Effects of a short-term increase in physical activity on arterial stiffness during hyperglycemia

Ryota Kobayashi,1,* Kaori Sato,2 Toshihiko Takahashi,3 Kenji Asaki,4 Soichiro Iwanuma,5 Nobuyuki Ohashi5 and Takeo Hashiguchi5

1Center for Fundamental Education, 2Department of Tokyo Judo Therapy and 3Department of School Education, Teikyo University of Science, 2-2-1 Senju, Sakuragi, Adachi-ku, Tokyo 120-0045, Japan
2College of Liberal Arts, International Christian University, 3-10-2 Osawa, Mitaka-shi, Tokyo 181-8585, Japan
3Adachi-ku Track and Field Association, 1-33-22 Yanaka, Adachi-ku, Tokyo 120-0006, Japan

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We examined the effects of increasing physical activity on arterial stiffness during hyperglycemia. Nineteen glucose-intolerant elderly participated in the study. We randomly assigned 10 participants to increase their daily activity in everyday life, regardless of the time or intensity, for 1 month (PAI group) (age, 74.6±1.3 years; mean±SE) and nine participants to maintain their level of activity (CON group) (age, 79.2±2.1 years; mean±SE). The 75-g oral glucose tolerance test was conducted in each participant in both groups before and after the start of the intervention to confirm glucose intolerance. Brachial-ankle pulse wave velocity and cardio-ankle vascular index significantly increased from baseline at 30, 60, and 90 min after the 75-g glucose ingestion after the intervention in the CON group (p<0.05), but not in the PAI group. Heart-brachial pulse wave velocity did not change compared to baseline after the 75-g glucose ingestion in either group and did not change from baseline at 30, 60, and 90 min after the 75-g glucose ingestion before and after the intervention in both groups. The present findings indicate that a short-term increase in physical activity suppresses the increase in arterial stiffness after glucose intake.

Key Words: increased physical activity, arterial stiffness, blood pressure, glucose ingestion, blood glucose

A diet high in carbohydrates increases the risk of diabetes. Increased arterial stiffness can result from diabetes, and aortic and peripheral arterial disease is one of the leading causes of mortality in diabetic patients. Even after adjusting for other risk factors, diabetic patients are two to four times more likely to die than non-diabetic patients. Therefore, suppressing arterial stiffness is important to minimize cardiovascular risk.

A postprandial increase in arterial stiffness is associated with cardiovascular disease risk. In fact, arterial stiffness increases rapidly during hyperglycemia. Gordin et al. reported increased arterial stiffness due to elevated postprandial blood glucose levels in healthy middle-aged and elderly people and patients with type 2 diabetes. Thus, data consistently show that arterial stiffness increases during hyperglycemia. Arterial stiffness also increases with age. Japan is a super-aging society, and controlling the increase in arterial stiffness during acute hyperglycemia in the elderly is considered important.

Individuals with an active lifestyle have a reduced risk of cardiovascular disease due to a suppresses increases in age-related arterial stiffness. In interventional studies, routinely increasing aerobic exercise in daily life leads to a significant decrease in arterial stiffness in elderly people. Vaitkevicius et al. found that moderate physical activity is effective in improving arterial stiffness. Moreover, our recent study reported that older people with lower physical activity (daily step count: 3,649.8±559 steps/day) have increased arterial stiffness after 75 g glucose intake, but older people with higher physical activity (daily step count: 10,628.6±1,578 steps/day) show no change. Thus, increasing one’s physical activity may suppress the increased arterial stiffness that occurs during hyperglycemia. However, the effect of increasing daily physical activity on the arterial stiffness response to hyperglycemia has not yet been tested.

We hypothesized that increasing daily physical activity prevents the increase in arterial stiffness during acute hyperglycemia in elderly, glucose-intolerant people. We examined the effects of increasing daily physical activity on arterial stiffness during hyperglycemia.

Materials and Methods

Participants. Nineteen glucose-intolerant elderly participated in the study. We randomly assigned 10 participants to increase their daily activity in everyday life, regardless of the time or intensity, for 1 month (PAI group) (age, 74.6±1.3 years; height, 153.3±2.7 cm; weight, 56.2±2.6 kg; mean±SE) and nine participants to maintain their level of activity (CON group) (age, 79.2±2.1 years; height, 152.6±3.5 cm; weight, 56.0±3.1 kg; mean±SE). All participants were normotensive (Japanese standard value: <140/90 mmHg), non-smokers, and had a sedentary lifestyle (≥1 year without exercise; assessed with an international physical activity questionnaire). Before the experiment, participants underwent a 75-g oral glucose tolerance test (OGTT) to confirm impaired glucose tolerance and to confirm that all participants were in the judgment category of the Japan Diabetes Society (140 to 199 mg/dl). All participants were fully informed about the experimental procedures as well as the purpose of the study before providing written informed consent to participate. The Ethics Committee at Teikyo University of Science approved this study, which proceeded in accordance with the guidelines for human experimentation published by our Institutional Review Board. This study also conformed to the principles of the Declaration of Helsinki (Table 1).

Sample size. Power analysis was performed with G*Power 3 to obtain an appropriate sample size. In our laboratory, we assumed that the magnitude of the effect on arterial stiffness was 0.5. The calculation showed that each group should include eight participants to detect differences, with an 80% power and 5% one-sided alpha using analysis of variance. In this study, 19 participants were tested.
**Study design.** We randomly assigned 10 participants to increase their daily activity in everyday life for 1 month (PAI group) and nine participants to maintain their level of daily activity (CON group). The PAI group was asked to increase their daily living activities every day regardless of strength and time for 1 month. Specifically, participants could go shopping, walk in the garden, clean up, prepare meals, ride a bicycle, go out with a child, play with a child, walk a dog, etc (Table 2). Activities performed while sitting were not considered part of the increase in activity. We did not set a goal time or target step number so that participants could increase their activity according to their own lifestyle. This setting is intended to investigate whether physical activity as close as possible to the subject’s lifestyle can suppress the increase in arteriosclerosis during hyperglycemia, for consideration of clinical application. Participants in the CON group were asked to continue their daily activity level for 1 month. All Participants did not change their eating habits during the intervention.

The 75-g OGTT was conducted in each group before and after the start of the intervention. After 10 min of supine rest, systemic and aortic arterial stiffness, brachial and ankle blood pressure (BP), heart rate (HR), and blood glucose (BG) were measured before (baseline), and at 30, 60, and 90 min after the 75-g OGTT (Fig. 1). Both groups were asked to fill out an activity diary and wear an activity meter to monitor their activity during this experiment. The booklet we created asked them to describe the activity time and activity in as much detail as possible. Participants were instructed to maintain the same diet as before the intervention. The participants abstained from alcohol, caffeine, and intense physical activity (exercise) for 24 h, and fasted for at least 10–12 h before being assessed in a quiet room at a temperature between 23°C and 26°C.

### Table 1. Summarizes the characteristics of both groups (n = 19)

| Variable                  | PAI group         | CON group         |
|---------------------------|-------------------|-------------------|
|                           | Pre | Post | Pre | Post |
| Age (years)               | 74.6 ± 1.3       | 74.6 ± 1.3       | 79.2 ± 2.1   | 79.2 ± 2.1   |
| Sex                       | 4 male, 6 female | 4 male, 6 female | 2 male, 7 female | 2 male, 7 female |
| Height (cm)               | 153.3 ± 2.7      | 153.3 ± 2.7      | 152.6 ± 3.5  | 152.6 ± 3.5  |
| Weight (kg)               | 56.2 ± 2.6       | 56.2 ± 2.6       | 56.0 ± 3.1   | 55.6 ± 3.0   |
| Body fat (%)              | 31.0 ± 1.8       | 30.6 ± 2.0       | 33.5 ± 1.7   | 33.2 ± 1.7   |
| BMI (kg/m²)               | 23.9 ± 0.8       | 23.9 ± 0.8       | 23.9 ± 0.7   | 23.8 ± 0.6   |

Values are mean ± SE. BMI, body mass index; PAI, physical activity increases; CON, control.

### Table 2. The lit physical activities

| Walking                      | Housework                               | Other                           |
|------------------------------|-----------------------------------------|----------------------------------|
| Go shopping on foot          | Wipe the floor                          | Play with their grandchildren    |
| Use the stairs (Do not use escalators or elevators) | Vacuum the room                        | Get up early                     |
| Dog-walking                  | Fold up the bedding and put it in the closet | Do not lay down in the afternoon |
| Go out as mush as possible   | Sweep and clean the entrance and/or near the park | Talking while standing |
| Make a detour                | Do the gardening                        |                                  |
| Walk briskly                 |                                        |                                  |

**Fig. 1.** Study design. 75-g OGTT, 75-g oral glucose tolerance test.
Physical activity. Daily physical activity was measured using a triaxial accelerometer (HJA-750C, Active Style Pro, Omron, Kyoto, Japan). All subjects wore the triaxial accelerometer on the waist 14 days before intervention and continuously for 1 month, except during sleeping and bathing, and data from a continuous, all-day period were used to assess physical activity [daily living activity (kcal/day), daily step activity (kcal/day), daily step count (steps/day), Total physical activity (light, moderate and vigorous) level, (min/day)].

Body composition. Height was measured in units of 0.1 cm using a height gauge. Body weight was measured in units of 0.1 kg using a body weight/body composition meter (WB-150 PMA, Tanita, Tokyo, Japan).

Arterial stiffness. The brachial-ankle (ba) and heart-brachial (hb) pulse wave velocity (PWV) of all participants were measured using an automatic oscillographic device (form PWV/ABI, Colin Medical Technology, Komaki, Japan). Measurement of baPWV and hbPWV were carried out as described in previous studies. The cardio-ankle vascular index (CAVI) of all participants was measured using an automatic oscillographic device (VaSera VS-1500AE, Fukuda-Denshi, Tokyo, Japan) as described in a previous study. CAVI is a measurement method that does not depend on BP. All measurements were performed with the participants in a supine position in a quiet room. The daily coefficients of variation (CVs) at the laboratory were 5 ± 1%, 5 ± 2%, and 3 ± 1% for baPWV, hbPWV, and CAVI, respectively.

BP and HR. Brachial and ankle systolic BP (SBP), mean BP (MBP), diastolic BP (DBP), pulse pressure (PP), and HR at rest in the supine position were measured using the automatic oscillographic PWV/ABI device (Omron-Colin, Tokyo, Japan) over the brachial and ankle arteries.

BG. Venous blood was drawn from the left fingertip of the participants before (baseline) and 30, 60, and 90 min after the 75-g OGTT. BG was measured with the flavin-adenine dinucleotide glucose dehydrogenase method using a Glutest Neo Alpha glucometer (Sanwa Kagaku Kenkyusho, Tokyo, Japan). The daily coefficients of variation (CVs) at the laboratory was 5 ± 3% for BG.

75-g OGTT. The 75-g OGTT was performed with the Trelan G75 (Ajinomoto Pharmai, Tokyo, Japan) in the morning after fasting overnight (10 to 12 h). The glucose drink (225 ml) was within the adult standard and was consumed within 5 min. This method is recognized in the Japan Diabetes Guidelines.

Statistical analysis. All data are presented as means ± SE. The normal distribution of all data was confirmed using Kolmogorov–Smirnov tests. The two groups of means were compared using an independent t test. Data were analyzed using a repeated-measures 2-way analysis of variance (group × time). Significant differences between means were identified using the Bonferroni post-test. Data were statistically analyzed using SPSS ver. 22 (IBM, Armonk, NY). Statistical significance was set at p<0.05.

Results

Physical characteristics. Table 1 summarizes the characteristics of both groups. Age, height, weight, body fat and BMI before and after the intervention was not significantly different between the groups.

Arterial stiffness. Figure 2A show changes in the baPWV after the 75-g OGTT in both groups. baPWV significantly increased from baseline at 30 (p<0.01), 60 (p<0.01), and 90 (p<0.01) min after the 75-g OGTT before the intervention in both groups and did not differ between groups. baPWV significantly increased from baseline at 30 (p<0.01), 60 (p<0.01), and 90 (p<0.01) min after the 75-g OGTT after the intervention in the CON group, but not in the PAI group and did not differ between groups. Figure 2B shows changes in the hbPWV after the 75-g OGTT. hbPWV significantly increased from baseline at 30 (p<0.01), 60 (p<0.01), and 90 (p<0.01) min after the 75-g OGTT before and after the intervention in both groups. The changes in CAVI after the intervention in the CON group were not significantly different from the PAI group. **p<0.01 and *p<0.05 vs baseline.
OGTT in both groups, hbPWV did not change from baseline at 30, 60, and 90 min after the 75-g OGTT before and after the intervention in both groups, and did not differ between them. Figure 2C show changes in the CAVI after the 75-g OGTT in both groups. CAVI significantly increased from baseline at 30 \((p<0.01)\), 60 \((p<0.01)\), and 90 \((p<0.01)\) min after the 75-g OGTT before the intervention in both groups and did not differ between groups. CAVI significantly increased from baseline at 30 \((p<0.01)\), 60 \((p<0.05)\), and 90 \((p<0.05)\) min after the 75-g OGTT after the intervention in the CON group, but not in the PAI group and did not differ between groups.

**BP and HR.** Table 3 shows changes in brachial BP and HR after the 75-g OGTT in both groups. Brachial SBP, MBP, DBP, PP and HR did not change from baseline at 30, 60, and 90 min after the 75-g OGTT before and after the intervention in both groups and did not differ between them. Table 4 shows changes in ankle BP after the 75-g OGTT in both groups. Ankle DBP did not change from baseline at 30, 60, and 90 min after the 75-g OGTT before and after the intervention in both groups and did not differ between them. Ankle SBP, MBP, and PP significantly increased from baseline at 30 \((p<0.01)\), 60 \((p<0.01)\), and 90 \((p<0.01)\) min after the 75-g OGTT after the intervention in the CON group, but not in the PAI group and did not differ between groups.

**BG.** Table 5 shows changes in BG after the 75-g OGTT in both groups. BG significantly increased from baseline at 30 \((p<0.01)\), 60 \((p<0.01)\), and 90 \((p<0.01)\) min after the 75-g OGTT before and after the intervention in both groups did not differ between groups.
Table 5. Changes in blood glucose before (baseline) and after glucose ingestion in both groups

| Variable                | Group    | Baseline | Post 30 min | Post 60 min | Post 90 min |
|-------------------------|----------|----------|-------------|-------------|-------------|
| Blood glucose (mg/dl)   | Pre      | CON group| 103.1 ± 4.5 | 148.1 ± 8.2*| 153.1 ± 10.5*| 162.9 ± 10.3*|
|                         | PAI group|          | 103.2 ± 7.4 | 149.4 ± 6.5*| 158.0 ± 8.1*| 162.5 ± 9.1*|
|                         | Post     | CON group| 104.7 ± 3.9 | 154.4 ± 14.5*| 156.1 ± 14.1*| 162.6 ± 11.0*|
|                         | PAI group|          | 98.0 ± 4.2  | 131.5 ± 3.7*| 132.8 ± 5.0*| 149.1 ± 12.8*|

Values are mean ± SE. PAI, physical activity increases; CON, control. *p<0.01 vs baseline.

Table 6. Changes in physical activity between the pre (baseline) and post (4-weeks) values in both groups

| Variable                          | PAI group          | CON group          |
|-----------------------------------|--------------------|--------------------|
|                                   | Pre                | Post               | Pre                | Post               |
| Daily living activity (kcal/day)  | 74.7 ± 1.7         | 205.6 ± 31.6**     | 74.1 ± 7.3         | 75.5 ± 16.9        |
| Daily step activity (kcal/day)    | 208.0 ± 4.4        | 338.4 ± 23.8**     | 208.5 ± 13.3       | 210.0 ± 28.3       |
| Daily step counts (counts/day)    | 3,015.8 ± 134.3    | 9,025.1 ± 43.8**   | 3,073.8 ± 417.9    | 3,064.5 ± 537.3    |
| Total physical activity (light)   | 217.1 ± 2.3        | 307.4 ± 14.6**     | 219.6 ± 27.7       | 215.1 ± 16.4       |
| level (min/day)                   | 10.3 ± 0.3         | 23.8 ± 3.3**       | 10.5 ± 1.8         | 9.9 ± 1.5          |
| Total physical activity (vigorous)| 0.3 ± 0.1          | 0.5 ± 0.2†         | 0.1 ± 0.02         | 0.1 ± 0.03         |
| level (min/day)                   |                     |                    |                    |                    |

Values are mean ± SE. PAI, physical activity increases; CON, control. *p<0.01 vs Pre. †p<0.01 vs CON group (Post).

Physical activity. Table 6 shows changes in physical activity between the pre (baseline) and post (4-weeks) values in both groups. Daily living activity (kcal/day), daily step activity (kcal/day), daily step counts (counts/day), total physical activity (Light and Moderate) level (min/day) significantly increased after the intervention compared with before the intervention in PAI group (p<0.01), but did not change in CON group. Daily living activity (kcal/day), daily step activity (kcal/day), daily step counts (counts/day), total physical activity (Light, Moderate, Vigorous) level (min/day) were significantly higher after the intervention in the PAI group compared with the CON group (p<0.01).

Discussion

The key novel finding of this study was that an increase in daily physical activity for a short period, compared with no increase in daily physical activity, suppressed the increase in acute arterial stiffness induced by a glucose load. These results suggest that increasing daily physical activity suppresses increases in arterial stiffness during acute hyperglycemia.

BG acutely increases after glucose ingestion in physically active and physically inactive humans. Mikus et al. later found that BG levels do not differ after glucose ingestion in active compared to inactive groups. Our results concurred with these findings. Weiss et al. found insulin sensitivity is higher in people with higher physical activity than those with low physical activity. In addition, insulin sensitivity is positively correlated with physical activity. Regular aerobic exercise increases glucose uptake by skeletal muscle. In fact, Frois et al. reported that 3 weeks of leg endurance training increases glucose uptake and decreases muscle insulin levels in the leg skeletal muscles. Thus, insulin resistance may have been lower in the PAI group than in the CON group. Therefore, increases in arterial stiffness during acute hyperglycemia may be influenced by blood insulin levels after glucose ingestion. However, we did not measure blood insulin levels, which is an important limitation of this study.

Arterial stiffness acutely increases during acute hyperglycemia. Aortic arterial stiffness increases at 60 min after glucose ingestion in obese individuals. Furthermore, in previous studies, aortic stiffness rigidity before breakfast did not differ and does not increase in nondiabetic patients compared with diabetic patients, although peripheral arterial stiffness increases in diabetic patients. 

We found that systemic PWV increased from baseline after the 75-g OGTT in the CON group, whereas proximal aorta PWV did not change after the 75-g OGTT in either group. Low levels of high-density lipoprotein cholesterol are associated with increased arterial stiffness. Although aortic arterial stiffness increases in middle-aged and older persons with metabolic syndrome after ingesting glucose, stiffness does not change in healthy subjects. High-density lipoprotein cholesterol was lower in individuals with metabolic syndrome than in healthy subjects.

Thus, increases in aortic arterial stiffness during acute hyperglycemia may have been higher in obese than in non-obese adult individuals. In this context, the aortic PWV during acute hyperglycemia should be compared between obese and healthy individuals.

A physically active lifestyle is linked with a decreased risk of cardiovascular diseases and events at all ages through improvements in arterial stiffness that reflect arterial remodeling. Furthermore, in previous studies, aortic arterial stiffness is associated with arterial remodeling. Weiss et al. reported lower arterial stiffness in their physical activity group (daily physical activity: 360 ± 12 kcal/day) than in their physical inactivity group (daily physical activity: 148 ± 4 kcal/day). In addition, higher levels of moderate-to-vigorous physical activity and avoidance of sedentary behavior are each associated with a slower age-related progression of aortic stiffness independent of conventional vascular risk factors among older individuals. Moreover, previous findings suggest that physical activity (Medical Outcomes Study 36-item Short Form: SF-36) is associated with peripheral arterial stiffness and SBP, but not with reduced aortic arterial stiffness in healthy humans. Thus, increasing physical activity may attenuate increases in arterial stiffness during acute hyperglycemia. We found that aortic PWV did not change from baseline after the 75-g OGTT after the intervention in both groups. PWV is associated with arterial stiffness, arterial diameter, and wall thickness. Thus, the finding of no change in arterial stiffness after the 75-g OGTT in the PAI group may be associated with stress on the peripheral arterial walls by increased ankle SBP after the 75-g OGTT.

Changes in arterial stiffness are influenced by vascular endothelial function, which decreases during acute hyperglycemia. Nitric oxide (NO) involved in vascular endothelial function increases after aerobic exercise training. MBP is determined by cardiac output and peripheral vascular resistance (e.g., peripheral endothelial function). We found that ankle MBP increased from baseline after the 75-g OGTT after the intervention in the CON group, whereas ankle MBP did not change after the intervention in the PAI group. Thus, increased arterial stiffness (mainly non-
BP dependent: CAVI) after glucose ingestion might be associated with impaired endothelial function after glucose ingestion. However, we did not measure vascular endothelial function, which is a limitation of this study. Lu et al. reported that sympathetic nervous system activity (low frequency/high frequency) determined by HR variability spectral analysis increases at 60 min after 500-kcal test meal comprising 17.5 g protein, 32.4 g fat, and 50.1 g carbohydrate. Thus, increased activity of the sympathetic nervous system may influence systemic arterial stiffness after glucose ingestion. However, we did not measure nervous system activity, which is a limitation of this study. The present findings require confirmation by further investigation into the mechanistic details of glucose-induced changes in systemic arterial stiffness.

Limitations of the present study include the small sample size and the fact that our participants were older adults with impaired glucose tolerance. Therefore, our findings cannot be generalized to other populations. Moreover, we did not measure insulin levels, endothelial function, and nervous system activity, which may have an important effect on arterial stiffness.

In conclusion, baPWV, CAVI, and ankle SBP were significantly lower after the 75-g OGTT in the PAI group compared to the CON group. These results suggest that increasing daily physical activity suppresses increases in arterial stiffness and ankle SBP, older adults with impaired glucose tolerance during acute hyperglycemia.

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Conflict of Interest

No potential conflicts of interest were disclosed.

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