# Pulse Wave Velocity as an Indicator of Atherosclerosis in Impaired Fasting Glucose

## The Tanno and Sobetsu Study

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**OBJECTIVE** — Brachial-ankle pulse wave velocity (baPWV), as an indicator of atherosclerosis in impaired fasting glucose (IFG), was studied in 232 subjects randomly selected from inhabitants of two rural communities in Japan.

**RESEARCH DESIGN AND METHODS** — BMI, systolic blood pressure (SBP), fasting blood glucose (FBS), lipid parameters, ankle brachial pressure index (ABI), and baPWV were measured in each subject. ABI and baPWV were measured using the recently developed device, form ABI/PWV. The subjects were divided into three groups according FBS level: a normal group consisting of subjects with FBS <110 mg/dl, an IFG group consisting of subjects with FBS 110–125 mg/dl, and a diabetic group consisting of subjects with FBS ≥126 mg/dl and subjects taking hypoglycemic agents. The parameters in the three groups were compared.

**RESULTS** — It was found that the baPWV value increased with increasing plasma glucose level. Significant differences were found between the baPWV values in the normal and IFG groups (1,518 vs. 1,673 cm/s, $P = 0.01$) and in the normal and diabetic groups (1,518 vs. 1,771 cm/s, $P < 0.0001$). The results of multiple regression analysis showed that FBS was closely related to baPWV as well as to age and SBP.

**CONCLUSIONS** — The relationship between IFG and atherosclerosis remains controversial. Further studies are needed to evaluate whether strict control of blood glucose level in patients with IFG will result in the prevention of atherosclerosis progression.

*Diabetes Care* **26:437–440, 2003**

Much interest has been shown over the past few decades in aortic pulse wave velocity (PWV) as a noninvasive method for assessing atherosclerosis, and there have been many recent reports on PWV and the development of atherosclerotic disease (1–4). In this study, we investigated the usefulness of PWV as an indicator of early-stage atherosclerosis in impaired fasting glucose (IFG) in inhabitants of two rural communities in Japan by using a new device for measuring PWV.

## RESEARCH DESIGN AND METHODS

— The subjects included 232 men (mean age 65.2 ± 9.5 years) selected from 1,479 inhabitants of the towns of Tanno and Sobetsu in Hokkaido who underwent medical examinations in 2000. Systolic blood pressure (SBP), diastolic blood pressure, BMI, and levels of fasting blood glucose (FBS), $HbA_{1c}$, total cholesterol, triglyceride, and HDL were measured in all subjects. Bilateral brachial-ankle PWV (baPWV) was measured in all subjects using a new device, form ABI/PWV (BP-203RPE; Nihon Colin).

Form ABI/PWV is a device with four cuffs that can simultaneously measure blood pressure levels in both arms and both legs and automatically calculate the ankle brachial pressure index (ABI). This device can also record pulse waves by sensors in the cuffs, store data on the start point of each pulse wave in the right arm and both legs in memory, record the time difference between transmission time to arm and transmission time to ankle as "transmission time," calculate the transmission distance from the right arm to each ankle according to body height, and automatically compute and output the baPWV values by transmission time and transmission distance. This device is useful for mass medical examinations and mass studies because it enables measurements of ABI and baPWV in a short time without influence of the operator's technique. Figure 1 shows a relationship between left and right baPWV. Since there was a significant positive correlation between left and right baPWV ($r = 0.91$, $P < 0.0001$), we used a mean right/left baPWV value during analysis.

The subjects were divided into three groups based on levels of FBS reported by the American Diabetes Association (ADA) (5): a normal group consisting of 185 subjects with FBS <110 mg/dl, an IFG group consisting of 24 subjects with FBS of ~110–125 mg/dl, and a diabetic group consisting of 23 subjects with FBS ≥126 mg/dl and subjects taking hypoglycemic agents. The parameters in the three groups were compared.

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Received for publication 22 April 2002 and accepted in revised form 5 November 2002.
**Abbreviations:** ABI, ankle brachial pressure index; ADA, American Diabetes Association; baPWV, brachial-ankle pulse wave velocity; FBS, fasting blood glucose; IFG, impaired fasting glucose; PWV, pulse wave velocity; SBP, systolic blood pressure.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

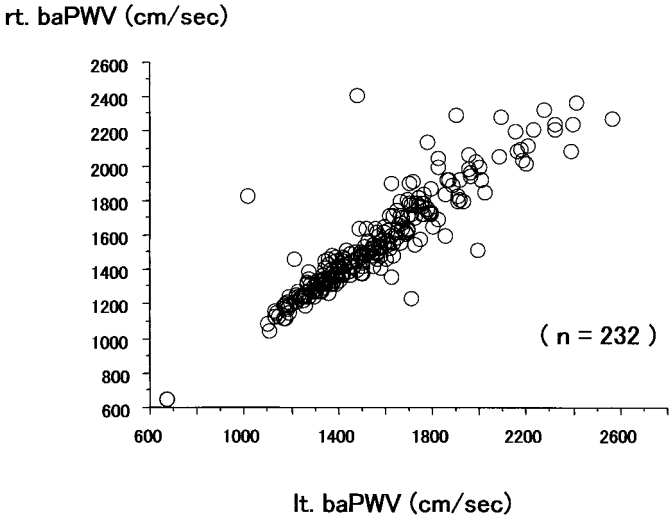


**Figure 1**—*Correlation between left (lt.) and right (rt.) baPWV. There was a significant positive correlation between left and right baPWV* (r = *0.91,* P < *0.0001).*

In this study, the subjects were randomly selected according to the ID number of the medical examination, and the 10% prevalence of diabetes was compatible with the known prevalence of diabetes in Japan.

The Statview package (Version 5.0J) was used for statistical analysis. All numerical values are expressed as means ± SD. The unpaired *t* test was used for examination of intergroup differences and frequency comparison. The significance level was set at $P < 0.05$.

**RESULTS** — Table 1 shows the characteristics of the subjects in the normal, IFG, and diabetic groups. Average age and total cholesterol were higher in the diabetic group than in the normal group, and BMI and SBP were higher in the IFG group than in the normal group.

There were no subjects with symptoms of arterial obstruction, and only 2.2% of the subjects had ABI <0.9. There was no significant correlation between FBS and ABI in all subjects, and there was no significant intergroup difference in the value of ABI.

However, there was a significant positive correlation between FBS and mean right/left baPWV ($r = 0.329$, $P < 0.0001$) (Fig. 2). There was also a significant positive correlation between $HbA_{1c}$ and mean right/left baPWV ($r = 0.289$; left baPWV: $r = 0.281$, $P < 0.0001$) (Fig. 2). A comparison of the values of baPWV in the three groups showed that the baPWV value increased with increasing plasma glucose level (Fig. 3). Significant differences were found between the baPWV values in the normal and IFG groups (1,518 vs. 1,673 cm/s, $P = 0.01$) and in the normal and diabetic groups (1,518 vs. 1,771 cm/s, $P < 0.0001$). The results of multiple regression analysis showed that FBS was closely related to baPWV, as well as to age and SBP (Table 2), suggesting that FBS is independently related to baPWV.

**CONCLUSIONS** — Much interest has been shown over the past few decades in PWV as a noninvasive method for assessing atherosclerotic diseases. It has been reported that both the frequency of calcification of the aorta, as seen on computed tomography images, and carotid intima-media thickness, as measured on ultrasonography images, increase as PWV increases (6). Shirakawa et al. (7) examined the relationship between PWV and coronary and cerebral arteries in autopsy and reported that the more advanced the atherosclerosis, the higher the PWV value. It has been shown in many studies that the values of PWV in subjects with hypertension and diabetes are higher than those in normal subjects (8–12). Blacher et al. (9) reported that the value of PWV in subjects with atherosclerotic disease was significantly higher than that in normal subjects. They also reported that the higher the PWV value, the higher the risk of cardiovascular disease in the normal subjects. It has been pointed out in several reports that atherosclerosis first develops in the aorta and then develops in the cerebral and coronary artery (1–3,7,13). PWV has therefore been reported to be a useful method for assessing early-stage atherosclerosis.

However, past methods used for measuring carotid-femoral PWV have required complex techniques and have not



**Table 1**—*Basal characteristics of three groups, classified by plasma glucose level*

| | Normal group | IFG group | Diabetic group |
|---|---|---|---|
| *n* | 185 | 24 | 23 |
| Age (years) | 64.7 ± 10.1 | 65.6 ± 5.9 | 69.2 ± 6.9* |
| BMI (kg/m$^2$) | 23.3 ± 2.8 | 25.0 ± 2.8† | 23.5 ± 2.7 |
| SBP (mmHg) | 129.6 ± 18.5 | 138.5 ± 16.3* | 130.7 ± 18.8 |
| DBP (mmHg) | 77.9 ± 11.1 | 80.3 ± 10.5 | 74.3 ± 10.9 |
| FBS (mg/dl) | 94.6 ± 6.6 | 115.5 ± 5.0† | 143.4 ± 41.3† |
| $HbA_{1c}$ (%) | 5.0 ± 0.3 | 5.6 ± 0.3† | 6.6 ± 1.2† |
| Total cholesterol (mg/dl) | 186.4 ± 30.6 | 186.8 ± 34.7 | 200.7 ± 31.4* |
| Triglyceride (mg/dl) | 116.6 ± 70.7 | 144.8 ± 111.1 | 125.3 ± 60.0 |
| HDL cholesterol (mg/dl) | 53.3 ± 13.7 | 47.9 ± 12.4 | 55.9 ± 16.9 |

Data are means ± SD. Normal group: FBS <110 mg/dl; IFG group: FBS 110–125 mg/dl; diabetic group: FBS ≥126 mg/dl or therapy for diabetes. *$P < 0.05$, †$P < 0.01$ vs. normal group. DBP, diastolic blood pressure.

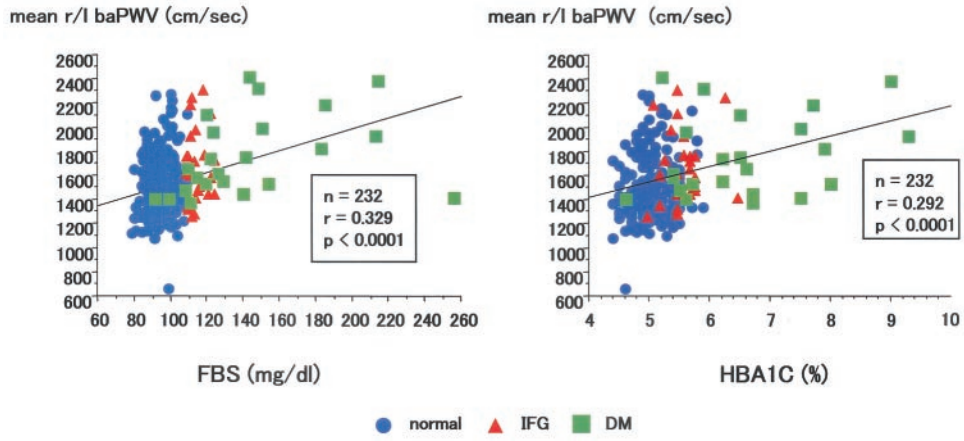


**Figure 2**—*Correlation between baPWV and FBS and $HbA_{1c}$. r/l, right/left. There was a significant positive correlation between FBS and mean baPWV (r = 0.329, P < 0.0001). There was also a significant positive correlation between $HbA_{1c}$ and baPWV (r = 0.281, P < 0.0001).*

demonstrated reproducibility. Form ABI/PWV, a recently developed device, enables simultaneous measurements of blood pressure levels of limbs and can calculate ABI and baPWV in a short time. Moreover, reproducible results can be obtained regardless of the operator's technique (intraobserver reproducibility is 10% [14]). This measurement method is different from the method of carotid-femoral PWV, and it is not simple to compare values of baPWV with values of PWV obtained by using past methods. However, it has been reported that the value of baPWV has a significant positive correlation with the value of PWV obtained by using the past method. It has also been reported that the value of baPWV has a positive correlation with carotid IMT obtained by us (15). Therefore, this test might predict the risk of atherosclerosis and that its high values may mean that the atherosclerotic process is already well established.

In this present study, we measured the values of baPWV in 232 men randomly selected from 1,479 inhabitants of two rural communities in Japan. The values of blood pressure and lipid parameters in the subjects were similar to the standard values in Japanese men. Therefore, the values of baPWV in the subjects are thought to reflect the values in the general population of Japanese men.

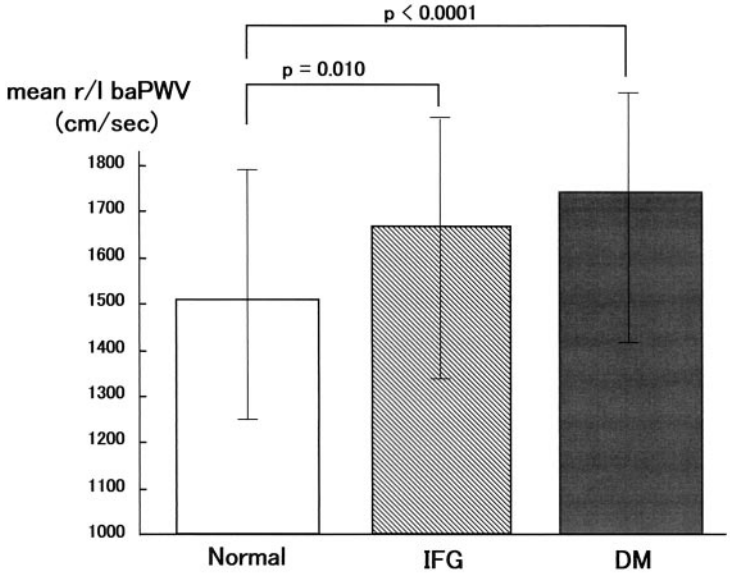


**Figure 3**—*Value of baPWV in three groups classified by plasma glucose level. Normal: FBS <110 mg/dl; IFG: FBS 110–125 mg/dl; DM (diabetes mellitus): FBS ≥126 mg/dl or therapy for diabetes. r/l, right/left. The higher the plasma glucose level, the higher the baPWV value. Significant differences were found between the baPWV values in the normal and IFG groups (1,518 vs. 1,673 cm/s; P = 0.01) and in the normal and DM groups (1,518 vs. 1,771 cm/s; P < 0.0001).*

Since none of the subjects in the present study underwent an oral glucose tolerance test, a diagnosis of impaired glucose tolerance could not be made; therefore, IFG based on ADA criteria (5) was used. It was found that the baPWV value increased with increasing plasma glucose level, and a significant difference was found between the baPWV values in the normal and IFG groups. It was therefore thought that atherosclerosis had already occurred in the IFG group. It has been reported that atherosclerosis has already developed in subjects with IFG as well as in those with diabetes, and that the risk of cardiovascular disease occurring in subjects with IFG is higher than that in normal subjects (16–18). Since borderline risk factors, such as high-normal blood pressure level and overweight (not obese), often coexist with IFG, it is thought that development of atherosclerosis in subjects with IFG is due to their combined effect. In this present study, we found that BMI and SBP were higher in the IFG group than in the normal group, and these high levels may be related to the development of atherosclerosis. However, the results of multiple regression analysis showed that FBS was closely related to baPWV regardless of age, SBP, and BMI. It is thought that plasma glucose level is independently related to atherosclerosis in subjects with IFG. The rela-

**Table 2—*Multiple regression analysis of the relationship between baPWV and other associated variables***

| | Regression coefficient | SE | Standardized coefficient | *t* value | *P* value |
|---|---|---|---|---|---|
| Age | 12.304 | 1.549 | 0.413 | 7.941 | <0.0001 |
| SBP | 5.874 | 0.828 | 0.376 | 7.093 | <0.0001 |
| FBS | 3.031 | 0.682 | 0.220 | 4.443 | <0.0001 |
| Total cholesterol | 0.570 | 0.480 | 0.063 | 1.187 | 0.2366 |
| BMI | −0.179 | 5.699 | −0.002 | −0.031 | 0.9750 |

tionship between IFG and atherosclerosis remains controversial, and further studies need to be performed to evaluate whether strict control of blood glucose level in patients with IFG will result in prevention of progression of atherosclerosis.

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