Arterial stiffness during hyperglycemia in older adults with high physical activity vs low physical activity

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We compared arterial stiffness after glucose intake in active and inactive elderly people with impaired glucose tolerance and clarified whether physical activity was associated with arterial stiffness after ingestion of glucose. Twenty older adults with impaired glucose tolerance were analyzed in a cross-sectional design. Based on the international physical activity questionnaire, participants were divided into the active group (daily step count: 10,175.9 ± 485.9 steps/day, n = 10) or the inactive group (daily step count: 4,125.6 ± 485.9 steps/day, n = 10). Brachial-ankle (systemic) and heart-brachial (aortic) pulse wave velocity and cardio-ankle vascular index (systemic) were increased at 30, 60, and 90 min compared to baseline after a 75-g oral glucose tolerance test in the inactive but not the active group. Heart-brachial pulse wave velocity did not change compared to baseline after a 75-g oral glucose tolerance test in either group. The area under the curve for brachial-ankle pulse wave velocity was associated with daily living activity (r = -0.577, p = 0.008), daily step activity (r = -0.546, p = 0.013), and the daily step count (r = -0.797, p = 0.0001). The present findings indicate that physical activity or inactivity is associated with arterial stiffness following glucose ingestion.

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

Elevated blood glucose (BG) after glucose intake is associated with the incidence of cardiovascular disease1–3 and an increase in arterial stiffness is involved.4,5 In fact, systemic and peripheral arterial stiffness are acutely increased during hyperglycemia.4–7 Increased central, peripheral, and systemic arterial stiffness increases the incidence of cardiovascular disease.8,9 Therefore, suppression of increased arterial stiffness is considered necessary. Adults with pre-diabetes and type 2 diabetes who spend the majority of the day with postprandial hyperglycemia are in a high priority group for preventive lifestyle interventions to prevent cardiovascular disease.10 Additionally, the magnitude of the fluctuation in postprandial glucose over the course of the day has become a major clinical focus of treatment strategies.11 Therefore, increases in arterial stiffness during hyperglycemia should be suppressed in people with high BG levels after meals.

In the older population in Japan, the incidence of cardiovascular disease in adults older than 55 years has increased significantly.12 In Japan, only about 40% of men and 35% of women over the age of 60 currently participate in physical activity.13 Therefore, the Japanese Ministry of Health, Labour, and Welfare published official physical activity guidelines to promote health, called “Healthy Japan 21.” These guidelines are based on scientific evidence, and the main recommendation is “10,000 steps per day.”14

Physical activity decreases arterial stiffness. Iemitsu et al.15 reported lower arterial stiffness in a physically active group compared with a physically inactive group of older Japanese subjects. Vaïtkevicius et al.16 showed that arterial stiffness is lower in physically active persons than in inactive persons. Thus, because physical activity may be important to prevent cardiovascular disease in aged persons, further research is needed to determine the role of “physical activity” in postprandial arterial stiffness in the population older than 55 years. However, whether habitual physical activity actually suppresses increased arterial stiffness during hyperglycemia in older individuals with high postprandial BG (impaired glucose tolerance) is unclear.

The study compared arterial stiffness after glucose ingestion in active and inactive older adults with impaired glucose tolerance and investigated the relationship between arterial stiffness after glucose ingestion and physical activity (calories burned, step count). We hypothesized that active older individuals with impaired glucose tolerance exhibit lower arterial stiffness during hyperglycemia compared with their age-matched inactive counterparts. We also postulated that arterial stiffness during hyperglycemia is correlated with the physical activity index (calories burned, step count).

Materials and Methods

Subjects. The participants were 20 elderly people. Older adults were classified into a habitual exercise group (age, 75.7 ± 1.8 years; n = 10; active) or a non-habitual exercise group (age, 78.5 ± 1.9 years; n = 10; inactive) using the international physical activity questionnaire. The active group had an active lifestyle (≥1 year with exercise; daily step count, 10,175.9 ± 837.8 steps/day, assessed with a triaxial accelerometer), and the inactive group had a sedentary lifestyle (≥1 year without exercise; daily step count, 4,125.6 ± 485.9 steps/day). All participants were normotensive (Japanese standard value: <140/90 mmHg) and non-smokers. 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).17 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 present study was conducted in accor-

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dance with the Declaration of Helsinki and was approved by the ethical committee of the Teikyo University of Science (Table 1).

Sample size. Power analysis was performed with G*Power 3 to obtain an appropriate sample size. According to our previous data, we assumed that the magnitude of the effect on arterial stiffness was a total of 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, 20 participants (10 participants per group) were tested.

Study design. The participants abstained from alcohol, caffeine, and exercise for 24 h, fasted for at least 10 to 12 h, and then reported to a quiet room at a temperature of 25°C. After resting for 15 min, brachial and ankle blood pressure (BP), arterial stiffness, heart rate (HR), high-density lipoprotein (HDL) cholesterol, and BG were measured before baseline (the 75-g OGTT, and brachial and ankle BP, arterial stiffness, HR, and BG were measured 30, 60, and 90 min after a 75-g OGTT (Fig. 1). Physical activity was assessed for 14 days after baseline measurements.

Physical activity. Daily physical activity was measured using a triaxial accelerometer (HJA-750C, Active Style Pro, Omron, Kyoto, Japan). With the exception of sleep and bathing, all participants wore the triaxial accelerometer on their waist for 14 consecutive days, and the data from 7 consecutive days were used for assessment of physical activity [daily living activity (kcal/day), daily step activity (kcal/day), daily step count (steps/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 oscillometric 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 oscillometric device (VaSera VS-100, Colin Medical Technology, Komaki, Japan).

Table 1. Subject characteristics (n = 20)

| Variable                        | Inactive group (n = 10) | Active group (n = 10) | p value |
|---------------------------------|-------------------------|-----------------------|---------|
| Age (years)                     | 78.5 ± 1.9              | 75.7 ± 1.8            | 0.305   |
| Sex                             | 3 male, 7 female        | 3 male, 7 female      | N/A     |
| Height (cm)                     | 150.7 ± 2.7             | 154.0 ± 3.2           | 0.431   |
| Weight (kg)                     | 53.7 ± 3.7              | 57.5 ± 2.6            | 0.420   |
| HDL cholesterol (mg/dl)         | 69.0 ± 4.2              | 69.1 ± 5.2            | 0.983   |
| BMI (kg/m²)                     | 23.5 ± 1.2              | 21.6 ± 2.5            | 0.487   |
| Daily living activity (kcal/day)| 281.7 ± 18.8            | 415.4 ± 29.1          | p<0.01  |
| Daily step activity (kcal/day)  | 91.3 ± 16.9             | 230.7 ± 42.3          | p<0.01  |
| Daily step counts (counts/day)  | 4,125.6 ± 485.9         | 10,175.9 ± 837.8      | p<0.01  |

Values are mean ± SE. BMI, body mass index; HDL, high-density lipoprotein.

Fig. 1. Study design. 75-g OGTT, 75-g Oral Glucose Tolerance Test. IPAQ, International Physical Activity Questionnaires.
BG and HDL cholesterol. 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 coefficient of variation in the laboratory was 5 ± 3%. BG was measured before and 30, 60, and 90 min after the 75-g OGTT. Serum concentrations of HDL cholesterol were determined with standard enzymatic techniques. HDL cholesterol was measured only before the 75-g OGTT.

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 90-min total areas under the curve (AUC) were analyzed using a repeated-measures 2-way analysis of variance (group × time). Significant differences between means were identified using the Bonferroni post-test. Correlations among baPWV AUC and physical activity (daily step count, calories consumed by daily living activities, and daily step activity) were examined using the Pearson product-moment correlation coefficient. Data were statistically analyzed using SPSS ver. 22 (IBM, Armonk, NY). Statistical significance was set at p<0.05.

Results

Summary of group characteristics. The active group had a higher daily living activity (p<0.01), daily step activity (p<0.05), and daily step count (p<0.01) than the inactive group.

Arterial stiffness. baPWV was significantly increased at 30 (p<0.05), 60 (p<0.01), and 90 (p<0.01) min compared to baseline after the 75-g OGTT in the inactive but not the active group. baPWV did not differ between the groups (Fig. 2A). The baPWV AUC was significantly lower in the active than in the inactive group (p=0.01) (Fig. 2B). hbPWV was not different at 30, 60, and 90 min compared to baseline after the 75-g OGTT in either group and showed no significant difference (Fig. 2C). The hbPWV AUC was not different between the groups (Fig. 2D). CAVI was significantly increased at 30 (p<0.01), 60 (p<0.01), and 90 (p<0.01) min compared to baseline after the 75-g OGTT in the inactive but not the active group. CAVI was significantly higher at 30 (p<0.05) min after the 75-g OGTT in the inactive group compared with the active group (Fig. 2E). The CAVI AUC was significantly lower in the active than in the inactive group (p<0.01) (Fig. 2F).

BP and HR. Brachial SBP, MBP, DBP, PP, ankle SBP, MBP, DBP, PP, and HR did not change at 30, 60, and 90 min compared to baseline after the 75-g OGTT in either group, and brachial and ankle SBP, MBP, DBP, PP, and HR showed no significant difference between groups. Ankle SBP was significantly increased at 30 (p<0.05), 60 (p<0.05), and 90 min (p<0.01) compared to baseline after the 75-g OGTT in the inactive but not the active group. Ankle MBP was significantly increased at 60 (p<0.05) and 90 min (p<0.05) compared to baseline after the 75-g OGTT in the inactive but not the active group (Table 2).

BG. BG was significantly increased at 30 (p=0.01), 60 (p<0.01), and 90 (p<0.01) min compared to baseline after the 75-g OGTT in both groups. BG did not differ between the groups (Table 3).

Arterial stiffness and physical activity. baPWV AUC was associated with the daily step count (r=−0.797, p=0.0001, Fig. 3A), daily step activity (r=−0.546, p=0.013, Fig. 3B) and daily living activity (r=−0.577, p=0.008, Fig. 3C).

Discussion

The key novel finding of this study was that baPWV and CAVI were significantly increased compared to baseline after the 75-g OGTT in the inactive but not the active group in older people with impaired glucose tolerance. In addition, baPWV AUC was associated with daily living activity, daily step activity, and daily step counts. These results suggest that physical activity or inactivity is associated with an increase in arterial stiffness following glucose ingestion.

BG levels increase rapidly after glucose intake in both physically active and inactive humans. Weiss et al., Mikus et al., and Kobayashi et al. showed that BG levels after glucose intake do not differ between active and inactive groups. Our current study showed similar results. However, BG levels after a 75-g OGTT were lower in a master athlete runner group (averaged 77 km/week running) than in a healthy control group of middle-aged and older adults. In this study, according to the international physical activity questionnaire, physical activity of elderly individuals includes walking and living activities (housework, cleaning, cooking), and no intense exercise was required. That is, the subject’s exercise intensity was considered to be low. Athlete-level exercise (exercise intensity) may be required to lower BG levels after glucose intake.

Arterial stiffness increases rapidly after eating. In previous studies, aortic rigidity after breakfast did not differ and did not increase in nondiabetic patients compared with diabetic patients, although peripheral arterial stiffness increased in diabetic patients. The present results show that baPWV increased from baseline after the 75-g OGTT in the inactive group, whereas hbPWV, an indicator of the proximal aorta, did not change after the 75-g OGTT in either group. Thus, we conclude that impaired glucose tolerance in older adults is associated with pathological changes in the smaller arteries (mainly leg arterial stiffness), whereas in hyperglycemic conditions, the active group may show less peripheral arterial stiffness than the inactive group. However, in the present study, we did not measure leg arterial stiffness, which is a limitation of this research. Aortic arterial stiffness increases during hyperglycemia in obese people.

Increased arterial stiffness is associated with low levels of HDL cholesterol. Although aortic stiffness increases in middle-aged and older persons with metabolic syndrome after ingesting glucose, stiffness does not change among healthy subjects, and HDL cholesterol is lower in individuals with metabolic syndrome than in healthy subjects. In this study, HDL cholesterol was within the normal level. Thus, changes in aortic arterial stiffness after glucose intake may be associated with HDL cholesterol levels. Detailed examination of the mechanism by which aortic and peripheral arterial stiffness increase after glucose intake will be necessary in the future.

Several studies have reported that arterial stiffness is lower in physically active people compared to sedentary people. For example, Lemitsu et al. reported lower systemic arterial stiffness in a physically active group than in a physically inactive group. Gando et al. and Nishiwaki et al. showed that physical activity reduces arterial stiffness in older adults. The present
results show that baPWV and CAVI were significantly increased from baseline after the 75-g OGTT in the inactive but not the active group in older people with impaired glucose tolerance. Furthermore, in this study, the baPWV AUC was associated with daily living activity, step activity, and the step count during daily living.

The influence of momentum in the improvement of arterial stiffness is considered to be large. The Japanese Ministry of
Health, Labour, and Welfare published official physical activity guidelines to promote health, called “Healthy Japan 21”. The guidelines are based on scientific evidence, and the main recommendation is “10,000 steps per day”.  

A previous study indicated that an increase in arterial stiffness can be prevented by exceeding 6,600 steps/day. In the present study, the daily step counts in the inactive and active groups were 4,125.6 ± 485.9 steps and 10,175.9 ± 837.8 steps, respectively. Therefore, physical activity may be an important factor in suppressing an increase in arterial stiffness during hyperglycemia. Investigation of the detailed mechanism is needed in the future.

Although the present study was not designed to examine possible mechanisms by which physical activity affects arterial stiffness after glucose ingestion, we propose the following explanations. Physical activity or inactivity is associated with lower extremity arterial stiffness and SBP but not with aortic stiffness. Previous studies reported a correlation between arterial stiffness and SBP after glucose ingestion. We found that ankle SBP was significantly increased at 30, 60, and 90 min compared to baseline after the 75-g OGTT in the inactive but not the active group. Thus, an increase in ankle SBP after glucose intake may increase baPWV (perhaps peripheral stiffness).

Table 2. Changes in brachial an ankle SBP, MBP, DBP and PP before (baseline) and after glucose ingestion in both groups

| Variable         | Group      | Baseline         | Post 30 min | Post 60 min | Post 90 min |
|------------------|------------|------------------|-------------|-------------|-------------|
| Brachial SBP (mmHg) | Inactive   | 127.8 ± 2.8      | 130.9 ± 5.0 | 130.3 ± 3.5 | 130.3 ± 3.7 |
|                  | Active     | 128.2 ± 2.1      | 130.3 ± 4.3 | 129.0 ± 6.0 | 132.2 ± 5.6 |
| Brachial MBP (mmHg) | Inactive   | 93.5 ± 2.4       | 93.6 ± 3.1  | 92.4 ± 2.6  | 93.2 ± 2.5  |
|                  | Active     | 95.7 ± 1.8       | 95.8 ± 2.3  | 94.8 ± 3.7  | 97.1 ± 3.6  |
| Brachial DBP (mmHg) | Inactive   | 76.3 ± 2.8       | 74.9 ± 2.6  | 73.5 ± 2.6  | 74.6 ± 2.8  |
|                  | Active     | 79.4 ± 2.5       | 78.5 ± 2.0  | 77.7 ± 3.1  | 79.5 ± 3.2  |
| Brachial PP (mmHg)  | Inactive   | 51.5 ± 3.1       | 56.0 ± 3.7  | 56.8 ± 2.7  | 55.7 ± 4.0  |
|                  | Active     | 48.8 ± 3.4       | 51.8 ± 4.0  | 51.3 ± 4.8  | 52.7 ± 4.4  |
| Ankle SBP (mmHg)  | Inactive   | 150.0 ± 7.3      | 160.5 ± 6.9*| 165.2 ± 5.8*| 164.7 ± 7.8**|
|                  | Active     | 144.7 ± 4.9      | 146.8 ± 5.5 | 142.5 ± 4.7 | 144. ± 6.3  |
| Ankle MBP (mmHg)  | Inactive   | 96.6 ± 2.9       | 102.0 ± 4.7 | 106.5 ± 4.4*| 105. ± 4.8* |
|                  | Active     | 97.4 ± 1.7       | 97.0 ± 2.7  | 94.5 ± 2.0  | 97.3 ± 3.6  |
| Ankle DBP (mmHg)  | Inactive   | 69.9 ± 3.7       | 72.8 ± 4.1  | 77.1 ± 4.2  | 76.4 ± 3.8  |
|                  | Active     | 73.8 ± 1.3       | 72.1 ± 2.0  | 70.5 ± 1.7  | 73.5 ± 2.9  |
| Ankle PP (mmHg)   | Inactive   | 80.1 ± 9.2       | 87.7 ± 4.8  | 88.1 ± 3.8  | 88.3 ± 5.7  |
|                  | Active     | 70.9 ± 5.4       | 74.7 ± 4.9  | 72.0 ± 4.8  | 71.3 ± 5.1  |
| Heart rate (beats/min) | Inactive | 68.0 ± 2.7       | 70.5 ± 3.0  | 67.7 ± 2.7  | 67.3 ± 2.6  |
|                  | Active     | 63.8 ± 2.9       | 63.2 ± 2.4  | 62.2 ± 2.8  | 61.7 ± 2.5  |

Values are mean ± SE. SBP, systolic blood pressure; MBP, mean blood pressure; DBP, diastolic blood pressure; PP, pulse pressure. **p<0.01 and *p<0.05 vs baseline.

Table 3. Changes in blood glucose before (baseline) and after glucose ingestion in both groups

| Variable         | Group      | Baseline | 30 min  | 60 min  | 90 min  |
|------------------|------------|----------|---------|---------|---------|
| Blood glucose (mg/dl) | Inactive   | 105.4 ± 6.3 | 160.8 ± 9.9* | 167. ± 10.0* | 169.4 ± 9.9* |
|                  | Active     | 104.7 ± 5.6 | 154.3 ± 9.3* | 167.7 ± 8.6* | 158.6 ± 9.0* |

Values are mean ± SE. *p<0.01 vs baseline.

Fig. 3. Correlation between arterial stiffness and physical activity. Values are mean ± SE. baPWV, brachial-ankle pulse wave velocity; AUC, area-under-the-curve.
In addition, this study evaluated CAVI, an indicator of BP-independent systemic arterial stiffness. In this study, CAVI after 75-g OGTT was significantly higher in the inactive group than in the age-matched active group. Thus, after considering the influence of BP, we infer that physical activity itself can suppress an increase in arteriosclerosis after glucose intake. CAVI is well known to affect nitric oxide (NO) as a confounding factor. The NO level decreases after glucose ingestion (28). Peripheral endothelial cells play an important role in regulating vascular activity via NO and are involved in the regulation of arterial stiffness. (29) Vascular endothelial function is transiently reduced during hyperglycemia. (40) Moreover, Boyle et al. (41) showed that a decrease in daily physical activity for 5 days (transition from >10,000 to <5,000 steps/day) impairs vascular endothelial function in lower extremity arteries but not brachial arteries. BP is determined by peripheral vascular resistance (e.g., endothelial function). In this study, MBP in the ankles was significantly increased at 60 min compared to baseline after the 75-g OGTT in the inactive but not the active group. Thus, an increase in arteriosclerosis (mainly CAVI) following glucose intake in the inactive group may be associated with a decrease in endothelial function. However, as we have not obtained direct evidence (e.g., Flow Mediated Dilation: FMD) to support this concept, further studies are needed. The present study was limited by the sample size and because our participants were older adults with impaired glucose tolerance; therefore, our findings cannot be generalized to healthy people. Moreover, this study did not include measures such as oxidative stress, insulin levels, and endothelial function (e.g., FMD), which can have an important effect on arterial stiffness. We will examine the mechanism in future studies.

In conclusion, baPWV and CAVI were significantly increased compared to baseline after the 75-g OGTT in the inactive but not the active group in older people with impaired glucose tolerance, and the baPWV AUC and CAVI AUC were lower in the active group than the inactive group. In addition, the baPWV AUC was associated with daily living activity, daily step activity, and the daily step count. These results suggest that physical activity or inactivity is associated with an increase in arterial stiffness following glucose ingestion.

Conflict of Interest

No potential conflicts of interest were disclosed.

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