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Reproducibility of Regional Pulse Wave Velocity in Healthy Subjects

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Abstract

Background: Pulse wave velocity (PWV), which is inversely related to the distensibility of an arterial wall, offers a simple and potentially useful approach for an evaluation of cardiovascular diseases. In spite of the clinical importance and widespread use of PWV, there exist no standard either for pulse sensors or for system requirements for accurate pulse wave measurement. Objective of this study was to assess the reproducibility of PWV values using a newly developed PWV measurement system in healthy subjects prior to a large-scale clinical study.

Methods: System used for the study was the PP-1000 (Hanbyul Meditech Co., Korea), which provides regional PWV values based on the measurements of electrocardiography (ECG), phonocardiography (PCG), and pulse waves from four different sites of arteries (carotid, femoral, radial, and dorsalis pedis) simultaneously. Seventeen healthy male subjects with a mean age of 33 years (ranges 22 to 52 years) without any cardiovascular disease were participated for the experiment. Two observers (observer A and B) performed two consecutive measurements from the same subject in a random order. For an evaluation of system reproducibility, two analyses (within-observer and between-observer) were performed, and expressed in terms of mean difference ± 2SD, as described by Bland and Altman plots.

Results: Mean and SD of PWVs for aorta, arm, and leg were 7.07 ± 1.48 m/sec, 8.43 ± 1.14 m/sec, and 8.09 ± 0.98 m/sec measured from observer A and 6.76 ± 1.00 m/sec, 7.97 ± 0.80 m/sec, and 7.97 ± 0.72 m/sec from observer B, respectively. Between-observer differences (mean ± 2SD) for aorta, arm, and leg were 0.14 ± 0.62 m/sec, 0.18 ± 0.84 m/sec, and 0.07 ± 0.86 m/sec, and the correlation coefficients were high especially 0.93 for aortic PWV. Within-observer differences (mean ± 2SD) for aorta, arm, and leg were 0.01 ± 0.26 m/sec, 0.02 ± 0.26 m/sec, and 0.08 ± 0.32 m/sec from observer A and 0.01 ± 0.24 m/sec, 0.04 ± 0.28 m/sec, and 0.01 ± 0.20 m/sec from observer B, respectively. All the measurements showed significantly high correlation coefficients ranges from 0.94 to 0.99.

Conclusion: PWV measurement system used for the study offers comfortable and simple operation and provides accurate analysis results with high reproducibility. Since the reproducibility of the measurement is critical for the diagnosis in clinical use, it is necessary to provide an accurate algorithm for the detection of additional features such as flow wave, reflection wave, and dicrotic notch from a pulse waveform. This study will be extended for the comparison of PWV values from patients with various vascular risks for clinical application. Data acquired from the study could be used for the determination of the appropriate sample size for further studies relating various types of arteriosclerosis-related vascular disease.

Keywords: Pulse wave velocity; cardiovascular disease; reproducibility; pulse sensor; arterial stiffness

INTRODUCTION

Measurements of velocity for pulse waves in human have been studied and proposed as one way to diagnose and evaluate distensibility of large arteries. Since aortic stiffness is an important index, which might reflects hypertension, arteriosclerosis, arterial aging and diabetes, several methods for assessing large arteries' distensibility have been utilized[1-6]. Among those, most

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noninvasive systems are computerized tomography (CT), magnetic resonance image (MRI), and ultrasound based equipments such as doppler measurement, echocardiography, and high resolution echo-tracking. However, such instruments are sophisticated to operate, limited to an examination for acute patients, and only reserved for a few clinical research labs.[7,8] It calls for the development of a device, which is not only accurate for diagnosis but also simple to operate routinely for clinical use.

Pulse wave velocity (PWV), which is inversely related to arterial wall distensibility, offers a simple and potentially useful approach for an evaluation of cardiovascular diseases. In spite of the clinical importance and widespread use of PWV, there exist no standard for a PWV measurement system for either pulse sensors or system requirements for accurate measurements of pulse waves. Moreover, extraction of transit time from pulse waves requires accurate algorithm for the detection of exact point from each pulse wave.[9,10] Since the most important requirements for PWV measurement system are the stability and reproducibility of pulse waveforms, design of pulse sensors, system hardware, and analysis algorithm should be carefully considered.

Sensors currently used for the measurement of pulse waves are classified largely into two types, ultrasonic doppler sensors and pressure sensors. The latter is more comfortable and economical for clinical application, and widely used pressure sensors are applanation tonometry sensors. However, tonometry sensor has to be used on top of the skin surface, that is, patient has to take off the cloth for the measurement of pulse wave from the femoral or dorsalis pedis arteries. It calls for the development of a sensor, which could detect pulse waves easily even not directly on the surface of the skin. Moreover, since the reproducibility of the measurement is critical for diagnosis in clinical use, it is necessary to provide the stable and accurate waveforms.

Widespread method for the calculation of PWV utilizes intersecting tangent algorithm, which detects starting point of each pulse wave. Then, PWV values are calculated based on the extraction of foot-to-foot transit time, which is determined by the time difference between upstroke points of two pulse waves obtained from two different sites[11,12]. However, pulse waves are affected by many factors such as blood pressure, heart rate, respiration, and age, which may cause the changes in the shape of waveforms.[13] For example, pulse waves from femoral arteries fluctuate according to the respiratory rhythm, and the shape of the waveforms from those patients provide incorrect information, which may affect the detection of correct upstroke point.

Table 1. Clinical information of the participants for the experiment.

Subjects N = 17	Mean ± SD	Min ~ Max
Age(yr)	32.9 ± 7.1	22~52
Height(cm)	176.6 ± 7.2	163 ~ 189
Weight(kg)	76.5 ± 7.6	63 ~ 89
BMI(kg/m^2)	24.6 ± 2.9	19.6 ~ 29.8
SBP(mmHg)	116.5 ± 7.8	105.4 ~ 132.1
DBP(mmHg)	66.1 ± 5.9	53.5 ~ 75.8
MBP(mmHg)	82.9 ± 6.0	70.8 ~ 94.5
HR(bpm)	61.7 ± 7.9	46.2 ~ 76.5

Abbreviation : BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; HR, heart rate

Table 2. Mean and standard deviation of regional PWV values obtained from two observers, A and B.

PWV(m/s)	Observer A			Observer B		
	1st PWV	2nd PWV	Ave	1st PWV	2nd PWV	Ave
Aortic	7.08 ± 1.57	7.07 ± 1.40	7.07 ± 1.48	6.75 ± 1.04	6.76 ± 0.96	6.76 ± 1.00
Arm	8.42 ± 1.14	8.45 ± 1.16	8.43 ± 1.14	7.92 ± 0.81	8.00 ± 0.81	7.97 ± 0.80
Leg	8.02 ± 1.02	8.18 ± 0.97	8.09 ± 0.98	7.98 ± 0.73	7.96 ± 0.72	7.97 ± 0.72

Table 3. Summary of the reproducibility analysis results for between-observer and within-observer for each regional PWV.

items	Between-observer				Within-observer(A)				Within-observer(B)			
variable	M	SD	Std.E	r	M	SD	Std.E	r	M	SD	Std.E	r
Aortic	0.14	0.31	0.15	0.93**	0.01	0.13	0.03	0.99**	0.01	0.12	0.03	0.98**
Arm	0.18	0.42	0.10	0.50**	0.02	0.13	0.03	0.95**	0.04	0.14	0.03	0.94**
Leg	0.07	0.43	0.10	0.58*	0.08	0.16	0.04	0.97**	0.01	0.10	0.03	0.96**

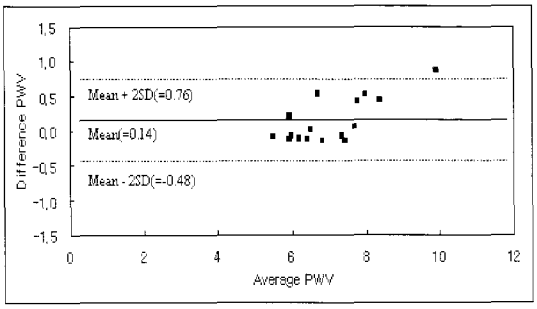
M = mean difference, SD = standard deviation of mean difference, Std. E = standard error, r = correlation coefficient
*p<0.05, **p<0.01

Therefore, it is also important to establish an accurate algorithm, which correctly detects upstroke points from the waveform under any possible circumstances. Objective of this study was to assess the reproducibility of PWV values determined from a newly developed PWV measurement system in healthy subjects prior to a large-scale clinical study. The study was focused on the evaluation of a computerized algorithm for PWV determination utilizing ECG, PCG, and four pulse waves from different site of arteries. Results from this study could be used for an application of the system to the diagnosis of various types of arteriosclerosis-related vascular disease.

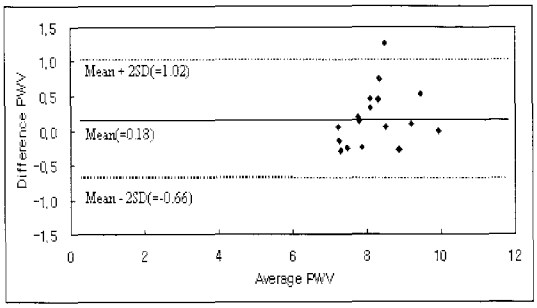
METHODS

System used for the study was the PP-1000 (Hanbyul Meditech Co., Korea), which provides regional PWV values based on the measurements of electrocardiography (ECG), phonocardiography (PCG), and pulse waves from four different sites of arteries (carotid, femoral, radial, and dorsalis pedis) simultaneously. ECG signals were acquired from both forceps, and the PCG sensor, designed using piezopolymer film contact microphone, was placed on the chest. Sensors used for pulse wave measurement were semiconductor pressure sensors with gel-filled, and the housing was designed to afford the applied pulse pressure from the artery. Sensor housing was attached to an elastic band with velcro, which could be easily strapped around the arteries, carotid, radial, femoral, and dorsalis pedis. Cutoff frequency of analog filters for pulse waves was set at 0.05~20Hz.

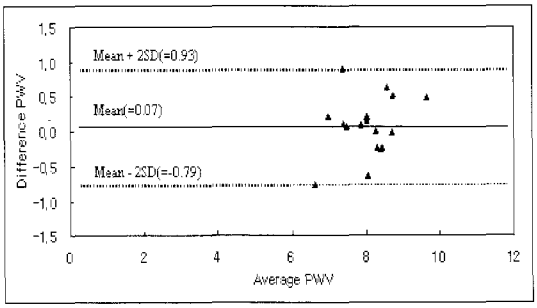
Seventeen healthy male subjects with mean age of 33 years (range 22 to 52 years) without any cardiovascular



(a) Aortic PWV

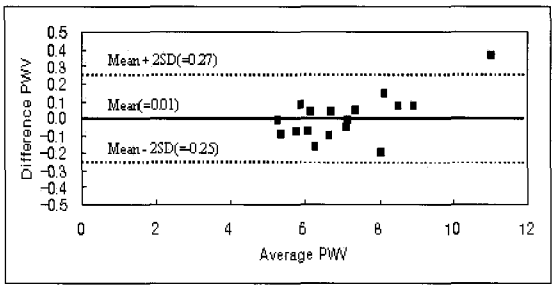


(b) Arm PWV

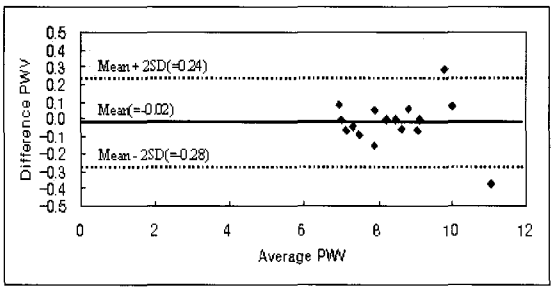


(c) Leg PWV

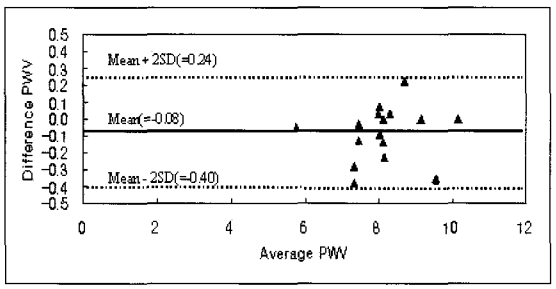
Figure 1. Scatter plots showing reproducibility of the averaged differences between PWV values obtained from two observers, A and B.



(a) Aortic PWV

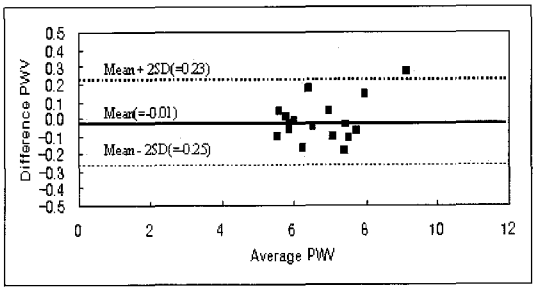


(b) Arm PWV

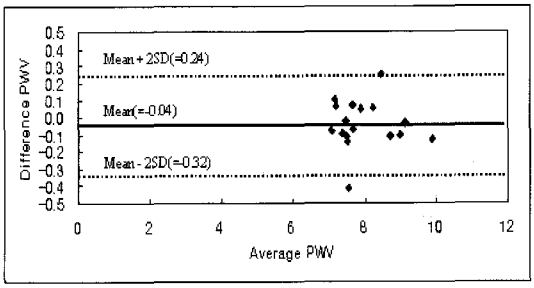


(c) Leg PWV

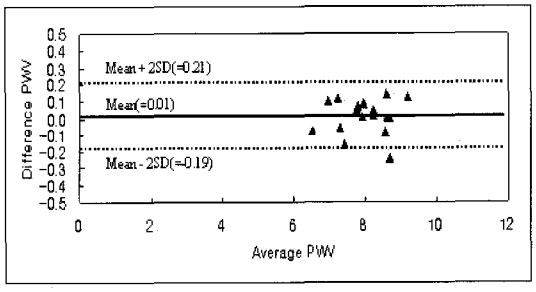
Figure 2. Scatter plots showing reproducibility of the averaged differences between consecutive PWV values obtained from observer A.



(a) Aortic PWV



(b) Arm PWV



(c) Leg PWV

Figure 3. Scatter plots showing reproducibility of the averaged differences between consecutive PWV values obtained from observer B.

disease were participated for the experiment, and the data acquisition was performed at the Heart Research Institute (University Hospital of Wales, Cardiff, UK). Two observers (observer A and B) performed two consecutive measurements from the same subject in a random order. Once an observer A finishes two consecutive measurements from one subject, all the sensors were detached, and an observer B attached sensors again to the same subject. Six signals, ECG, PCG, and four pulse waves from carotid, radial, femoral, and dorsalis pedis arteries on the left side of the body, were recorded simultaneously for the duration of 10 seconds. For an automatic determination of PWV values, surface distances between the two recording sites of pulse waves were measured and input to the system to allow the calculation of PWV values. Table 1 summaries the clinical information of the participants for the experiment.

Once data collection is finished, the system extracts characteristic points from each signal. R-peaks of ECGs were detected using time division adaptive threshold algorithm. Also, discrimination between 1st and 2nd heart sounds was performed based on the R-peaks of ECG, and the starting points of 2nd heart sounds were found using enveloping detection and threshold method. Also, peak points and dicrotic notches of carotid artery pulse waves were found based on the features acquired from

ECG and PCG. Finally, based on the time-domain scales obtained from the above values, upstroke points of pulse waves at the carotid, radial, femoral, and dorsalis pedis arteries were detected using intersecting tangent methods.

Time differences of upstroke points between two different sites were used to calculate regional PWV values. Three different PWV values, aortic, arm, and leg PWVs, were calculated as regional PWVs. Aortic PWV represents the velocity between carotid artery and femoral artery. Arm PWV and leg PWV were calculated based on the carotid-radial and the femoral-dorsalis pedis pulse transit time, respectively. For an evaluation of system reproducibility, two analyses, within-observer and between-observer, were performed, and expressed in terms of mean difference ± 2SD, as described by Bland and Altman. Correlation coefficients, regression equation, and standard errors were acquired through linear regression analysis using SPSS 10.0.

RESULTS

Three different regional PWV values, arotic, arm, leg PWVs, are summarized in table 2. As can be seen from the table 2, mean and SD of PWVs for aorta, arm, and leg were 7.07 ± 1.48 m/sec, 8.43 ± 1.14 m/sec, and 8.09 ± 0.98 m/sec measured from observer A and 6.76 ± 1.00 m/sec, 7.97 ± 0.80 m/sec, and 7.97 ± 0.72 m/sec from observer B, respectively. There was no trend of variations for the measurements with the underlying mean values or of the systematic bias. Results for the reproducibility are summarized in Table 3, which includes mean differences, standard deviations of mean differences, standard errors, and correlation coefficients for each regional PWV values for between-observer and within-observer studies.

Between-observer reproducibility was analyzed using Bland-Altman plots and reproducibility was expressed in terms of the mean difference and standard deviation between the measurements obtained from two observers. Results are shown in Figure 1 as scatter plots. The between-observer differences (mean ± 2SD) for aorta, arm, and leg were 0.14 ± 0.62 m/sec, 0.18 ± 0.84 m/sec, and 0.07 ± 0.86 m/sec, and the correlation coefficients were significantly high, especially 0.93 for aortic PWV.

Reproducibility of regional PWV values for two consecutive measurements from the same subject was also analyzed using Bland-Altman plots. Results of within-observer difference for observer A and B are shown in Figure 2 and Figure 3, respectively. Within-observer differences (mean ± 2SD) for aorta, arm, and leg were 0.01 ± 0.26 m/sec, 0.02 ± 0.26 m/sec, and 0.08 ± 0.32 m/sec from observer A and 0.01 ± 0.24 m/sec, 0.04 ± 0.28 m/sec, and 0.01 ± 0.20 m/sec from observer B, respectively. However, all the measurements showed significantly high correlation coefficients ranges from 0.94 to 0.99.

DISCUSSION

Bland-Altman presents the statistical methods for assessing agreement between two values under separate measurements. Reproducibility was reported as a mean and SD of difference between two methods14). They recommended 95% limits of agreement, mean difference plus or minus 2SD which would shows how far apart measurements by the two methods were likely to be for most individuals. Asmar et. al. studied on the assessment of arterial distensibility by automatic PWV measurement, and the accuracy and reproducibility for the automatic measurement of PWV were compared with the manual calculation[15]). Wilkinson et. al., analyzed the mean difference and SD of PWV values between different subjects and observers for the reproducibility study[16]). In this study, PWV values were compared by intra-observer and between-observer methods for evaluating reproducibility of the newly developed PWV measurement system, and the results were expressed based on the Bland-Altman plot.

The results of between-observer reproducibility (Mean±SEM) were 0.14 ± 0.15 m/s, 0.07 ± 0.10 m/s, and 0.18 ± 0.10 m/s for aortic, leg, and arm PWV, respectively. Reproducibility coefficients(2SD) were ±0.62 m/s for aortic PWV, ±0.86 m/s for leg PWV, and ±0.84 m/s for arm PWV. The results show that the agreement and reproducibility of between-observer values were higher than that of the previous studies for aortic and brachial PWV using applanation tonometery [16,17]). The results of within-observer reproducibility using consecutive measurement by one observer (Mean±SEM) were 0.01 ± 0.03 m/s, 0.01 ± 0.03 m/s for aortic PWV, 0.08 ± 0.04 m/s, 0.01 ± 0.03 m/s for leg PWV, and 0.02 ± 0.03 m/s, 0.04 ± 0.03 m/s for

arm PWV. Reproducibility coefficients (2SD) were in the range of 0.21~0.32 m/s for all regional PWV. Within-observer study showed higher reproducibility than that of the between-observer study, which is because of the possibility for more consistent placement of the sensors.

The results of evaluating reproducibility by between-observer and within-observer methods indicate that the newly developed system showed high reproducibility. It was possible since the sensors for obtaining pulse waves were designed to minimize the motion artifact to remove the operation errors caused by an observer. Moreover, the system utilized a precise algorithm for the detection of the important characteristics from the pulse waves, which leads to provide an accurate PWV values. The system could provide the regional PWV values by measuring pulse waves from different sites of arteries. This study could be extended for the comparison of PWV values from the patients with various vascular risks including arteriosclerosis, dyslipidemia, and hypertension for clinical application.

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