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

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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 $\pm$ SE) and nine participants to maintain their level of activity (CON group) (age, 79.2 ± 2.1 years; mean $\pm$ 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.^(1,2) Increased arterial stiffness can result from diabetes, and aortic and peripheral arterial disease is one of the leading causes of mortality in diabetic patients.⁽³⁾ Even after adjusting for other risk factors, diabetic patients are two to four times more likely to die than non-diabetic patients.⁽⁴⁻⁶⁾ Therefore, suppressing arterial stiffness is important to minimize cardiovascular risk.⁽⁷⁾

A postprandial increase in arterial stiffness is associated with cardiovascular disease risk.⁽⁸⁾ In fact, arterial stiffness increases rapidly during hyperglycemia. Gordin *et al.*⁽⁹⁾ 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.⁽¹⁰⁾ 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.^(11,12) In interventional studies, routinely increasing aerobic exercise in daily life leads to a significant decrease in arterial stiffness in elderly people.⁽¹³⁾ Vaitkevicius *et al.*⁽¹⁴⁾ 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: $3,649.8 \pm 559$ steps/day) have increased arterial stiffness after 75 g glucose intake, but older people with higher physical activity (daily step count: $10,628.6 \pm 1,578$ steps/day) show no change.⁽¹⁵⁾ 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 $\pm$ 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 $\pm$ 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).⁽¹⁶⁾ 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.⁽¹⁷⁾ 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.

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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	56.3 ± 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/m ²)	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
<ul style="list-style-type: none"> • Go shopping on foot • Use the stairs (Do not use escalators or elevators) • Dog-walking • Go out as much as possible • Make a detour • Walk briskly 	<ul style="list-style-type: none"> • Wipe the floor • Vacuum the room • Fold up the bedding and put it in the closet • Sweep and clean the entrance and/or near the park • Do the gardening 	<ul style="list-style-type: none"> • Play with their grandchildren • Get up early • Do not lay down in the afternoon • Talking while standing

Fig. 1. Study design. 75-g OGTT, 75-g oral glucose tolerance test.

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.

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)].⁽¹⁸⁾

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 oscillometric device (form PWV/ABI; Colin Medical Technology, Komaki, Japan). Measurement of baPWV and hbPWV were carried out as described in previous studies.^(19,20) The cardio-ankle vascular index (CAVI) of all participants was measured using an automatic oscillometric device (VaSera VS-1500AE; Fukuda-Denshi, Tokyo, Japan) as described in a previous study.⁽²¹⁾ 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 $5 \pm 1\%$, $5 \pm 2\%$, and $3 \pm 1\%$ 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 oscillometric PWV/ABI device (Omron-Colin, Tokyo, Japan) over the brachial and ankle arteries.⁽¹⁹⁾

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).⁽²²⁾ The daily coefficients of variation (CVs) at the laboratory was $5 \pm 3\%$ for BG.

75-g OGTT. The 75-g OGTT was performed with the Trelan-G75 (Ajinomoto Pharma, 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.⁽¹⁶⁾

Statistical analysis. All data are presented as means $\pm$ 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 $\times$ 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

Fig. 2. Changes in arterial stiffness before and after the 75-g OGTT in both groups. Values are the mean $\pm$ SE. PAI, physical activity increases; CON, control; baPWV, brachial-ankle pulse wave velocity; hbPWV, heart-brachial pulse wave velocity; CAVI, cardio-ankle vascular index. * $p < 0.05$ and ** $p < 0.01$ vs baseline.

Table 3. Changes in brachial an BP and HR before (baseline) and after glucose ingestion in both groups

Variable	Group	Baseline	Post 30 min	Post 60 min	Post 90 min
Brachial SBP (mmHg)	Pre	CON group	133.9 ± 6.5	132.6 ± 5.7	137.3 ± 8.2
		PAI group	133.2 ± 2.0	134.5 ± 2.8	136.7 ± 5.2
	Post	CON group	133.6 ± 6.8	130.6 ± 4.6	132.9 ± 4.9
		PAI group	131.0 ± 5.9	131.2 ± 4.3	130.3 ± 5.1
Brachial MBP (mmHg)	Pre	CON group	95.5 ± 4.3	93.7 ± 3.9	97.0 ± 5.1
		PAI group	95.9 ± 4.2	96.6 ± 2.0	96.0 ± 3.8
	Post	CON group	94.9 ± 4.5	91.8 ± 3.4	93.0 ± 3.7
		PAI group	93.7 ± 3.6	93.8 ± 3.3	92.5 ± 3.4
Brachial DBP (mmHg)	Pre	CON group	76.2 ± 3.4	74.3 ± 3.1	76.9 ± 3.7
		PAI group	77.3 ± 1.8	77.7 ± 2.2	76.6 ± 3.3
	Post	CON group	75.6 ± 3.8	72.4 ± 3.0	73.1 ± 3.3
		PAI group	75.0 ± 2.9	75.1 ± 3.1	73.6 ± 2.9
Brachial PP (mmHg)	Pre	CON group	57.7 ± 3.9	58.2 ± 3.3	60.4 ± 5.0
		PAI group	55.9 ± 2.8	56.8 ± 2.8	58.3 ± 3.2
	Post	CON group	57.9 ± 4.7	58.1 ± 2.5	59.8 ± 2.8
		PAI group	56.0 ± 4.3	56.1 ± 2.6	56.7 ± 3.1
Heart rate (beats/min)	Pre	CON group	67.9 ± 1.5	68.1 ± 1.7	68.4 ± 1.7
		PAI group	64.3 ± 2.4	63.5 ± 2.5	62.5 ± 2.2
	Post	CON group	68.6 ± 1.6	68.4 ± 2.0	69.9 ± 2.8
		PAI group	63.1 ± 2.3	63.1 ± 1.7	63.0 ± 1.8

Values are mean ± SE. PAI, physical activity increases; CON, control; SBP, systolic blood pressure; MBP, mean blood pressure; DBP, diastolic blood pressure; PP, pulse pressure.

Table 4. Changes in ankle an BP before (baseline) and after glucose ingestion in both groups

Variable	Group	Baseline	Post 30 min	Post 60 min	Post 90 min
Ankle SBP (mmHg)	Pre	CON group	145.7 ± 7.6	161.5 ± 8.2**	158.7 ± 8.6**
		PAI group	149.9 ± 5.3	164.5 ± 5.5**	165.1 ± 5.9**
	Post	CON group	145.0 ± 7.9	154.5 ± 7.0*	154.8 ± 6.9**
		PAI group	151.8 ± 5.9	153.7 ± 5.2	152.0 ± 5.5
Ankle MBP (mmHg)	Pre	CON group	97.8 ± 4.5	103.1 ± 4.6**	103.5 ± 5.4**
		PAI group	99.9 ± 3.5	106.5 ± 3.0**	107.1 ± 4.1**
	Post	CON group	97.1 ± 4.5	100.9 ± 4.4*	101.6 ± 4.8**
		PAI group	100.4 ± 3.5	100.8 ± 3.6	99.9 ± 3.4
Ankle DBP (mmHg)	Pre	CON group	73.9 ± 3.6	73.9 ± 3.1	75.9 ± 4.2
		PAI group	74.9 ± 2.9	77.5 ± 2.4	78.1 ± 3.7
	Post	CON group	73.1 ± 3.3	74.1 ± 3.3	75.0 ± 4.0
		PAI group	74.7 ± 3.0	74.4 ± 3.2	73.9 ± 3.0
Ankle PP (mmHg)	Pre	CON group	71.8 ± 5.6	87.5 ± 5.9	82.7 ± 5.8
		PAI group	75.0 ± 3.7	87.0 ± 4.6	87.0 ± 4.3
	Post	CON group	71.9 ± 6.0	80.4 ± 4.1	79.8 ± 4.0
		PAI group	77.1 ± 4.7	79.3 ± 3.8	78.1 ± 4.6

Values are mean ± SE. PAI, physical activity increases; CON, control; SBP, systolic blood pressure; MBP, mean blood pressure; DBP, diastolic blood pressure; PP, pulse pressure. * $p < 0.05$ and ** $p < 0.01$ 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 before the intervention in both groups and did not differ between groups. Ankle SBP, MBP, and PP significantly increased from baseline at 30 ($p < 0.05$), 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*
		PAI group	103.2 ± 7.4	149.4 ± 6.5*	158.0 ± 8.1*
	Post	CON group	104.7 ± 3.9	154.4 ± 14.5*	156.1 ± 14.1*
		PAI group	98.0 ± 4.2	131.5 ± 3.7*	132.8 ± 5.0*

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) level (min/day)	217.1 ± 2.3	307.4 ± 15.6* [†]	219.6 ± 27.7	215.1 ± 16.4
Total physical activity (moderate) level (min/day)	10.3 ± 0.3	23.8 ± 3.3* [†]	10.5 ± 1.8	9.9 ± 1.5
Total physical activity (vigorous) level (min/day)	0.3 ± 0.1	0.5 ± 0.2 [†]	0.1 ± 0.02	0.1 ± 0.03

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 increases 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.^(23,24) Mikus *et al.*⁽²⁵⁾ 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.*⁽²⁴⁾ 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,⁽²⁶⁾ and regular aerobic exercise increases glucose uptake by skeletal muscle. In fact, Frøsig *et al.*⁽²⁷⁾ reported that 3 weeks of leg endurance training increases glucose uptake and decreases blood 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.⁽⁷⁾ Furthermore, in previous studies, aortic rigidity after breakfast does not differ and does not increase in nondiabetic patients compared with diabetic patients, although peripheral arterial stiffness increases in diabetic patients.⁽⁸⁾ 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.⁽²⁸⁾ 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.⁽²⁹⁾ 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. Iemitsu *et al.*⁽³⁰⁾ 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.⁽³¹⁾ 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.⁽³²⁾ Thus, increasing physical activity may attenuate increases in arterial stiffness during acute hyperglycemia. We found that aortic PWV did not change from baseline at 30, 60, and 90 min after the 75-g OGTT after the intervention in both groups. PWV is associated with arterial stiffness, arterial diameter, and wall thickness.⁽³³⁾ 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,⁽³⁴⁾ which decreases during acute hyperglycemia.⁽³⁵⁾ Nitric oxide (NO) involved in vascular endothelial function increases after aerobic exercise training.⁽³⁶⁾ 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.*⁽³⁷⁾ reported that sympathetic nervous system activity (low frequency/high frequency) determined by HR variability spectral analysis increases at 60 min after a 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.

References

- Blacher J, Asmar R, Djane S, London GM, Safar ME. Aortic pulse wave velocity as a marker of cardiovascular risk in hypertensive patients. *Hypertension* 1999; **33**: 1111–1117.
- van Sloten TT, Schram MT, van den Hurk K, *et al.* Local stiffness of the carotid and femoral artery is associated with incident cardiovascular events and all-cause mortality: the Hoorn study. *J Am Coll Cardiol* 2014; **63**: 1739–1747.
- Hietanen H, Pääkkönen R, Salomaa V. Ankle blood pressure as a predictor of total and cardiovascular mortality. *BMC Cardiovasc Disord* 2008; **8**: 3.
- Newman AB, Sciscovick DS, Manolio TA, *et al.* Ankle-arm index as a marker of atherosclerosis in the Cardiovascular Health Study. Cardiovascular Health Study (CHS) Collaborative Research Group. *Circulation* 1993; **88**: 837–845.
- Steg PG, Bhatt DL, Wilson PW, *et al.* One-year cardiovascular event rates in outpatients with atherothrombosis. *JAMA* 2007; **297**: 1197–1206.
- Kallio M, Forsblom C, Groop PH, Groop L, Lepäntalo M. Development of new peripheral arterial occlusive disease in patients with type 2 diabetes during a mean follow-up of 11 years. *Diabetes Care* 2003; **26**: 1241–1245.
- Baynard T, Carhart RL Jr, Weinstock RS, Ploutz-Snyder LL, Kanaley JA. Short-term exercise training improves aerobic capacity with no change in arterial function in obesity. *Eur J Appl Physiol* 2009; **107**: 299–308.
- Blendea MC, Bard M, Sowers JR, Winer N. High-fat meal impairs vascular compliance in a subgroup of young healthy subjects. *Metabolism* 2005; **54**: 1337–1344.
- Gordin D, Saraheimo M, Tuomikangas J, *et al.* Influence of postprandial hyperglycemic conditions on arterial stiffness in patients with type 2 diabetes. *J Clin Endocrinol Metab* 2016; **101**: 1134–1143.
- Tanaka H, Miyachi M, Murakami H, Maeda S, Sugawara J. Attenuated age-related increases in arterial stiffness in Japanese and American women. *J Am Geriatr Soc* 2015; **63**: 1170–1174.
- Park W, Park HY, Lim K, Park J. The role of habitual physical activity on arterial stiffness in elderly individuals: a systematic review and meta-analysis. *J Exerc Nutrition Biochem* 2017; **21**: 16–21.
- Alkatan M, Machin DR, Baker JR, Akkari AS, Park W, Tanaka H. Effects of swimming and cycling exercise intervention on vascular function in patients with osteoarthritis. *Am J Cardiol* 2016; **117**: 141–145.
- Koshihara H, Maeshima E. Effects of exercise intervention on arterial stiffness in middle-aged and older females: evaluation by measuring brachial-ankle pulse wave velocity and cardio-ankle vascular index. *J Phys Ther Sci* 2019; **31**: 88–92.
- Vaitkevicius PV, Fleg JL, Engel JH, *et al.* Effects of age and aerobic capacity on arterial stiffness in healthy adults. *Circulation* 1993; **88** (4 Pt 1): 1456–1462.
- Kobayashi R, Sato K, Takahashi T, *et al.* Arterial stiffness during hyperglycemia in older adults with high physical activity vs low physical activity. *J Clin Biochem Nutr* 2019; **65**: 146–152.
- Seino Y, Nanjo K, Tajima N, *et al.* Report of the Committee on the Classification and Diagnostic Criteria of Diabetes Mellitus. *J Diabetes Investig* 2010; **1**: 212–228.

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.

- Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 2007; **39**: 175–191.
- Gando Y, Yamamoto K, Murakami H, *et al.* Longer time spent in light physical activity is associated with reduced arterial stiffness in older adults. *Hypertension* 2010; **56**: 540–546.
- Okamoto T, Masuhara M, Ikuta K. Combined aerobic and resistance training and vascular function: effect of aerobic exercise before and after resistance training. *J Appl Physiol* (1985) 2007; **103**: 1655–1661.
- Sugawara J, Tomoto T, Tanaka H. Arterial path length estimation for heart-to-brachium pulse wave velocity. *Hypertens Res* 2018; **41**: 444–450.
- Nishiwaki M, Takahara K, Matsumoto N. Arterial stiffness in young adult swimmers. *Eur J Appl Physiol* 2017; **117**: 131–138.
- Algov I, Grushka J, Zarivach R, Alfonsa L. Highly efficient flavin-adenine dinucleotide glucose dehydrogenase fused to a minimal cytochrome c domain. *J Am Chem Soc* 2017; **139**: 17217–17220.
- Zhu W, Zhong C, Yu Y, Li K. Acute effects of hyperglycaemia with and without exercise on endothelial function in healthy young men. *Eur J Appl Physiol* 2007; **99**: 585–591.
- Weiss EP, Royer NK, Fisher JS, Holloszy JO, Fontana L. Postprandial plasma incretin hormones in exercise-trained versus untrained subjects. *Med Sci Sports Exerc* 2014; **46**: 1098–1103.
- Mikus CR, Oberlin DJ, Libla JL, Taylor AM, Booth FW, Thyfault JP. Lowering physical activity impairs glycemic control in healthy volunteers. *Med Sci Sports Exerc* 2012; **44**: 225–231.
- Ekelund U, Brage S, Griffin SJ, Wareham NJ, ProActive UK Research Group. Objectively measured moderate- and vigorous-intensity physical activity but not sedentary time predicts insulin resistance in high-risk individuals. *Diabetes Care* 2009; **32**: 1081–1086.
- Frøsig C, Rose AJ, Treebak JT, Kiens B, Richter EA, Wojtaszewski JF. Effects of endurance exercise training on insulin signaling in human skeletal muscle: interactions at the level of phosphatidylinositol 3-kinase, Akt, and AS160. *Diabetes* 2007; **56**: 2093–2102.
- Roes SD, Alizadeh Dehnavi R, *et al.* Assessment of aortic pulse wave velocity and cardiac diastolic function in subjects with and without the metabolic syndrome: HDL cholesterol is independently associated with cardiovascular function. *Diabetes Care* 2008; **31**: 1442–1444.
- Jahn LA, Hartline L, Rao N, *et al.* Insulin enhances endothelial function throughout the arterial tree in healthy but not metabolic syndrome subjects. *J Clin Endocrinol Metab* 2016; **101**: 1198–1206.
- Iemitsu M, Maeda S, Otsuki T, *et al.* Arterial stiffness, physical activity, and atrial natriuretic peptide gene polymorphism in older subjects. *Hypertens Res* 2008; **31**: 767–774.
- Ahmadi-Abhari S, Sabia S, Shipley MJ, *et al.* Physical activity, sedentary behavior, and long-term changes in aortic stiffness: the Whitehall II Study. *J Am Heart Assoc* 2017; **6**: e005974.
- Yamada S, Inaba M, Goto H, *et al.* Associations between physical activity,

- peripheral atherosclerosis and bone status in healthy Japanese women-
Atherosclerosis 2006; **188**: 196–202.
- 33 Cho JY, Kim KH. Evaluation of arterial stiffness by echocardiography: methodological aspects. *Chonnam Med J* 2016; **52**: 101–106.
 - 34 Wilkinson IB, Franklin SS, Cockcroft JR. Nitric oxide and the regulation of large artery stiffness: from physiology to pharmacology. *Hypertension* 2004; **44**: 112–116.
 - 35 Mah E, Noh SK, Ballard KD, Matos ME, Volek JS, Bruno RS. Postprandial hyperglycemia impairs vascular endothelial function in healthy men by inducing lipid peroxidation and increasing asymmetric dimethylarginine:arginine. *J Nutr* 2011; **141**: 1961–1968.
 - 36 Tsukiyama Y, Ito T, Nagaoka K, Eguchi E, Ogino K. Effects of exercise training on nitric oxide, blood pressure and antioxidant enzymes. *J Clin Biochem Nutr* 2017; **60**: 180–186.
 - 37 Lu CL, Zou X, Orr WC, Chen JD. Postprandial changes of sympathovagal balance measured by heart rate variability. *Dig Dis Sci* 1999; **44**: 857–861.