial PWV, femoral PWV, and VO2max). However, because female sex has been associated with lower aerobic endurance in subjects with type 2 diabetes (24), there is the possibility that a significant training effect was obscured by sex differences. Congruent with the most recent meta-analysis literature (25), we did not detect any significant interaction between sex and the effects of training on weight, BMI, waist circumference, and fasting blood glucose (Table 2). This observed lack of a sex effect needs to be interpreted with caution because our study had insufficient numbers to adequately assess sex differences in the training response.

Because our exercise intervention was completed by a relatively small number of subjects, the benefits of aerobic training on arterial stiffness need to be confirmed by larger studies. The fact that a short 3-month intervention produced a sizable decrease in arterial stiffness suggests that larger exercise studies in this high-risk group are practicable and might be able to demonstrate training-induced improvements in mortality or cardiovascular event rates.

In summary, we demonstrated that aerobic exercise reduces multifactorial (type 2 diabetes, aging, hypertension, and hypercholesterolemia) arterial stiffness with a relatively short intervention. Aerobic exercise should be first-line therapy for arterial stiffness, regardless of the underlying etiology.

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