Association of Risk Factors With Increased Pulse Wave Velocity Detected by a Novel Method Using Dual-Channel Photoplethysmography

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Background: Pulse wave velocity (PWV) is correlated with cardiovascular risk. This study presents a new method for measuring the arterial PWV by simultaneously recording the digital volume pulse through the finger and the toe by way of dual-channel photoplethysmography (PPG).

Methods: In this study, 100 asymptomatic subjects (54 men and 46 women, 19 to 64 years of age) were enrolled. The PWV was measured both by dual-channel PPG (PWV-DVP) and by the standard method that current used applanation tonometry (PWV-AT). The developed dual-channel PPG system recorded digital volume pulse simultaneously from both the finger and toe. Time of pulse transition was measured on the time delay difference between two digital volume pulses. The PWV was calculated by dividing the distance between finger and toe by that of transit time.

Results: The PWV-DVP was significantly correlated with PWV-AT ($r = 0.678$, $P < .01$). With multivariate analysis controlled for age, heart rate, systolic blood pressure, and diastolic blood pressure, PWV-DVP was still significantly correlated with PWV-AT ($r = 0.669$, $P < .01$). Subjects with hypertension and dyslipidemia had significant higher PWV detected by both methods.

Conclusion: This study showed that PWV measured with dual-channel PPG system correlated very well with that measured using the traditional method. Am J Hypertens 2005;18:1118–1122 © 2005 American Journal of Hypertension, Ltd.

Key Words: Pulse wave velocity, photoplethysmography, hypertension, dyslipidemia.

Increased stiffness of the large arteries is associated with increased cardiovascular risk in hypertension. An elevated aortic PWV is not only associated with increased cardiovascular risks in hypertension, but also plays a prognostic factor in patients with end-stage renal disease. Arterial stiffness increases with age and concomitant cardiovascular risk factors. An arterial pulse wave is generated by the contraction of the left ventricle and the ejection of blood into the ascending aorta. Subsequently, pulse waves propagate throughout the arterial tree at a finite speed. The transit time between two different sites in the arterial tree can be measured using applanation tonometry. The PWV can be recorded by calculating the distance between these two arterial tree sites divided by the transit time.

A digital volume pulse (DVP) can be obtained using photoplethysmography (PPG). The DVP can be rapidly and simply detected by measuring the transmission of infrared light through the finger pulp. A previous study has demonstrated that the contour of DVP is similar to that of a peripheral pressure pulse. The contour of the DVP is determined by the systemic circulation including pressure wave reflection and PWV in the aorta and large arteries. The amplitude of reflection wave is affected by the degree of peripheral vasodilation and can be changed by vasoactive drugs. Both nitroglycerin and $\beta_2$-adrenergic agonist can attenuate the amplitude of reflection wave. Previous studies have demonstrated that...
the degree of attenuation of the reflection wave after β2-
adrenergic agonist can be useful in evaluating endothelium-dependent vasodilation. A stiffness index for large arteries can also be derived from an analysis of the contour of the DVP. The first peak of DVP is formed mainly by pressure transmitted along a direct path from the left ventricle to the finger, and the second peak is formed by the reflection wave reflected back up from the lower extremities. The short interval time between the first and second peaks can be used to infer the transit time needed for the pressure wave to propagate along the aorta and large arteries. The stiffness index can be calculated from the body height divided by this transit time and has been found to correlate well with PWV.

This novel method has been developed to measure PWV directly from DVP. Given that the contour of DVP is similar to peripheral pulse, the time difference between two different DVP sites can be regarded as the transit time between two pulses. The PWV can then be calculated by dividing the distance between these two sites by the transit time. To automate and facilitate the process, a system has been developed featuring two PPG sensors that detect DVP from two different sites simultaneously; in addition, this system has software that analyze the DVP and measure exactly the time difference between these two DVP roots.

To test the validity of our new method, this new system was used to detect the PWV in asymptomatic subjects, and results were compared with those obtained with the standard method based on applanation tonometry.

Methods

Study Population

A total of 100 asymptomatic hospital staff members (54 men and 46 women, mean age 38 ± 10 years, range 19 to 64 years) were included in this study. All subjects were apparently healthy and free of any vascular disease symptoms. Risk factors were carefully evaluated. Hypercholesterolemia was defined as a total serum cholesterol concentration ≥200 mg/dL or as use of lipid-lowering therapy. Hypertension was diagnosed if blood pressure (BP) was >140/90 mm Hg on three occasions or if the subject was taking any antihypertensive medication. Diabetes mellitus was diagnosed if the fasting plasma glucose concentration was >125 mg/dL on two separate occasions or if the subject was treated with insulin or oral hypoglycemic agents. Smokers were defined as those who smoked regularly at the start of this study. All subjects were in normal sinus rhythm. All gave their written informed consent for this study, and the Human Research Committee of the hospital approved this study.

Measurement of PWV by the New Dual-Channel PPG System

This new PWV measurement system was consisted of a portable interception device and pulse wave analytic software. The interception device is a PPG with two infrared sensors emitting a wavelength of 940 nm. Signals detected by infrared sensors are transmitted to an analog signal processor unit and a mixed signal microprocessor. The DVP signals are stored in a high-capacity memory unit to form a pulse wave database. The pulse wave analytic software uses a Visual Basic interface (Microsoft Corporation, Redmond, WA) that can analyze two DVP simultaneously and measure the time difference between the two roots of DVP (Fig. 1).

One infrared sensor is placed on the right index finger and the other is placed on the right second toe. For each measurement, DVP are recorded simultaneously from both sites for a 5-sec duration. The transit time is calculated as the average of all time differences measured during this 5-sec period. The finger-to-toe distance is the difference on the distance measured from the sternal notch to the right index toe and from the sternal notch to the right index finger. The software automatically calculates PWV after the finger-to-toe distance measurement is entered.

Measurement of PWV by Applanation Tonometry

To test the validity of the new system, PWV was also measured by applanation tonometry. Right carotid and femoral pulse waves were detected directly by using a Millar piezo-resistive pressure transducer (Millar SPT 301, Millar Instruments, Houston, TX) coupled into a Sphygmocor device (AtCor, Sydney, Australia). The timing of these waveforms was compared with that of the R wave on a simultaneously recorded electrocardiogram. The carotid-to-femoral PWV is calculated by dividing the transit time by the distance between these two pulses.

Protocol

Before any testing, all subjects rested in a supine position for 20 min in a quiet, temperature-controlled (26 °C ± 1°C) room. The PWV was measured both by our new dual-channel PPG system (represented as PWV-DVP) and by applanation tonometry (represented as PWV-AT). To test
the reproducibility of our new method, PWV-DVP was measured twice, 20 min apart, in 20 subjects.

**Statistical Analysis**

Association between PWV-DVP and PWV-AT was tested by the Spearman correlation test. Influences of continuous variables on PWV were also tested by the Spearman correlation test and by linear regression analysis with 95% confidence interval (95% CI). The association between PWV-DVP and PWV-AT was also examined by multiple linear regression controlling for age, BP, and heart rate. Effects of risk factors on PWV were tested by unpaired t test and by multiple logistic regression analysis controlling age. Data were expressed as mean ± standard deviation. Statistical analyses were performed using SPSS software, version 10.0 for Windows (SPSS Inc., Chicago, IL). A P value < .05 was regarded as statistically significant.

**Results**

**Reproducibility of PWV-DVP**

The intra-class correlation coefficient between the two separate measurements of PWV-DVP was high (r = 0.959, P < .01). There were no significant differences between the two measurements (6.37 ± 1.05 vs 6.29 ± 1.00 m/sec, P = .276; mean difference 0.09 ± 0.35 m/sec). The coefficient of variation was 5.8% as calculated by using a method reported in a previous study.15

**Correlation Between PWV-DVP and PWV-AT**

Mean systolic BP of the subjects was 126 ± 19 mm Hg and mean diastolic BP was 75 ± 12 mm Hg. The PWV-DVP was significantly correlated with PWV-AT (r = 0.678, P < .01) (Fig. 2). Both PWV-DVP and PWV-AT were significantly correlated with age, heart rate, and BP (Table 1). After multivariate analysis controlling for age, heart rate, systolic BP, and diastolic BP, PWV-DVP was still significantly correlated with PWV-AT (r = 0.669, P < .01).

**Effects of Risk Factors**

Among 100 subjects, 10 subjects had hypertension, 12 were smokers, 16 had hypercholesterolemia, and one subject had diabetes mellitus. Of the 10 hypertension subjects, two (20%) were untreated, two (20%) were treated with calcium-channel blockers, two (20%) with angiotensin-converting enzyme inhibitors, three (30%) with β-blockers, and one (10%) with diuretics. Subjects with hypertension had significantly higher PWV than those without hypertension as determined by either tonometry (8.14 ± 1.49 vs 6.51 ± 1.01, P = .007, 95% CI of difference 0.57 to 2.70) or PPG (8.04 ± 1.83 vs 6.49 ± 0.92, P < .01, 95% CI of difference 0.86 to 2.24). Subjects with hypercholesterolemia also had higher PWV than that of their counterparts (PWV-DVP 7.27 ± 1.55 vs 6.39 ± 0.93 m/sec, P = .044, 95% CI of difference 0.03 to 1.72; PWV-AT 7.30 ± 1.37 vs 6.40 ± 1.03 m/sec, P = .023, 95% CI of difference 0.14 to 1.67). Multivariate analysis showed that subjects with hypertension had higher PWV than those without hypertension as determined by both methods (PWV-DVP odds ratio 2.28, 95% CI 1.19 to 4.37; PWV-AT odds ratio 2.47, 95% CI 1.26 to 4.84).

**Discussion**

In the current study, a new method was developed using a dual-channel PPG with good reproducibility for measuring PWV. The PWV detected by the new method was well correlated with that obtained by the standard method. Increasing PWV was associated with risk factors.

Arterial stiffness is increased in subjects with coronary heart disease, diabetes mellitus, and end-stage renal diseases.4,9 Arterial stiffness is also an important prognostic factor for cardiovascular events in these patients.4,10 Among various indices of arterial stiffness, PWV is a reliable and reproducible method.10 The development of tonometry and its computerized automatic procedure for measuring arterial pulses in the aorta and extremity branches provide good reproducibility for measuring PWV.15,16 Pulse wave velocity has been studied extensively for assessing the cardiovascular risks in various conditions.1,3,4 Two major drawbacks of this technique, however, are the expensive equipment needed and the high level of technical expertise needed for obtaining an adequate waveform for analysis.

Photoplethysmography is a noninvasive method for evaluation of peripheral hemodynamics and has been extensively used in evaluating the dynamic function of leg veins.17 Recently the application of PPG has been ex-
tended to arterial function, including arterial stiffness\(^\text{12}\) and endothelial function.\(^\text{13,14}\) In developing this novel method to measure PWV using dual-channel PPG, our data revealed that the PWV assessed by our method had good reproducibility and correlated closely with that of PWV measured by the traditional method. An increase in PWV was shown to be associated with increasing age and other risk factors according to both of these methods. The results indicated that PWV assessed by our new method can be used in evaluating cardiovascular risk factors. The correlation coefficient between the two methods with multivariate analysis was 0.669. This results indicated that PWV measured by these two methods were not completely identical. Carotid-to-femoral PWV measured by applanation tonometry is a direct measurement of aortic PWV, whereas PWV measured by DVP is the wave velocity traveling through aorta as well as arteries of upper and lower limbs. The PWV measured with traditional method provides an indicator of arterial stiffness only on a regional basis.\(^\text{15}\) However, PWV measured with our method implies stiffness of the global arterial system. Atherosclerosis rarely involves the brachial artery, unlike the femora and aorta. The PWV measurements could be different between our new method and the traditional method in subjects with advanced atherosclerosis. Therefore, our new method should be further validated in patients with different etiologies and diagnoses, and should be tested for clinical significance in regard to prognosis and response to therapy.

Stiffness index, as derived from body height divided by transit time between forward wave and reflective wave of DVP, has also been reported to correlate well with PWV.\(^\text{12}\) Although very well correlated, this index is only an indirect and rough assessment of pulse wave travel and is subject to change if the contour of DVP is not adequately detected by PPG.

The DVP signal from PPG has certain limitations. The amount of reflected light depends on several factors, including degree of skin pigmentation, individual tissue characteristics, and initial blood volume in the measured area.\(^\text{17}\) Our study data are also confined to asymptomatic subjects with normal sinus rhythm and no concomitant obvious atherosclerosis. The clinical significance and application of our method in subjects with vascular diseases and arrhythmia need further evaluation. The DVP contour is also influenced by vasodilators. The height of reflected wave was significantly decreased after intravenous nitroglycerin infusion, but the effects on transit time and PWV were only modest.\(^\text{16}\) However, whether the effects of drugs on PWV measured by two methods are different should be further evaluated. In addition, there were only 10 hypertensive subjects in our study, who were using various antihypertensive drugs. We would not able to distinguish the effects of antihypertensive drugs on BP because of the small sample. The lack of statistical analysis controlling for drug class was one limitation of the present study.

A drawback of DVP measurement is that the circulation in the tips of fingers or toes may depend on smoking status, local temperature, and degree of peripheral atherosclerosis. To record DVP is probably difficult in patients with Raynaud disease or migraine. The reproducibility of DVP recording can be also decreased in these situations. We tried to record a good DVP contour by keeping the extremities warm before each measurement. The DVP measurements were easily obtained and had good reproducibility in our asymptomatic subjects. However, our method was not applied to patients with diseases in peripheral circulation. It is important to test our method in different situations in the future.

The PWV assessed from dual-channel PPG is well correlated with the traditional method and can be used for evaluating cardiovascular risk factors. In comparison to applanation tonometry, our new system is advantageous in terms of lower expense (about 2000 US dollars), complete technical independence, and portability. Only two PPG sensors, a small interception device, and a notebook computer are needed.

### References


