

The study of the influence of systolic blood
pressure on discordance between brachial-ankle
pulse wave velocity and carotid-femoral pulse
wave velocity results

Min-Ho Han

The Graduate School
Yonsei University
Department of Biomedical Engineering

The study of the influence of systolic blood
pressure on discordance between brachial-ankle
pulse wave velocity and carotid-femoral pulse
wave velocity results

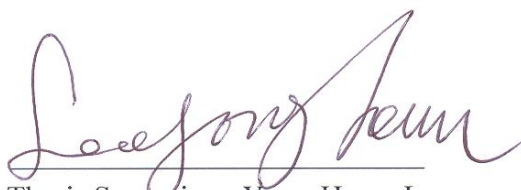
A Masters Thesis

Submitted to the Department of Biomedical Engineering
and the Graduate School of Yonsei University
in partial fulfillment of the
requirements for the degree of
Master of Biomedical Engineering

Min-Ho Han

June 2014

This certifies that the masters thesis of
Min-Ho Han is approved.



Thesis Supervisor: Yong-Heum Lee



Thesis Committee Member: Byung-Jo Jung



Thesis Committee Member: Sei-Young Lee

The Graduate School
Yonsei University
June 2014

ACKNOWLEDGEMENTS

I have been working during the day, and have then had to travel 3 hours from Seoul to Wonju where my graduate school is located every Tuesday to take classes. Looking back, graduate school has made me tired, but I had fun and was happy. I was eventually able to finish my Master's degree course with the help of many people to whom I'm grateful. First of all, I'd like to thank Professor Yong Heum Lee for giving me gracious advices and encouragement. I respect his outstanding passion and persistent effort in his studies and research. It was a great experience for me and helped me to study more and enjoy each step of the learning process.

I would also like to thank Professor Byung Jo Jung and Professor Sei Yung Lee for giving me valuable teaching and guidance, as well as Professor Ji Hoe Heo for providing me with valuable data for this thesis.

I would like to thank Hyo Sung Kim, who is a classmate and helped me to commute from Seoul to Wonju with her car, as well as others in graduate school who were an uplifting influence for me.

I was provided with a good environment for working and studying by my superiors, Woon Kyung Ko and Jung Hye Choi, and I was able to properly polish my writing with help from my colleague Yu Jin Yeo.

I owe this success to my attentive parents-in laws, who have always supported and helped me, and I hope they are always happy and healthy.

TABLE OF CONTENTS

I . INTRODUCTION	1
II . MATERIALS AND METHODS	2
1. Study population.....	2
2. Measurements of baPWV & ABI	3
3. Measurements of cfPWV	7
4. Risk factors	9
5. Statistical analysis	10
III. RESULTS.....	10
1. Demographic characteristics	10
2. Comparison of PWV between two subgroups in each bSBP, cSBP and a hypertension group	13
3. Association between discordance of PWV findings and SBP	15
IV. DISCUSSION	15
V . CONCLUSION.....	18
REFERENCES	18

LIST OF FIGURES

Figure 1. The baPWV equipment component list.....	5
Figure 2. Flowchart showing baPWV measurement according to the order	5
Figure 3. The transmission time obtained by PVR	6
Figure 4. The cfPWV equipment component list	7
Figure 5. Flowchart showing cfPWV measurement according to the order	8
Figure 6. The transmission distance (Lf-Lc)	9
Figure 7. The PWV finding categorized based on the xy-plane on the result tables	9

LIST OF TABLES

Table 1. Clinical characteristics and laboratory findings.....	12
Table 2. Comparison of PWV between two subgroups in each bSBP, cSBP and a hypertension group.....	14
Table 3. Association between discordance of findings and blood pressure	14

ABSTRACT

The study of the influence of systolic blood pressure on discordance between brachial-ankle pulse wave velocity and carotid-femoral pulse wave velocity results

Han, Min Ho

Dept. of Biomedical Engineering

The Graduate School

Yonsei University

Background: Pulse wave velocity (PWV) is related to cardiovascular disease and stroke as an independent risk factor that is available for estimating the arterial stiffness. There are two main causes of increased PWV. One is increased arterial stiffness derived from decreased elasticity, and the other is high systolic blood pressure (SPB) at the time when PWV is measured. Although the results of PWV appear abnormal on paper in patients with high SBP, it is hard to accurately determine if increased PWV is derived from arterial stiffness, high SBP or combination of both. The brachial-ankle PWV (baPWV) is more likely to be influenced by high blood pressure than carotid-femoral PWV (cfPWV), since baPWV includes some peripheral arterial components, which have less cushioning against high pressure than central arteries, in addition to central arterial components. So, it is feared that reliability of baPWV will decline in patients with high SBP.

Methods: We studied 114 patients with acute brain infarction or transient ischemic attack (TIA) who underwent both baPWV and cfPWV measurements. We investigated the

influence of SBP on discordance between baPWV and cfPWV results in patients with around 140 mmHg SBP.

Results: 114 patients were divided into accordance and discordance groups by matching both PWV results. In total group, brachial artery SBP (bSBP) was 140.4 ± 21.0 mmHg, central artery SBP (cSBP) was 128.8 ± 20.4 mmHg. Both SBPs were higher in the accordance group ($p=0.013$, $p=0.045$), whereas there was no statistically significant difference in the other risk factors. The percentage of an abnormal cfPWV was higher in the accordance group ($p<0.001$). However, the percentage of an abnormal baPWV was higher in the discordance group ($p=0.001$). The bSBP was categorized into two groups (<144 mmHg bSBP, and ≥ 144 mmHg bSBP) based on 144 mmHg bSBP. The cSBP also was categorized into two groups (<133 mmHg cSBP, and ≥ 133 mmHg cSBP) based on 133 mmHg cSBP. In multivariate analysis, after adjusting for confounding factors, <144 mmHg bSBP was independently associated with the discordance of PWV findings ($p=0.037$). However, <133 mmHg cSBP was not associated with the discordance of PWV findings.

Conclusion: It was found that baPWV was more affected by bSBP, and resulted in an abnormal finding in spite of a normal finding of the cfPWV measurement in the same subject with <144 mmHg bSBP. Our study suggests that cfPWV is more useful than baPWV to estimate the arterial stiffness in patients with around 140 mmHg bSBP.

Key words : discordance, systolic blood pressure, brachial-ankle pulse wave velocity, carotid-femoral pulse wave velocity

I . INTRODUCTION

Arterial stiffness has been closely associated with aging and hypertension of cardiovascular risk factors. The elevated arterial stiffness from aging and hypertension causes increased systolic blood pressure, decreased diastolic blood pressure, and consequently augmented pulse pressure due to increased pulse wave velocity and early return of reflected waves to the heart from the periphery[1]. These changes in pressure components increase myocardial oxygen demand and ventricular load, therefore inducing left ventricular hypertrophy. In addition, they decrease coronary perfusion, thereby inducing subendocardial ischemia[2]. Thus, it is important to measure arterial stiffness as the prevention against cardiovascular events.

Pulse wave velocity (PWV) is a noninvasive parameter that is used to assess arterial stiffness and is an independent predictor of the risk for stroke and cardiovascular disease[3]. There are two kinds of PWV that have been widely used for estimating the level of arteriosclerosis. One is carotid-femoral pulse wave velocity (cfPWV), which only reflects the stiffness of central arteries including abundant elastic components. The other is brachial-ankle pulse wave velocity (baPWV), which reflects mainly the stiffness of central arteries and partially that of peripheral arteries, which have less elastic components than central arteries[4]. The pathophysiological reasons, that lead to increased PWV, are mainly reduced elasticity caused by arteriosclerosis[2, 3], and a synergistic effect from high systolic blood pressure (SBP)[5-7]. Although the results from measurements show increased PWV in patients with high SBP, their results cannot be

taken at face value, because PWV might be influenced by high SBP regardless of arterial stiffness. So, it is difficult to determine if increased PWV is truly caused by arterial stiffness, a synergistic effect, or a combination of both causes. baPWV may respond especially sensitively to high SBP, since it additionally includes stiffer peripheral arterial elements, which play a less important role in cushioning against high pressure than central arteries[1, 2]. Therefore, even if cfPWV is normal, there might be a possibility that baPWV is abnormal in patients with around 140 mmHg SBP, which is on the border of hypertension and is somewhat higher than normal. In this study we sought to determine whether the influence of SBP on discordance between baPWV and cfPWV results exists in patients with around 140 mmHg SBP.

II. MATERIALS AND METHODS

1. Study population

This was a hospital-based, retrospective cross-sectional study. The candidates were patients who had been admitted between June 2012 and March 2013 with acute brain infarction or transient ischemic attack (TIA) within seven days of symptom onset and were registered in the Yonsei Stroke Registry. Among them, we enrolled patients who underwent both baPWV and cfPWV measurements. All of the enrolled patients were evaluated with 12-lead electrocardiography, chest x-ray, and standard blood tests including lipid profile. baPWV and cfPWV were measured on a single visit using two

different devices. We excluded patients with (1) arrhythmia that could interfere with accurate assessment of PWV, (2) peripheral arterial occlusive disease (PAOD) or ankle brachial blood pressure index (ABI) <0.90, which could produce inaccurate measurement of PWV, (3) only one result for baPWV or cfPWV on account of non-cooperation, such that baPWV could not be compared with cfPWV under the same condition of SBP. This study was approved by the Institutional Review Board of Severance Hospital, Yonsei University Health System.

2. Measurements of baPWV & ABI

Bilateral baPWV, blood pressures, ABI, electrocardiogram (ECG), and heart sounds were simultaneously measured with a plethysmographic apparatus (VP-1000, Colin Co. Ltd, Komaki, Japan, Figure 1) according to methods previously reported[8-11]. Before the measurement, patients lay down on the bed in a quiet, supine resting conditions. Then, the cuffs connected to the oscillometric and plethysmographic sensors were wrapped around both upper arms and ankles in order to measure blood pressures of bilateral limbs and record arterial pulse waveforms. ECG electrodes were placed on both wrists and heart sound microphone was placed on the left sternal border (Figure 2). The bilateral extremities pressure waveforms were stored for sampling time of 10 seconds with automatic gain analysis and quality adjustment. On the basis of the information from an apparatus, the baPWV was automatically calculated by taking the distance between two arterial recording sites and dividing it by the transmission time. The transmission distance (La-Lb) between the right brachium and ankle was automatically determined by the patient's height. The transmission time (ΔT_{ba}) was considered as the delay time from the

ascending point of the right brachial artery waveform to the ascending point of each tibial artery waveform (Figure 3). The baPWV was calculated by the following equations:

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

The La is the path length from the entrance of the aortic valve to ankle ($\text{La} = 0.8129 \times \text{height}\{\text{cm}\} - 2.0734$), the Lb is the path length from the entrance of the aortic valve to brachium ($\text{Lb} = 0.2195 \times \text{height}\{\text{cm}\} - 12.328$)[12]. The mean of bilateral baPWV value converted into m/s was used for the statistical analysis.

The bilateral ABI was simultaneously obtained with baPWV via the same device. The ABI is an established clinical test as a simple marker of peripheral arterial stenosis, and associated with risk of myocardial infarction and stroke in general population[13-15]. The ABI is simply calculated as the ratio of the higher of both brachial SBPs and each tibial SBP. The ABI is calculated by the following equations: $\text{ABI} = \text{each tibial SBP} / \text{the higher brachial SBP}$.

The SBP of lower extremities is usually higher than upper extremities due to the higher arterial resistance derived from many branching and tapering arteries[1]. Therefore, the ABI is usually >0.95 in people free from atherosclerosis. The $\text{ABI} < 0.90$ was defined as low. The patients with low ABI were excluded from this study, because the baPWV reliability is diminished by low ABI[16].

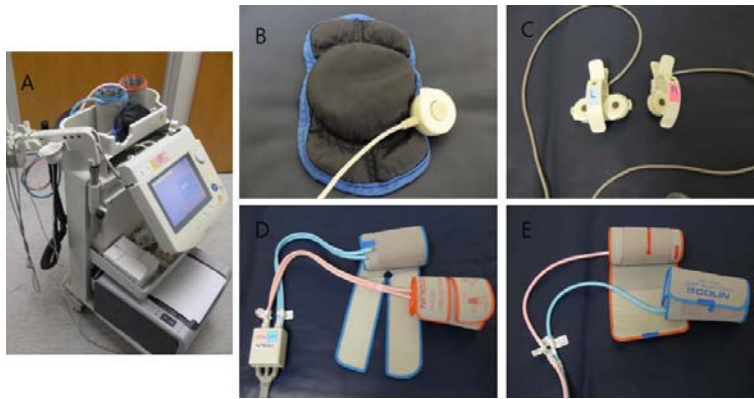


Figure 1. The baPWV equipment component list
A, main body; B, heart sound microphone; C, ECG electrodes; D, ankle cuffs; E, arm cuffs.



Figure 2. Flowchart showing baPWV measurement according to the order
1, ankle cuffs were wrapped around both ankles;
2, arm cuffs were wrapped around both upper arms;
3, ECG electrodes were placed on both wrists;
4, heart sound microphone was placed on the left sternal border;
5, a scene of a patient with all the sensors attached;
6, pulse volume record (PVR) was recorded.

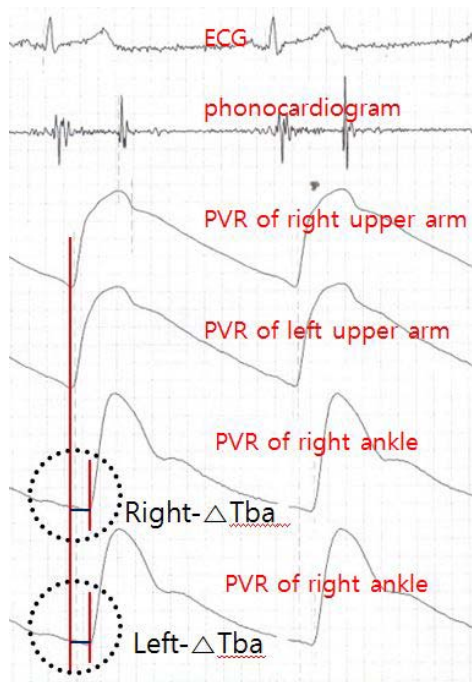


Figure 3. The transmission time obtained by PVR

3. Measurements of cfPWV

The principal of cfPWV measurement is the same as baPWV, but its measuring region and device differ from baPWV. Prior to cfPWV measurements, the brachial blood pressure was measured from a healthy arm of a patient in the supine position after at least 5 minutes rest, with an OMRON HEM-7220 device (Omron Healthcare, Kyoto, Japan). The cfPWV was performed with a tonometric device (SphygmoCor, AtCor Medical, NSW, Australia, Figure 4). The pulse waves of the carotid artery on the unilateral side were detected and those of the femoral artery on the same side were sequentially recorded using a probe attached to tonometric sensor. In addition, ECG was simultaneously recorded by attaching electrodes to both arms and the left leg during the test (Figure 5). The transmission time (ΔT_{cf}) was considered as the delay time from the ascending point of unilateral carotid artery waveform to the ascending point of the ipsilateral femoral artery waveform. The transmission distance ($L_f - L_c$) was calculated by subtracting the sternal notch-unilateral carotid site (L_c) from the ipsilateral femoral site-sternal notch distances (L_f), after measuring each interval with a ruler on the body surface (Figure 6). The cfPWV was calculated by the following equations: $cfPWV = L_f - L_c / \Delta T_{cf}$ (m/s).

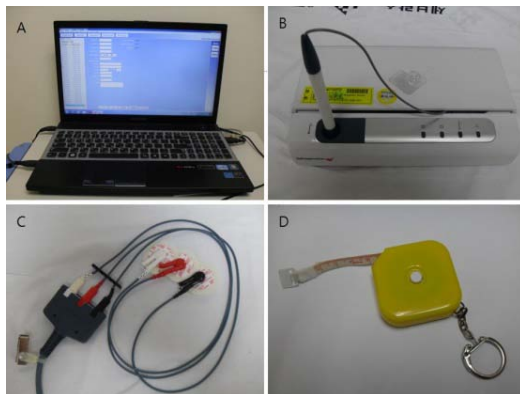


Figure 4. The cfPWV equipment component list

A, laptop computer; B, electronics module with a tonometer; C, ECG cable and lead; D, measuring tape.

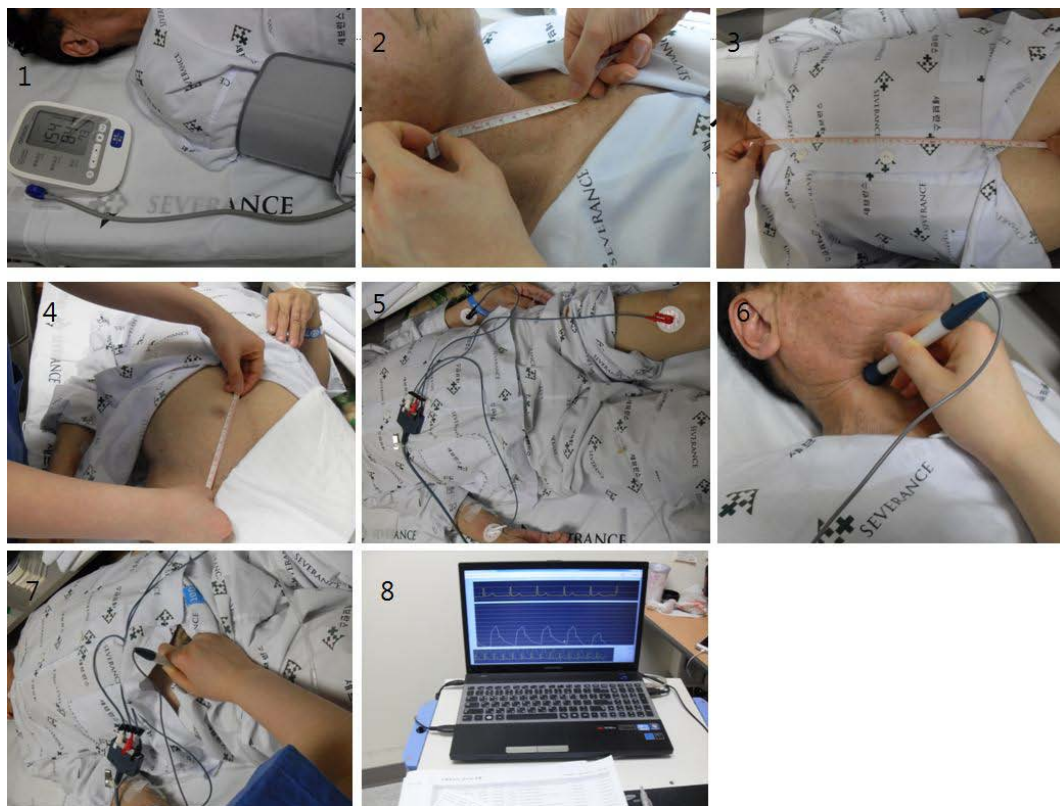


Figure 5. Flowchart showing cfPWV measurement according to the order

- 1, the brachial blood pressure was measured from a healthy arm of a patient in the supine position after at least 5 minutes rest;
- 2, measurement from the sternal notch to unilateral carotid site;
- 3 and 4, measurement from the sternal notch to the ipsilateral femoral site;
- 5, ECG electrodes were placed on both wrists and a left leg;
- 6, pulse waves of a carotid artery on the unilateral side were detected using a probe;
- 7, pulse waves of a femoral artery on the same side were sequentially recorded using a probe;
- 8, PVR was recorded.

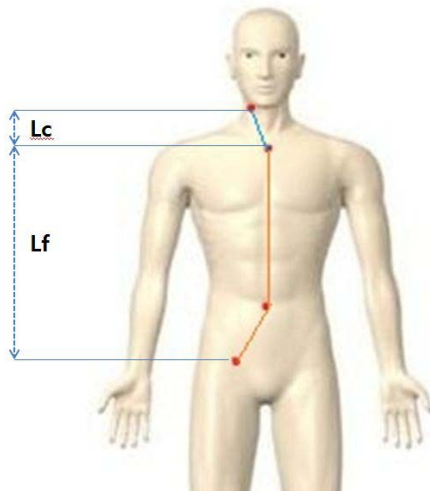


Figure 6. The transmission distance (Lf-Lc)
Lc, the distance from unilateral carotid site to sternal notch; Lf, the distance from sternal notch to ipsilateral femoral site.

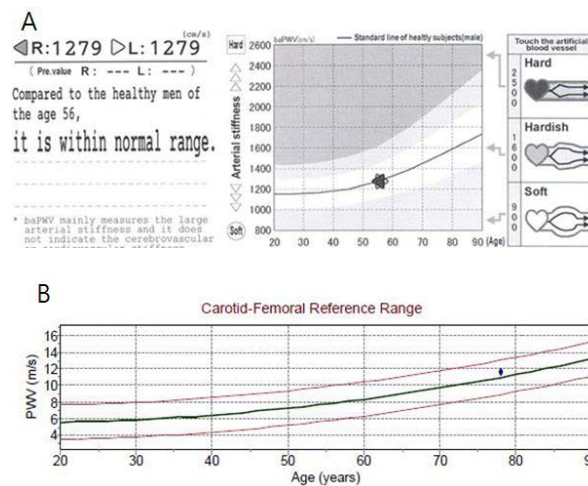


Figure 7. The PWV finding categorized based on the xy-plane on the result tables
A, baPWV result; B, cfPWV result.

4. Risk factors

The abnormal cfPWV and baPWV were defined as when the value of each PWV strayed out of the normal range in the xy-plane on the result tables with an upward trend. If either baPWV finding was abnormal in case of baPWV measurement, the results of baPWV were considered as abnormal findings (Figure 7). Hypertension was defined as a history of having used any antihypertensive drug after diagnosis of hypertension, resting blood pressures with high systolic pressure ≥ 140 mmHg, or diastolic pressure ≥ 90 mmHg on repeated measurements[17]. Diabetes mellitus (DM) was defined as a fasting plasma glucose ≥ 7.0 mmol/L or a history of having taken an oral hypoglycemic agent or insulin[18]. Hypercholesterolemia was defined as a history of having used lipid lowering agents after diagnosis of hypercholesterolemia, low-density lipoprotein cholesterol ≥ 4.1 mmol/L, or total cholesterol ≥ 6.2 mmol/L[19]. Current smoking was defined as having smoked a cigarette within 1 year prior to admission. Body mass index (BMI) was yielded by dividing kilograms of weight by height in meters squared (kg/m^2). Coronary heart disease was defined as the basis of unstable angina, coronary artery occlusive disease, or myocardial infarction. Brachial artery systolic blood pressure (bSBP) was obtained by measuring on a brachium which was free of any peripheral artery disease before the PWV measurement. Central artery systolic blood pressure (cSBP) and augmentation index (AI) were calculated by converting the radial pulse wave into the central pulse wave with the generalized transfer function of the device used to measure cfPWV. The waist was measured starting from the navel in a supine position.

5. Statistical analysis

Statistical analysis was performed using the windows SPSS package version 18.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as Mean \pm standard deviation or median [interquartile range (IQR)] as appropriate. Categorical variables were summarized as number (%). Demographic characteristics and risk factors were compared using independent sample t-tests or chi-square tests for categorical variable between the accordance and discordance groups based on results of both PWVs. Comparison of PWVs by categorized systolic pressures and hypertension was conducted using Mann-Whitney test. In addition to simple linear regression analysis which can estimate the relationship between discordance group and blood pressure-related variables, multiple linear regression analysis was performed to determine the influence of each variable on discordance. All statistical tests were two-tailed, and $p < 0.05$ was considered statistically significant.

III. RESULTS

1. Demographic characteristics

There were 171 patients with acute cerebral infarction or TIA during the study period. After the exclusion of 24 patients who were uncooperative during either PWV measurement, 2 patients with PAOD, 6 patients with ABI < 0.90 , and 25 patients with

arrhythmia, 114 consecutive patients were included in this study. All patients were divided into accordance and discordance groups by matching both results of PWVs. Table 1 shows the characteristics of the subjects. The accordance group contained 54 patients, and the discordance group contained 60 patients. The number of males in the accordance group was higher than that of the discordance group ($p=0.015$). In total group, bSBP was 140.4 ± 21.0 mmHg, cSBP was 128.8 ± 20.4 mmHg, and both SBPs were higher in the accordance group ($p=0.013$, $p=0.045$). There also was no statistically significant difference in risk factors such as hypertension, DM, hypercholesterolemia, current smoking, and coronary heart disease between both groups. The percentage of an abnormal cfPWV was 37.7% in total, and higher in the accordance group in comparison with the discordance group ($p<0.001$). However, the percentage of an abnormal baPWV was 88.6% in total, and higher in the discordance group ($p=0.001$). Fasting glucose, total cholesterol, triglyceride, HbA_{1c}, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol were not associated with an outstanding interval between both groups.

Table 1. Clinical characteristics and laboratory findings

Variable	Total (N = 114)	Accordance (N = 54)	discordance (N = 60)	p-value
Male sex *	69 (60.5)	39 (72.2)	30 (50.0)	0.015
Age (year)	62.04±11.01	61.39±10.56	62.63±11.46	0.549
Body mass index (kg/m ²)	24.02±3.06	24.27±3.19	23.80±2.94	0.415
Brachial artery systolic blood pressure (mmHg) *	140.4±21.0	145.5±22.1	135.8±19.0	0.013
Central artery systolic blood pressure (mmHg) *	128.8±20.4	132.8±21.6	125.2±18.6	0.045
Brachial-ankle pulse wave velocity (m/s)	19.18±4.86	19.58±5.30	18.82±4.44	0.405
Carotid-femoral pulse wave velocity (m/s) **	9.89±2.82	11.43±3.14	8.50±1.47	<0.001
Hypertension	72 (63.2)	36 (66.7)	36 (60.0)	0.461
Diabetes mellitus	42 (36.8)	21 (38.9)	21 (35.0)	0.667
Hypercholesterolemia	17 (14.9)	6 (11.1)	11 (18.3)	0.280
Current smoking	28 (24.6)	16 (29.6)	12 (20.0)	0.233
Coronary heart disease	39 (34.2)	18 (33.3)	21 (35.0)	0.851
Waist (cm)	86.54±8.70	87.38±9.21	85.78±8.21	0.334
Total cholesterol (mg/dl)	176.47±42.30	174.95±47.12	177.83±37.80	0.718
LDL-cholesterol (mg/dl)	100.76±31.41	101.96±29.10	99.70±33.55	0.704
HDL-cholesterol (mg/dl)	43.35±12.67	43.13±14.25	43.55±11.22	0.862
Triglyceride (mg/dl)	130.69±78.23	127.15±72.61	133.75±83.29	0.658
HbA _{1c} (%)	6.56±1.19	6.64±1.24	6.50±1.15	0.538
Plasma glucose (mg/dl)	144.41±58.10	146.89±49.44	142.18±65.26	0.668
Carotid augmentation index(HR75) (%)	24.46±9.56	23.22±9.12	25.58±9.89	0.189
Abnormal carotid-femoral pulse wave velocity **	43 (37.7)	42 (77.8)	1 (1.7)	<0.001
Abnormal brachial-ankle pulse wave velocity *	101 (88.6)	42 (77.8)	59 (98.3)	0.001

Values are mean±standard deviation or number(%). *, p<0.05 between accordance and

discordance; **, $p < 0.001$ between accordance and discordance.

2. Comparison of PWV between two subgroups in each bSBP, cSBP and a hypertension group

The bSPB was categorized into two subgroups (<144 mmHg bSBP, and ≥ 144 mmHg bSBP) based on 144mmHg bSBP which is around 140mmHg that can become a criterion of hypertension. The cSBP also was categorized into two subgroups (<133 mmHg cSBP, and ≥ 133 mmHg cSBP) based on 133 mmHg which was obtained by subtracting about 11mmHg, the mean value of differences between each bSBP and cSBP from 144mmHg. We carried out the Mann-Whitney test to compare each PWV between two subgroups in each bSBP, cSBP and a hypertension group. Table 2 showed that both PWVs were increased in a higher SBP subgroup in each bSBP and cSBP, and in a hypertension subgroup ($p < 0.001$ in all the groups).

Table 2. Comparison of PWV between two subgroups in each bSBP, cSBP and a hypertension group

			cfPWV		baPWV	
		Number	Median (IQR)	p-value	Median (IQR)	p-value
bSBP	<144 mmHg	69	8.70 (2.6)	<0.001 **	16.23 (4.5)	<0.001 **
	≥144 mmHg	45	10.70 (3.0)		20.44 (7.5)	
cSBP	<133 mmHg	68	8.70 (2.9)	<0.001 **	16.29 (4.7)	<0.001 **
	≥133 mmHg	46	10.55 (3.0)		20.43 (6.7)	
Hypertension	No	42	8.55 (2.6)	<0.001 **	15.91 (4.7)	<0.001 **
	Yes	72	9.75 (3.4)		19.30 (7.3)	

IQR, interquartile range; bSBP, brachial artery systolic blood pressure; cSBP, central artery systolic blood pressure; cfPWV, carotid-femoral pulse wave velocity; baPWV, brachial-ankle pulse wave velocity; **, p<0.001 between subgroups in each bSBP, cSBP and a hypertension group.

Table 3. Association between discordance of findings and blood pressure

Characteristic	Univariate			Multivariate		
	Odds ratio	Standard error	p-value	Odds ratio	Standard error	p-value
<144 bSBP (mmHg)	2.33	0.39	0.031 *	13.76	1.26	0.037 *
<133 cSBP (mmHg)	1.60	0.38	0.221	0.13	1.24	0.099
Hypertension	0.75	0.39	0.462	1.82	0.55	0.281
baPWV (m/s)	0.97	0.04	0.403	1.28	0.09	0.004 *
cfPWV (m/s)	0.53	0.13	<0.001 **	0.39	0.19	<0.001 **

bSBP, brachial artery systolic blood pressure; cSBP, central artery systolic blood pressure; cfPWV, carotid-femoral pulse wave velocity; baPWV, brachial-ankle pulse wave velocity; *, p<0.05; **, p<0.001.

3. Association between discordance of PWV findings and SBP

Univariate analysis showed that <144mmHg bSBP was significantly associated with the discordance of PWV findings ($p=0.031$), and cfPWV was negatively associated with the discordance of PWV findings ($p<0.001$). After adjustment of confounding factors on multivariate analysis, <144mmHg bSBP and cfPWV were still independently associated with the discordance of PWV findings ($p=0.037$, $p<0.001$). In addition, baPWV had a positive association with that ($p=0.004$). However, <133mmHg cSBP was not associated with the discordance of PWV findings (Table 3).

IV. DISCUSSION

Age and blood pressure are known to be major determinants of PWV[5]. Of them, blood pressure, which is affected by a variety of conditions such as emotional stress, physical activities, and/or the surrounding environment, is variable and modifiable[6]. Consistently elevated blood pressure causes the structural and functional faculties of the central elastic artery to be damaged, and consequently induces arteriosclerosis[1]. It also promotes an increase in PWV itself[6]. Therefore, it is difficult to determine whether an increased PWV finding actually represents the progress of atherosclerosis in light of the arterial stiffness or instead originates from a synergistic effect of elevated blood pressure in patients with hypertension. Increased PWV which is caused by the synergistic effect may occur predominantly in peripheral arteries which have less buffering effect than

central arteries. These situations could cause discordance between both results of PWV in patients with about 140mmHg bSBP, which is one criterion for hypertension. Our study demonstrated a significant association between the discordance of both PWV findings and bSBP, but not cSBP. Previous studies sought to compare baPWV with cfPWV, which is the gold standard non-invasive examination for estimating central arterial stiffness, and then reported that baPWV was as useful as cfPWV[4]. Also, many researchers have used either PWV or both PWVs together to strictly evaluate arterial stiffness in various studies related to cardiovascular disease[8, 9, 11, 20, 21], stroke[3, 22], and end-stage renal disease[23-25]. Some researchers have attempted to correct PWV in patients with hypertension by modifying their blood pressure[5, 26], and Kohji et al. suggested cardio-ankle vascular index (CAVI) which could reflect arteriosclerosis of the aorta, femoral artery, and tibial artery by separating from an influence of a blood pressure, but CAVI still needs to be proved through additional studies[7]. Hirofumi et al., as mentioned earlier, conducted a study with a total of 2287 adults (1265 men and 1022 women) in six different institutions in Japan and one in the USA to determine associations between cfPWV and baPWV. This study which reported that there was a significant positive relationship between cfPWV and baPWV, but baPWV results were approximately 20% higher than cfPWV results due to peripheral arterial stiffness in addition to central arterial stiffness[4]. The baPWV might diminish the reliability of the prediction for cardiac or cerebral arteriosclerosis, because it includes a peripheral component from the femoral artery to the posterior tibial artery, which means that the prognostic value of the femoral-ankle PWV is controvertible in comparison with cfPWV[27]. As yet, there have been no studies about the influence of such difference between baPWV and cfPWV on discordance between two PWV results in the same patient. The present study, along with

previous findings, demonstrated that baPWV value was higher than cfPWV value, and the PWV was positively correlated with SBP in light of Table 2. In addition, our study newly confirmed that there was a significant association between the discordance of both PWV findings and <144mmHg bSBP, except for <133mmHg cSBP. This fact implies that the higher the SBP is, the more the two PWV findings correspond with each other. In other words, a higher SBP leads both PWV values to increase and go off the normal range by promoting not only arterial stiffness, but also a synergistic effect. In contrast, the finding of baPWV was abnormal despite the normal finding of cfPWV in patients who had lower bSBP than 144mmHg bSBP, which might be more predominant around 140mmHg bSBP, since baPWV is more vulnerable to blood pressure, and consequently prone to be abnormal in comparison with cfPWV. However, we could not demonstrate whether there exists an association between the discordance of results and a SBP subgroup with around 140mmHg among several groups classified according to SBP, on account of a small sample size. The cSBP, which reflects only conditions of the central artery, did not affect the discordance between both results of PWV, because it may equally affect both PWV measurements. Therefore, we suggest that the result of cfPWV may be more useful for exactly estimating a patient's arterial stiffness (by excluding some influence on blood pressure) when the patient, who has undergone both PWV measurements, has <144mmHg bSBP.

This study has several limitations. First, the subjects of our study were stroke patients. Therefore, it is uncertain whether the association of the result's discordance and <144mmHg bSBP can be generalized to other populations. Second, the sample size of subjects is small, while there were over 500 people in preceding PWV related studies[3, 4]. Originally, we sought to verify if there was an association between the results'

discordance and a specific bSBP subgroup by minutely classifying subjects according to bSBP. However, we were unable to do so due to a small sample size, so the results of our study should be reconfirmed with a larger number of participants to investigate in detail the relationship with a certain subgroup with around 140mmHg bSBP. Finally, because there have been no studies using the PWV which have resulted in normal finding or abnormal finding according to the intact measurement results on paper, many additional studies are needed to validate and strengthen the reliability of this study.

V. CONCLUSION

In this study, baPWV was more affected by bSBP, and consequently resulted in abnormal finding in spite of normal finding of the cfPWV measurement in a same subject with <144mmHg bSBP. However, <133mmHg cSBP was not associated with the discordance of PWV findings. Our study suggests that cfPWV is more useful than baPWV for estimating arterial stiffness in patients with around 140mmHg bSBP.

REFERENCES

- [1] Nichols, W. W. 2005. "Clinical measurement of arterial stiffness obtained from noninvasive pressure waveforms". *Am J Hypertens*, 18(1 Pt 2): 3S-10S.
- [2] Watanabe, H., Ohtsuka, S., Kakihana, M., and Sugishita, Y. 1993. "Coronary circulation in dogs with an experimental decrease in aortic compliance". *J Am Coll Cardiol*, 21(6): 1497-1506.
- [3] Mattace-Raso, F. U., van der Cammen, T. J., Hofman, A., van Popele, N. M., Bos, M. L., Schalekamp, M. A., Asmar, R., Reneman, R. S., Hoeks, A. P., Breteler, M. M., and Witteman, J. C. 2006. "Arterial stiffness and risk of coronary heart disease and stroke: the Rotterdam Study". *Circulation*, 113(5): 657-663.
- [4] Tanaka, H., Munakata, M., Kawano, Y., Ohishi, M., Shoji, T., Sugawara, J., Tomiyama, H., Yamashina, A., Yasuda, H., Sawayama, T., and Ozawa, T. 2009. "Comparison between carotid-femoral and brachial-ankle pulse wave velocity as measures of arterial stiffness". *J Hypertens*, 27(10): 2022-2027.
- [5] Asmar, R., Benetos, A., Topouchian, J., Laurent, P., Pannier, B., Brisac, A. M., Target, R., and Levy, B. I. 1995. "Assessment of arterial distensibility by automatic pulse wave velocity measurement. Validation and clinical application studies". *Hypertension*, 26(3): 485-490.
- [6] Park, H. J., Rho, T. H., Park, C. S., Jang, S. W., Shin, W. S., Oh, Y. S., Lee, M. Y., Cho, E. J., Seung, K. B., Kim, J. H., and Choi, K. B. 2007. "The relationship between the acute changes of the systolic blood pressure and the brachial-ankle pulse wave velocity". *Korean J Intern Med*, 22(3): 147-151.
- [7] Shirai, K., Utino, J., Otsuka, K., and Takata, M. 2006. "A novel blood pressure-independent arterial wall stiffness parameter; cardio-ankle vascular index (CAVI)". *J Atheroscler Thromb*, 13(2): 101-107.

- [8] Chae, M. J., Jung, I. H., Jang, D. H., Lee, S. Y., Hyun, J. Y., Jung, J. H., Ahn, D. S., Lim, D. S., and Lee, S. J. 2013. "The Brachial Ankle Pulse Wave Velocity is Associated with the Presence of Significant Coronary Artery Disease but Not the Extent". *Korean Circ J*, 43(4): 239-245.
- [9] Chow, B. and Rabkin, S. W. 2013. "Brachial-ankle pulse wave velocity is the only index of arterial stiffness that correlates with a mitral valve indices of diastolic dysfunction, but no index correlates with left atrial size". *Cardiol Res Pract*, 2013: 986847.
- [10] Kawai, T., Ohishi, M., Onishi, M., Ito, N., Takeya, Y., Maekawa, Y., and Rakugi, H. 2013. "Cut-off value of brachial-ankle pulse wave velocity to predict cardiovascular disease in hypertensive patients: a cohort study". *J Atheroscler Thromb*, 20(4): 391-400.
- [11] Liu, D. H., Wang, Y., Liao, X. X., Xu, M. G., Wang, J. M., Yang, Z., Chen, L., Lu, M. D., Lu, K., and Tao, J. 2006. "Increased brachial-ankle pulse wave velocity is associated with impaired endothelial function in patients with coronary artery disease". *Chin Med J (Engl)*, 119(22): 1866-1870.
- [12] Matsui, Y., Kario, K., Ishikawa, J., Eguchi, K., Hoshide, S., and Shimada, K. 2004. "Reproducibility of arterial stiffness indices (pulse wave velocity and augmentation index) simultaneously assessed by automated pulse wave analysis and their associated risk factors in essential hypertensive patients". *Hypertens Res*, 27(11): 851-857.
- [13] Busch, M. A., Lutz, K., Rohl, J. E., Neuner, B., and Masuhr, F. 2009. "Low ankle-brachial index predicts cardiovascular risk after acute ischemic stroke or transient ischemic attack". *Stroke*, 40(12): 3700-3705.

- [14] Rabkin, S. W., Chan, S. H., and Sweeney, C. 2012. "Ankle-brachial index as an indicator of arterial stiffness in patients without peripheral artery disease". *Angiology*, 63(2): 150-154.
- [15] Wild, S. H., Byrne, C. D., Smith, F. B., Lee, A. J., and Fowkes, F. G. 2006. "Low ankle-brachial pressure index predicts increased risk of cardiovascular disease independent of the metabolic syndrome and conventional cardiovascular risk factors in the Edinburgh Artery Study". *Diabetes Care*, 29(3): 637-642.
- [16] Motobe, K., Tomiyama, H., Koji, Y., Yambe, M., Gulinisa, Z., Arai, T., Ichihashi, H., Nagae, T., Ishimaru, S., and Yamashina, A. 2005. "Cut-off value of the ankle-brachial pressure index at which the accuracy of brachial-ankle pulse wave velocity measurement is diminished". *Circ J*, 69(1): 55-60.
- [17] Jones, D. W. and Hall, J. E. 2004. "Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure and evidence from new hypertension trials". *Hypertension*, 43(1): 1-3.
- [18] Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. 2003. "Report of the expert committee on the diagnosis and classification of diabetes mellitus". *Diabetes Care*, 26 Suppl 1: S5-20.
- [19] Expert Panel on Detection, E., and Treatment of High Blood Cholesterol in Adults. 2001. "Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III)". *JAMA*, 285(19): 2486-2497.
- [20] Munakata, M., Konno, S., Miura, Y., Yoshinaga, K., and Group, J. T. S. 2012. "Prognostic significance of the brachial-ankle pulse wave velocity in patients

- with essential hypertension: final results of the J-TOPP study". *Hypertens Res*, 35(8): 839-842.
- [21] Sugawara, J., Hayashi, K., Yokoi, T., Cortez-Cooper, M. Y., DeVan, A. E., Anton, M. A., and Tanaka, H. 2005. "Brachial-ankle pulse wave velocity: an index of central arterial stiffness?". *J Hum Hypertens*, 19(5): 401-406.
 - [22] Kim, J., Cha, M. J., Lee, D. H., Lee, H. S., Nam, C. M., Nam, H. S., Kim, Y. D., and Heo, J. H. 2011. "The association between cerebral atherosclerosis and arterial stiffness in acute ischemic stroke". *Atherosclerosis*, 219(2): 887-891.
 - [23] Blacher, J., Guerin, A. P., Pannier, B., Marchais, S. J., Safar, M. E., and London, G. M. 1999. "Impact of aortic stiffness on survival in end-stage renal disease". *Circulation*, 99(18): 2434-2439.
 - [24] Guerin, A. P., Blacher, J., Pannier, B., Marchais, S. J., Safar, M. E., and London, G. M. 2001. "Impact of aortic stiffness attenuation on survival of patients in end-stage renal failure". *Circulation*, 103(7): 987-992.
 - [25] London, G. M., Marchais, S. J., Safar, M. E., Genest, A. F., Guerin, A. P., Metivier, F., Chedid, K., and London, A. M. 1990. "Aortic and large artery compliance in end-stage renal failure". *Kidney Int*, 37(1): 137-142.
 - [26] Yamashina, A., Tomiyama, H., Arai, T., Koji, Y., Yambe, M., Motobe, H., Glunizia, Z., Yamamoto, Y., and Hori, S. 2003. "Nomogram of the relation of brachial-ankle pulse wave velocity with blood pressure". *Hypertens Res*, 26(10): 801-806.
 - [27] Pannier, B., Guerin, A. P., Marchais, S. J., Safar, M. E., and London, G. M. 2005. "Stiffness of capacitive and conduit arteries: prognostic significance for end-stage renal disease patients". *Hypertension*, 45(4): 592-596.

ABSTRACT(IN KOREAN)

수축기 혈압이 두 맥파전파속도의 결과 불일치에 미치는 영향 :
상완동맥-족부동맥 맥파전파속도, 경동맥-대퇴동맥 맥파전파속도

연세대학교 보건환경대학원 의공학과

한민호

배경 : 맥파전파속도(pulse wave velocity, PWV)는 뇌졸중과 심혈관질환의 독립적 위험요소인 동맥경직도를 측정할 수 있는 유용한 검사이다. 그 중 상완동맥-족부동맥 맥파전파속도(brachial-ankle PWV, baPWV)는 탄력성이 풍부한 중심동맥(대동맥)과 대동맥에 비해 적은 탄성과 직경이 가는 말초동맥(상완동맥, 대퇴동맥)의 동맥경직도가 혼합 반영되어 있어서 주로 중심동맥의 경직도만을 반영하는 경동맥-대퇴동맥 맥파전파속도(carotid-femoral PWV, cfPWV)보다 평균적으로 높은 경향이 있고, 또한 상대적으로 혈압에 민감하게 반응할 수 있기 때문에 측정 시 고혈압의 기준 중 하나인 상완동맥 수축기 혈압 140mmHg 근방의 혈압이 관찰되는 환자에서 두 맥파전파속도 결과의 불일치가 생길 가능성이 있다.

방법 : 본 연구는 baPWV와 cfPWV를 모두 시행한 급성 허혈성 뇌졸중 환자 114명을 대상으로 하였다. 우리는 측정 당시 수축기 혈압과 두 맥파전파속도 결과의 불일치간의 관련성을 연구하였다.

결과 : 전체 대상자는 114명이었으며, 두 검사 결과의 일치군과 불일치군은 각각 54, 60명이었다. 전체 대상자의 상완동맥에서 측정한 수축기 혈압은 $140.4 \pm 21.0 \text{ mmHg}$ 였고, 중심동맥의 수축기 혈압은 $128.8 \pm 20.4 \text{ mmHg}$ 였으며, 두 수축기 혈압 모두 일치군에서 유의하게 높았다 ($p=0.013$, $p=0.045$). 다른 심혈관 위험인자들에서는 두 군간의 통계적으로 유의한 차이는 보이지 않았다. 상완동맥의 수축기 혈압을 144 mmHg 를 기준으로 $<144 \text{ mmHg}$ bSBP군과 $\geq 144 \text{ mmHg}$ bSBP군으로 두 집단으로 나누고, 중심동맥의 수축기 혈압은 133 mmHg 를 기준으로 $<133 \text{ mmHg}$ cSBP군과 $\geq 133 \text{ mmHg}$ cSBP군으로 나누어 다변량 분석을 실시하였다. 그 결과 $<144 \text{ mmHg}$ bSBP는 두 맥파전파속도검사의 결과 불일치와 관련이 있는 독립적 인자였다 ($p=0.037$). 한편 $<133 \text{ mmHg}$ cSBP는 두 맥파전파속도검사의 결과 불일치와 통계적으로 유의한 관련은 없었다 ($p=0.099$).

결론 : baPWV는 cfPWV보다 bSBP에 의해 비교적 영향을 많이 받을 수 있기 때문에 $<144 \text{ mmHg}$ bSBP를 보이는 환자군에서 cfPWV가 정상범위에 있는데도 불구하고, baPWV가 정상범위를 넘어 높게 나타날 우려가 있다. 따라서 상완동맥 수축기 혈압 140 mmHg 근방의 혈압이 관찰되는 환자에서 동맥의 경직도를 파악할 때 baPWV보다는 cfPWV가 혈압에 덜 취약하므로 더 유용하게 사용될 수 있을 것으로 예상된다.

핵심되는 말 : 불일치, 수축기 혈압, 상완동맥-죽부동맥 맥파전파속도, 경동맥-대퇴동맥 맥파전파속도