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Original article

Clinical utility of heart-carotid pulse wave velocity in healthy Japanese subjects

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ABSTRACT

Background: Brachial-ankle pulse wave velocity (baPWV) is established as a reliable parameter of arterial stiffening and predictor of cardiovascular disease. However, the clinical significance of regional heart-carotid pulse wave velocity (hcPWV) has not been proven. In the current study, hcPWV was compared with common carotid arterial (CCA) stiffness index beta (stiffness beta), an established marker measured by ultrasonography.
Patients and methods: CCA and femoral arterial (FA) stiffness beta, hcPWV, baPWV, and peripheral femoral-ankle pulse wave velocity (faPWV) were measured in 276 healthy Japanese subjects.
Results: Analysis of covariance (ANCOVA) showed a significant correlation between the CV of hcPWV and CCA stiffness beta ($F = 79.65$, $P < 0.0001$). hcPWV was significantly and positively correlated with CCA stiffness beta ($r = 0.481$, $P < 0.0001$), whereas faPWV showed a tendency for a positive correlation with FA stiffness beta ($r = 0.118$, $P = 0.0584$). However, only 69 (25%) of the subjects were within the 95% confidence line for CCA stiffness beta based on hcPWV. hcPWV and CCA stiffness beta were significantly and positively correlated with age, systolic blood pressure (SBP), diastolic blood pressure, pulse pressure, total and LDL-cholesterol, and triglyceride; while body mass index and LDL-cholesterol/HDL-cholesterol ratio were only correlated with hcPWV. Among these parameters, SBP and total cholesterol were positive independent factors associated with hcPWV and CCA stiffness beta.
Conclusions: Heart-carotid PWV can be used as a measure of arterial stiffening with similar reliability to CCA stiffness beta in healthy Japanese subjects, but for different underlying reasons.

1. Introduction

Pulse wave velocity (PWV) is an index of arterial stiffness that is easily quantified using a simple device developed for measurement of the brachial-ankle PWV (baPWV) [1], which is a good independent predictor of the presence of coronary artery disease in men [2]. We have also shown the significance of baPWV in patients with subclinical hypothyroidism or hemiparesis [3,4]. Recent studies have suggested that arterial stiffness of different regions has different roles in various diseases, and we have reported greater stiffening of central arteries over peripheral arteries in patients with subclinical hypothyroidism or type 2 diabetes mellitus [5,6]. However, the clinical significance of regional PWV is still unclear.

Heart-carotid pulse wave velocity (hcPWV), which reflects the arterial stiffness from the aortic valve to the bulbs of the common carotid artery, can be determined using sensors simultaneously with baPWV [5,6], but this method is not broadly known. In contrast, the clinical value of measurement of common carotid arterial (CCA) stiffness beta [7–11] has been established by us and other investigators in patients with diabetes [7], hypertension [8], coronary heart disease [9], hyperthyroid Graves disease [10], and hypothyroidism [11]. CCA stiffness can be reproducibly obtained using phase-locked echo-tracking sonography, but this option is expensive and not commercially available.

This background prompted us to examine whether hcPWV could be used as a measure of arterial stiffness with a reliability similar to that of CCA stiffness beta in healthy Japanese subjects. In the study, we also determined the factors with an independent association with hcPWV that differed from those for CCA stiffness beta.

2. Patients and methods

2.1. Subjects

The subjects were healthy Japanese people ($n = 276$, M/F ratio: 107/169, mean age 51.5 ± 0.78 years old) who were consecutively recruited from those who participated in a local health check program at the Osaka City University Hospital from July to September

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Table 1
Baseline characteristics of the subjects.

Item	Subjects
Number of subjects	276
Gender (female/male)	107/169
Age (years)	51.5 ± 0.78
Body mass index (kg/m^2)	22.5 ± 0.19
Smoking index	199.4 ± 23.1
Systolic BP (mmHg)	123.9 ± 1.15
Diastolic BP (mmHg)	69.6 ± 0.66
Pulse pressure (mmHg)	55.0 ± 0.95
Pulse rate (/min)	66.2 ± 0.59
T. Chol (mmol/l)	5.53 ± 0.06
Triglyceride (mmol/l)	1.34 ± 0.07
LDL-C (mmol/l)	3.34 ± 0.05
HDL-C (mmol/l)	1.59 ± 0.03
baPWV (cm/s)	1301.3 ± 15.8
hcPWV (cm/s)	844.8 ± 17 0
faPWV (cm/s)	963.8 ± 9.64
CCA stiffness beta	10.1 ± 0.23
FA stiffness beta	11.25 ± 0.30

Data are expressed as means ± SE. Systolic BP: systolic blood pressure; Diastolic BP: diastolic blood pressure; T. Chol: total cholesterol; LDL-C: LDL-cholesterol; HDL-C: HDL-cholesterol; baPWV: brachial-ankle pulse wave velocity; hcPWV: heart-carotid pulse wave velocity; faPWV: femoral-ankle pulse wave velocity; CCA stiffness beta: common carotid arterial stiffness beta; FA stiffness beta: femoral arterial stiffness beta.

in 2007. Written informed consent was obtained from all subjects. Clinical variables are shown in Table 1. To avoid confounding factors, subjects were excluded if they suffered from diseases known to affect atherosclerosis, such as hypertension, hyperlipidemia, and diabetes mellitus (all subjects had HbA1c ≤ 5.7%); or were taking medication on a regular basis.

2.2. Serum parameters

Blood was drawn just before ultrasonography was performed after an overnight fast. Total cholesterol, triglyceride, high-density lipoprotein (HDL)- and low-density lipoprotein (LDL)-cholesterol levels were determined using an autoanalyzer.

2.3. Pulse wave velocity (PWV)

An automatic waveform analyzer (model BP-203RPE; Omron Colin Co., Tokyo, Japan) was used to measure baPWV [1,2–4] and regional PWV [5,6] simultaneously with blood pressure, electrocardiogram and heart sounds, as previously described [1,2–6]. Briefly, subjects were examined with electrocardiogram electrodes placed on both wrists, with a microphone for detecting heart sound S2 placed on the left edge of the sternum, and with cuffs wrapped around the brachium and the ankles. Pressure waveforms of the brachial and tibial arteries were recorded using the cuffs, which were connected to a plethymographic sensor that determines the volume pulse form, and an oscillometric pressure sensor that measures blood pressure. Pressure waveforms of the carotid and femoral arteries were recorded using multi-element tonometry sensors placed at the left carotid and left femoral arteries.

The path length of each segment was estimated automatically based on the height (HT, in centimeters), and PWVs were calculated using the following formulae:

$$\text{baPWV} = (\text{La} - \text{Lb}) / \Delta\text{Tba}$$

La (path length from the suprasternal notch to the ankle) = 0.8129 × HT + 12.328

Lb (path length from the suprasternal notch to the brachium) = 0.2195 × HT – 2.0734.

ΔTba (time interval between the brachial and ankle arteries) = the time interval between the wave front of the brachial waveform and that of the ankle waveform

$$\text{hcPWV} = \text{Dhc}/\text{T}_{\text{hc}}$$

Dhc (path length of the heart-carotid arterial segment) = 0.2473 × HT–18.999

T_{hc} (time interval between onset of heart sound S2 and the dicrotic notch of the carotid waveform)

$$\text{femoral-ankle pulse wave velocity (faPWV)} = \text{L}_{\text{fa}}/\text{T}_{\text{fa}}$$

L_{fa} (path length from the femoral artery to the ankle) = 0.2486 × HT + 30.709

T_{fa} (time interval between the wave front of the femoral waveform and the wave front of the ankle waveform).

Reproducibility of the PWV measurements was evaluated by repeating measurements in 20 healthy subjects on two different occasions. The CVs were 1.7%, 5.9% and 4.2% for baPWV, hcPWV and faPWV, respectively.

2.4. Measurement of CCA stiffness beta (arterial distensibility)

Vessel diameter and pulsatile diameter changes were measured by echo-tracking sonography [7–13] using an ultrasound echo-tracking instrument interfaced with a real-time ultrasound scanner and fitted with a 3.5- and 5-MHz linear array transducer (Aloka SSD610, Aloka Co. Ltd., Tokyo, Japan). This system can detect vessel wall movements of less than 10 μm at the level of bifurcation in the common carotid artery and femoral artery [7,10,11]. The distensibility of the arterial walls was expressed as stiffness beta [7,10,11], which was calculated as follows: Stiffness beta = [ln(Ps/Pd)] × Dd/(Ds – Dd). In this equation, Ps and Pd denote the maximal systolic and end-diastolic blood pressures (mmHg), respectively; and Ds and Dd are the systolic and diastolic inner diameters (mm) of the artery, respectively. Each subject was examined three times and stiffness was calculated from the corresponding values obtained for diameter, pulsatile diameter changes, and blood pressures measured with a sphygmomanometer using the auscultatory method [7,10,11].

2.5. Statistical analysis

Data are expressed as means ± SE unless otherwise indicated. Statistical analysis was performed with StatView version 5.0 (SAS Institute, Cary, NC). Differences in hcPWV and CCA stiffness beta divided by either mean were examined by a two-tailed Student *t* test for paired data. Analysis of covariance (ANCOVA) was used to analyze CVs for hcPWV and CCA stiffness beta. Correlation of PWV with CCA stiffness beta was examined by simple regression analysis, and relationships between pairs of parameters were evaluated by Spearman rank correlation. Stepwise multiple regression analysis with forward elimination was performed to assess the independent association of clinical variables with PWV or stiffness beta. The *F* value was set at 4.0 in each step. *P* values of less than 0.05 were considered to be statistically significant in all analyses.

3. Results

3.1. Comparison of the distribution between hcPWV and CCA stiffness beta

The mean ± SE and SD of hcPWV were 10.1 ± 0.20 and 3.7, and those for CCA stiffness beta were 845 ± 17 and 274 (Table 1). Analysis of paired hcPWV and CCA stiffness beta values divided by either mean gave a *P* value of 0.9989 in a two-tailed Student *t* test.