Association between the Postprandial Glucose Levels and Arterial Stiffness Measured According to the Cardio-ankle Vascular Index in Non-diabetic Subjects

Atsuko Tsuboi¹ ², Chikako Ito¹, Rumi Fujikawa¹, Hideya Yamamoto³ and Yasuki Kihara²

Abstract

Objective Although a relationship between post-challenge hyperglycemia and arterial stiffness has been reported, the relationship between the postprandial glucose levels and cardio-ankle vascular index (CAVI) in non-diabetic subjects is not clear. This study thus evaluated the association between the postprandial glucose levels after a composite meal and the degree of arterial stiffness measured according to CAVI in non-diabetic subjects.

Methods The subjects included 1,291 individuals (655 men and 636 women; mean age, 48.6 years; range, 23-85 years) who underwent medical examinations, including blood tests and CAVI assessments, between October 2005 and April 2012. The 1-hour postprandial glucose levels were determined after a 600-kcal traditional Japanese meal.

Results The CAVI values were significantly higher in the subjects with higher 1-hour postprandial glucose levels (≥140 mg/dL in men; ≥158 mg/dL in women). A simple regression analysis indicated that the CAVI values were significantly correlated with the 1-hour postprandial glucose levels in men (r=0.286, p<0.0001) and women (r=0.228, p<0.0001). After adjusting for age, BMI, systolic blood pressure, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, 1-hour postprandial glucose, homeostasis model assessment of insulin resistance, estimated glomerular filtration rate, and high sensitive C-reactive protein, stepwise multiple regression analysis demonstrated that the 1-hour postprandial glucose level was an independent predictor associated with the CAVI in men (p=0.003) and older women 50 years of age or older (p=0.003).

Conclusion This study demonstrated that the 1-hour postprandial glucose levels are associated with increased CAVI values in non-diabetic men and older women 50 years of age or older.

Key words: arterial stiffness, cardio-ankle vascular index, postprandial glucose

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Introduction

Arterial stiffness has been demonstrated to be a surrogate marker for determining the prognosis of cardiovascular disease (CVD) (1). Increased arterial stiffness is an important risk factor for CVD morbidity and mortality, and it is very important to estimate the degree of arteriosclerosis by examining the level of arterial stiffness in order to take preventative measures against cardiovascular events (2). Arterial stiffness can be evaluated using various methods. Pulse-wave velocity (PWV) is a traditional parameter reflecting the degree of arterial stiffness, although it is affected by the patient’s blood pressure (BP) at the time of measurement (3). As an alternative, the cardio-ankle vascular index (CAVI), which essentially represents the stiffness of the aorta, femoral artery and tibial artery (4), was recently developed. This parameter is essentially BP-independent due

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to adjustment for BP based on the inclusion of a stiffness parameter, β (5, 6). The CAVI values have been reported to be increased in patients with diabetes mellitus (6, 7) and are associated with other risk factors for CVD, such as hypertension (8-10), dyslipidemia (11), and smoking (12), thus reflecting the degree of atherosclerotic changes present in the general population and patients at high risk of CVD.

In individuals with impaired glucose tolerance, as determined by an oral glucose tolerance test (OGTT), postprandial hyperglycemia increases the risk of CVD, independent of the fasting glucose level. The Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) study reported the glucose concentration at two hours on OGTT to be a better predictor of CVD events and all-cause mortality than the fasting glucose level (13). In addition, the Funagata study reported that impaired glucose tolerance is a risk factor for CVD, but not impaired fasting glucose (14). However, most of these studies were based on assessments of the glucose concentration using OGTT (i.e. post-challenge blood glucose). The concern has been raised that OGTT testing does not involve the consumption of a composite meal and post-challenge hyperglycemia may only be a surrogate marker of postprandial hyperglycemia. The extent to which the post-challenge glucose level reflects the glucose concentration after a meal is not clear, as only a few studies have assessed this issue (15, 16).

A relationship between post-challenge hyperglycemia and arterial stiffness has been reported (17-20); however, these results were obtained using OGTT and thus cannot be extrapolated to postprandial (i.e. after a meal) conditions, and the relationship between postprandial hyperglycemia and arterial stiffness in non-diabetic populations is not clear.

The purpose of this study was therefore to evaluate whether postprandial hyperglycemia is associated with the degree of atherosclerosis in non-diabetic subjects. We examined the association between the 1-hour postprandial glucose levels observed after eating a 600 kcal traditional Japanese meal and the degree of arterial stiffness measured according to the CAVI in non-diabetic Japanese adults.

Materials and Methods

Subjects

The study subjects consisted of 1,291 individuals (655 men and 636 women) who underwent general health examinations between October 2005 and April 2012 at Grand Tower Medical Court. All participants were non-diabetic, and patients with a fasting plasma glucose level of ≥126 mg/dL or a hemoglobin A1c (HbA1c) level of ≥6.5% and those under treatment for diabetes mellitus were excluded. Another exclusion criterion was a previous history of CVD. The study protocol was approved by the Medical Ethics Committee of the Grand Tower Medical Court Life Care Clinic, and all subjects provided their written informed consent prior to inclusion.

Anthropometric measurements and laboratory methods

Blood samples were obtained after overnight fasting. BP was measured in the sitting position on the right arm. The body mass index (BMI) was calculated based on the patient’s height (m) and body weight (kg). The serum lipid levels were determined according to an enzymatic method [total cholesterol and triglycerides, low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol] using a Hitachi 7180 analyzer (Hitachi Medical, Tokyo, Japan). The plasma glucose levels were measured using the hexokinase method. The insulin levels were measured using a chemiluminescent enzyme immunoassay. The insulin resistance homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using a homeostasis model assessment, as follows: fasting insulin (μU/mL) × (22.5 e^{0.0177} - 1.094) for males and females (21). The HbA1c levels were determined according to an enzymatic method and as the National Glycohemoglobin Standardization Program (NGSP) values (22). The estimated glomerular filtration rate (eGFR) was used to estimate the kidney function calculated according to the following formulas: males: eGFR (mL min⁻¹ 1.73 m⁻²)=194×(serum creatinine)⁻¹.094 × age⁻⁰.²⁰⁷; females: eGFR=194×(serum creatinine)⁻¹.094 × age⁻⁰.²⁰⁷×0.739. The serum concentrations of high-sensitivity C-reactive protein (hs-CRP) were determined using a latex turbidimetric immunoassay. The serum levels of high-molecular-weight (HMW) adiponectin were measured using an enzyme-linked immunosorbent assay (Sekisui Medical, Tokyo, Japan) based on a monoclonal antibody for humans (23). The abdominal visceral fat area (VFA) and subcutaneous fat area (SFA) were measured using low-dose X-ray computed tomography at the level of the navel with a Hitachi Robusto (Hitachi Medical).

After the medical examinations, all subjects ingested a 600 kcal traditional Japanese meal. The composition of the meal was 20-21% protein, 15-23% fat and 56-65% carbohydrate with 3.5-4.0 g salt, which is typical for Japanese adults. Blood samples were also drawn after the start of the meal, and the plasma glucose level, in the form of the 1-hour postprandial glucose level, was measured.

Measurement of the CAVI

The CAVI values were recorded using a Vaser VS-1000 vascular screening system (Fukuda Denshi, Tokyo, Japan), as previously described (2). Briefly, cuffs were applied to the four extremities on both upper arms and ankles, electrocardiogram leads were attached to both wrists and a phonocardiogram was placed at the right sternal border in the second intercostal space. The subjects rested in the supine position for at least 10 minutes, and measurements were then performed automatically. The CAVI was calculated according to the following formula: CAVI=a[(2p/ΔP)×ln(Ps/Pd)×PWV]⁻¹+b, where Ps and Pd are systolic and diastolic BP, respectively, in mmHg, ΔP is Ps-Pd, p is the blood density and a and b are constants to match the aortic PWV. This
Table 1. Clinical Characteristics of the Subjects.

<table>
<thead>
<tr>
<th></th>
<th>Men (n = 655)</th>
<th>Women (n = 636)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>48.5 ± 10.7</td>
<td>48.7 ± 12.3</td>
<td>0.6888</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.0 ± 3.4</td>
<td>21.1 ± 3.1</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>122.8 ± 15.0</td>
<td>117.0 ± 15.5</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>77.7 ± 9.9</td>
<td>72.2 ± 9.9</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>120.0 (82 - 121)</td>
<td>71.0 (52.0 - 99)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>56.4 ± 13.8</td>
<td>69.4 ± 15.3</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>126.1 ± 31.6</td>
<td>120.2 ± 31.5</td>
<td>0.0008</td>
</tr>
<tr>
<td>VFA (cm²)</td>
<td>90.8 ± 46.9</td>
<td>41.5 ± 29.8</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>SFA (cm²)</td>
<td>131.9 ±62.6</td>
<td>147.7 ± 70.0</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HMW adiponectin (µg/mL)</td>
<td>1.2 (0.5 - 2.1)</td>
<td>3.6 (1.9 - 5.2)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.5 ± 0.5</td>
<td>5.4 ± 0.3</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.75 (1.14 - 2.60)</td>
<td>1.22 (0.86 - 1.80)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Fasting plasma glucose (mg/dL)</td>
<td>105.1 ± 14.8</td>
<td>95.9 ± 9.8</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>1-hour postprandial glucose (mg/dL)</td>
<td>133.8 ± 35.7</td>
<td>133.8 ± 29.1</td>
<td>0.9925</td>
</tr>
<tr>
<td>eGFR</td>
<td>76.3 ± 13.4</td>
<td>78.4 ± 15.0</td>
<td>0.0072</td>
</tr>
<tr>
<td>hs-CRP (mg/L)</td>
<td>0.076 (0.04 - 0.158)</td>
<td>0.038 (0.023 - 0.078)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hypertension (n, %)</td>
<td>114 (17.4)</td>
<td>63 (9.9)</td>
<td>0.0312</td>
</tr>
<tr>
<td>Hyperlipidemia (n, %)</td>
<td>74 (11.3)</td>
<td>48 (7.5)</td>
<td>0.6638</td>
</tr>
<tr>
<td>Smoking (n, %)</td>
<td>214 (32.7)</td>
<td>51 (8.1)</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Data are presented as number of subjects, mean ± standard deviation, or median (interquartile range).
BMI: body mass index, BP: blood pressure, HDL: high-density lipoprotein, LDL: low-density lipoprotein, VFA: visceral fat area, SFA: subcutaneous fat area, HMW: high molecular weight, HOMA: homeostasis model assessment for insulin resistance, eGFR: estimated glomerular filtration rate, hs-CRP: high-sensitivity C-reactive protein, CAVI: cardio-ankle vascular index

Results

Table 1 shows the clinical characteristics of the subjects. The study subjects included 1,291 individuals comprised of 655 men (mean age, 48.5 years; range, 23-84 years) and 636 women (mean age, 48.7 years; range 23-85 years). The serum triglycerides, LDL cholesterol, hs-CRP, fasting plasma glucose and HbA1c levels and BMI, systolic and diastolic BP, HOMA-IR, VFA and CAVI values were significantly higher in the men than in the women. In contrast, the HDL cholesterol and HMW adiponectin levels and SFA and eGFR values were significantly lower in the men than in the women. The 1-hour postprandial glucose levels were not significantly different between the men and women.

Fig. 1 shows the CAVI values according to the quintiles (Q) of the 1-hour postprandial glucose level. We classified the subjects according to five quintiles for men and women respectively; therefore, the classification differed between the sexes. In men, the quintiles of the 1-hour postprandial glucose level were classified as follows: Q1, ≤106; Q2, 107-122; Q3, 123-139; Q4, 140-157; and Q5, ≥158 mg/dL. The CAVI values in the Q4 and Q5 groups were significantly higher in the men than in the women. The 1-hour postprandial glucose levels were not significantly different between the men and women.

Statistical analysis

Categorical variables are presented as numbers (percentage) and continuous variables are presented as the mean ± standard deviation or median (interquartile range). Differences in the clinical variables between men and women were evaluated using Student’s t-test or the Wilcoxon rank-sum test. As the levels of triglycerides, HOMA-IR and hs-CRP were not normally distributed, logarithmic transformation was performed for the analysis. The association between the CAVI values and the postprandial glucose quintiles was evaluated using Dunnett’s test, taking multiplicity into account. A simple regression analysis was performed to evaluate the relationships between the CAVI values and various clinical parameters in both sexes. A stepwise multiple regression analysis was performed in the younger (under 50 years of age) and older (50 years of age or older) women because the median age of menopause in Japanese women is almost 50 years (28). Comparisons of the VFA, HMW adiponectin, and hs-CRP levels according to the 1-hour postprandial glucose levels were performed using Student’s t-test. All statistical analyses were performed using the JMP (version 8) statistical software package (SAS Institute, Cary, USA). A p value of <0.05 was considered to be statistically significant.
higher than those observed in the Q1 group in men (p=0.01 and p<0.0001, respectively). In women, the quintiles of the 1-hour postprandial glucose level were classified as follows: Q1, ≤109; Q2, 110-124; Q3, 125-139; Q4, 140-157; and Q5, ≥158 mg/dL. The CAVI values in the Q5 group were significantly higher than those observed in the Q1 group in women (p<0.0001).

The simple regression analysis (Table 2) showed that the CAVI values were significantly correlated with the postprandial glucose levels in both men (r=0.286, p=0.0001) and women (r=0.228, p=0.0001). As for other clinical variables, the CAVI values were significantly correlated with age, BMI, systolic and diastolic BP, VFA, SFA, HMW adiponectin, fasting plasma glucose, HbA1c, HOMA-IR, eGFR and hs-CRP in men and age, BMI, systolic and diastolic BP, triglycerides, LDL cholesterol, VFA, SFA, fasting plasma glucose and HbA1c in women.

Table 3 shows the results of the stepwise multiple regression analysis of the CAVI and clinical variables in both men and women. In men, the 1-hour postprandial glucose level remained an independent predictor of an increased CAVI value (p=0.003), in addition to age, BMI, systolic BP and HDL cholesterol. In women, only age, BMI, triglycerides and HOMA-IR were found to be independently associated with the CAVI values. A stepwise multiple regression analysis was performed to determine the predictors of the CAVI values in the groups of younger and older women. In the group of older women, the 1-hour postprandial glucose level...
remained an independent factor for an increased CAVI value (p=0.003), in addition to age, BMI, systolic BP and triglycerides. Hence, in the group of younger women, age, BMI and triglycerides remained independent factors for an increased CAVI value, but not the 1-hour postprandial glucose level (Table 4).

Fig. 2 shows the results of the comparisons of the VFA, HMW adiponectin and hs-CRP levels according to the 1-hour postprandial glucose levels. The 1-hour postprandial glucose levels were classified as follows: normal group<140, high group≥140 mg/dL in men; and normal group<158, high group≥158 mg/dL in women. In both sexes, the VFA and hs-CRP levels in the high group were significantly higher than those observed in the normal group. In contrast, the HMW adiponectin levels were not significantly different between the two groups.

### Discussion

In this study, we evaluated whether postprandial hyperglycemia is associated with the degree of atherosclerosis in non-diabetic subjects. The important difference in our study from other glucose-loading studies is that we prepared a 600-kcal traditional Japanese meal for all 1,291 subjects that met the characteristics of a typical daily meal for Japanese adults and subsequently evaluated the association between the postprandial glucose levels and degree of arterial stiffness measured according to the CAVI. Our results showed the 1-hour postprandial glucose levels to be positively correlated with the CAVI values in both sexes and an independent predictor of increased CAVI values in men and older women, after adjusting for age and other variables. These findings indicate that postprandial hyperglycemia is one of the most important factors significantly associated with the extent of atherosclerosis in non-diabetic subjects.

This study is meaningful and original for the following reasons. First, the postprandial glucose levels were determined 60 minutes after a meal. The glucose concentration peaks at approximately 60 minutes after the start of a meal in healthy individuals (29); therefore, we measured the 1-hour postprandial glucose level. The 1-hour postprandial glucose level may reflect the effects of plasma glucose excursions associated with meals in everyday life among non-diabetic subjects and differs from the glucose concentrations measured on OGTT. Second, all subjects ingested a 600-kcal traditional Japanese meal, the composition of which was typical for Japanese adults. According to the National Health and Nutrition Survey of Japan conducted in 2010, the average energy intake for Japanese individuals 20 years of age or older is 1,859 kcal, while that for main nutrients is 68.1 g (14.7%) of protein, 52.7 g (25.5%) of fat, and 259.8 g (55.9%) of carbohydrate. Furthermore, no reports are available on the relationship between the postprandial glucose level measured after a composite meal and the degree of arterial stiffness determined according to the CAVI in non-diabetic subjects. Third, the number of non-diabetic

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### Table 3. Stepwise Multiple Regression Analysis between CAVI and Clinical Variables in Men and Women.

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th></th>
<th>Women</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>β</td>
<td>p value</td>
<td>β</td>
<td>p value</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.049</td>
<td>&lt; 0.0001</td>
<td>0.052</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>-0.077</td>
<td>&lt; 0.0001</td>
<td>-0.107</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>0.005</td>
<td>0.12</td>
<td>0.794</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>-0.008</td>
<td>0.01</td>
<td>0.003</td>
<td>0.003</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>0.003</td>
<td>0.001</td>
<td>-0.313</td>
<td>0.016</td>
</tr>
<tr>
<td>1-hour postprandial glucose (mg/dL)</td>
<td>0.43</td>
<td>0.54</td>
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</table>

§ Log-transformed values

### Table 4. Stepwise Multiple Regression Analysis between CAVI and Clinical Variables in Younger and Older Women.

<table>
<thead>
<tr>
<th></th>
<th>Younger women (n=274)</th>
<th></th>
<th>Older women (n=362)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>β</td>
<td>p</td>
<td>β</td>
<td>p</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.033</td>
<td>&lt; 0.0001</td>
<td>0.056</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>-0.073</td>
<td>&lt; 0.0001</td>
<td>-0.115</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>0.006</td>
<td>0.39</td>
<td>0.713</td>
<td>0.002</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>0.828</td>
<td>&lt; 0.0001</td>
<td>0.004</td>
<td>0.03</td>
</tr>
<tr>
<td>1-hour postprandial glucose (mg/dL)</td>
<td>0.23</td>
<td>0.45</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The age of younger women was under 50, and the age of older women was 50 or older. Abbreviations are the same as in Table 1.

§ Log-transformed values
subjects was sufficiently large, and there were no differences in age or the 1-hour postprandial glucose levels between men and women. Fourth, the CAVI was measured as a marker of arterial stiffness in this study. The CAVI is a newly developed marker of arterial stiffness, considered to reflect the degree of atherosclerosis. The CAVI is easily measured clinically with good reproducibility and is a useful parameter for physicians and in subjects with masked hypertension because it is not affected by the patient’s blood pressure at the time of measurement.

Our findings indicate that postprandial hyperglycemia plays an important role in increasing the CAVI values in older women. In women, menopause may affect the progression of atherosclerosis. Takahashi et al. (30) reported that menopause augments the age-related increase in arterial stiffness. The median age of menopause among Japanese women has been reported to be almost 50 years (28). We therefore divided the subjects into two groups using the threshold of 50 years of age in this study. However, we were unable to clearly obtain data for the menopause status. Further studies are thus needed to evaluate the association between postprandial hyperglycemia and arterial stiffness measured using the CAVI in non-diabetic postmenopausal women.

The American Diabetes Association has stated that the issue of whether postprandial hyperglycemia is an independent risk factor for CVD remains controversial and requires additional studies (29). Few studies have specifically evaluated the cardiovascular risks associated with postprandial hyperglycemia in patients with type 2 diabetes. The Diabetes Intervention Study recently reported the role of postprandial blood glucose in predicting cardiovascular events in newly diagnosed type 2 diabetic patients (15). Elevation of the blood glucose level after breakfast, but not the fasting blood glucose level, has been found to predict myocardial infarction and mortality, and The San Luigi Gonzaga Diabetes Study demonstrated the independent predictive power of postprandial glucose on cardiovascular events in patients with type 2 diabetes (16). In these studies, the study populations consisted of treated type 2 diabetes mellitus patients, and the postprandial glucose levels were measured under different conditions because the composition of the meals differed in each subject. In contrast, our study included only non-diabetic subjects, all of whom ingested a standardized 600-kcal Japanese meal. In addition, the CAVI values were significantly correlated with the 1-hour postprandial glucose levels in both sexes, and the 1-hour postprandial glucose level was found to be one of the most significant factors in-

![Graph](image-url)

Figure 2. Comparison of the VFA, HMW adiponectin and hs-CRP levels according to the 1-hour postprandial glucose levels in men and women. The 1-hour postprandial glucose levels were classified as follows: normal group <140, high group ≥140 mg/dL in men; and normal group <158, high group ≥158 mg/dL in women. Black bar: VFA in the normal group. Gray bar: VFA in the high group. The VFA and hs-CRP levels were significantly higher in the high group than in the normal group. There were no significant differences in the HMW adiponectin levels between the two groups. *p<0.0001, **p<0.001, ***p<0.05, †Log-transformed values.
dependently associated with the CAVI values in men and older women. We therefore suggest that our findings provide potentially useful information regarding the atherosclerotic and cardiovascular risks associated with postprandial hyperglycemia.

Several studies have reported the mechanism by which postprandial hyperglycemia increases vascular stiffness. Nitric oxide (NO) is considered to play an important role in relaxing vascular smooth muscle cells by reducing the probability of calcium channel-dependent activation of the sarcoplasmic reticulum, which in turn decreases Ca$^{2+}$ influx (31). Acute hyperglycemia is associated with increased oxidative stress, which inactivates NO in vitro (32, 33), and the levels of oxidative stress under intermittently high glucose conditions are significantly greater than those observed under constantly high glucose conditions in vitro (34). The CAVI is a sensitive physiological index for monitoring the degree of stress on the arterial wall induced by a high level of blood glucose. The results of this study indicate that the intermittent hyperglycemia observed after meals in everyday life induces impaired NO bioactivity and impacts the increase in the CAVI, even in non-diabetic populations.

The VFA and hs-CRP values were significantly higher in the high postprandial glucose group than in the normal group in both sexes in the current study. The VFA is considered to play an important role in the onset of metabolic syndrome and atherosclerosis (35, 36), which is affected by age, gender and the level of obesity (37, 38). CRP is an inflammatory biomarker and strong independent predictor of diabetes (39) reported to be strongly correlated with metabolic risk factors (40). However, there were no significant differences in the HMW adiponectin levels between the normal and high postprandial glucose groups among both men and women in this study. Adiponectin is secreted by adipose tissue, which has anti-diabetic, anti-atherosclerotic, and anti-inflammatory biofunctions (41, 42). The HMW adiponectin level is a more useful marker for evaluating the degree of insulin resistance and metabolic syndrome (43). The subjects in this study were non-diabetic and relatively young. In addition, few of the subjects were excessively obese, and the VFA in women was half that observed in men. We speculate that these characteristics may have affected the relationship between postprandial hyperglycemia and adiponectin noted in this study.

The BMI values were negatively correlated with the CAVI values in men and women in this study. A high CAVI is associated with obesity, although some studies have reported a negative correlation between the BMI and CAVI. Park et al. reported that the amount of visceral adipose tissue and epicardial adipose tissue exhibits a significant correlation with the CAVI, whereas BMI is negatively correlated with the CAVI (44). Meanwhile, Choi et al. reported that visceral obesity is a possible risk factor for arterial stiffness, rather than general obesity (45). In the current study, the proportion of subjects with general obesity (BMI≥25) was low (37.0% in men and 14.3% in women), the VFA in women was half that observed in men and the SFA in women was higher than that seen in men. We again speculate that these characteristics and/or the number of obese subjects with lower VFA values in this study may have affected the relationship between the BMI and CAVI values.

The HDL cholesterol levels in men and women and the LDL cholesterol and triglycerides levels in men did not display any significant associations with the CAVI values in this study. The CAVI and dyslipidemia are likely not closely connected, and dyslipidemia per se does not immediately increase arterial stiffness. Takaki et al. reported that the CAVI has a poor relationship with both the total and LDL cholesterol levels, and there is no observed correlation between the CAVI values and triglyceride and HDL cholesterol levels (9). Satoh et al. reported that an increased CAVI is significantly correlated with the triglycerides and HDL cholesterol levels in men, but not women (46). This observation may reflect a difference in the pathophysiological mechanisms underlying dyslipidemia between men and women.

The limitations of this study are that causality between postprandial glucose and arterial stiffness could not be established because our data were cross-sectional. Longitudinal and interventional studies are thus needed to evaluate whether a reduction in the postprandial glucose level decreases arterial stiffness and helps to prevent future CVD events. Additionally, although the rate of active smoking was higher for men than for women (32.7% and 8.1%, respectively), there were no significant correlations between active smoking and the CAVI values in men (r=0.023, p=0.2436) or women (r=0.013, p=0.3452). Kubozono et al. reported that smoking is associated with a significant increase in arterial stiffness as measured by according to the brachial artery PWV and CAVI (12). Therefore, the results of this study may have been affected by the fact that ex-smokers were included as smokers. Unfortunately, we were unable to obtain details for these patients. Furthermore, we found that 10.7% and 7.1% of the subjects had been treated with medications for hypertension and dyslipidemia, respectively. Several blood pressure-lowering (47, 48) and lipid-lowering (49, 50) agents have been reported to decrease the CAVI. These factors may have influenced the CAVI values in this study and should be taken into account in future studies.

In conclusion, we demonstrated that the 1-hour postprandial glucose level measured after the consumption of a standardized composite meal (a 600-kcal traditional Japanese meal) is associated with increased CAVI values in non-diabetic men and older women 50 years of age or older. The results of this study indicate that the occurrence of postprandial hyperglycemia in everyday life may demonstrate an important association with the degree of atherosclerosis in non-diabetic subjects.

The authors state that they have no Conflict of Interest (COI).
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