



ORIGINAL ARTICLE

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The Influence of Systolic Blood Pressure on Discordance between Brachial-Ankle Pulse Wave Velocity and Carotid-Femoral Pulse Wave Velocity Results

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ABSTRACT

Background: The brachial-ankle pulse wave velocity (baPWV) is more likely to be influenced by high blood pressure than carotid-femoral pulse wave velocity (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 systolic blood pressure (SBP). **Methods:** We studied 114 patients with acute brain infarction or transient ischemic attack who underwent both baPWV and cfPWV measurements. We investigated the influence of SBP on discordance between baPWV and cfPWV results in patients with a slightly high SBP. **Results:** 114 patients were divided into accordance and discordance groups by matching both pulse wave velocity (PWV) results. 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 brachial artery systolic blood pressure (bSBP) was categorized into two groups (< 144 mmHg bSBP, and ≥ 144 mmHg bSBP) based on 144 mmHg bSBP. The central artery systolic blood pressure (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. **Conclusions:** 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 a slightly higher bSBP.

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Key Words: Discordance, Systolic blood pressure, Brachial-ankle pulse wave velocity, Carotid-femoral pulse wave velocity

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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 about 140 mmHg SBP, which is on the border of hypertension and is slightly 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. We used an arbitrary cut-off value of SBP to investigate the influence of SBP

on PWV.

MATERIALS AND METHODS

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.

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) according to methods previously reported.⁸ 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. 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 pa-

tient'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. The baPWV was calculated by the following equations: $baPWV = La - Lb / \Delta T_{ba}$ (cm/s).

The La is the path length from the entrance of the aortic valve to ankle ($La = 0.8129 \times \text{height}\{\text{cm}\} - 2.0734$), the Lb is the path length from the entrance of the aortic valve to brachium ($Lb = 0.2195 \times \text{height}\{\text{cm}\} - 12.328$).⁹ 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.¹⁰⁻¹² 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: $ABI = \text{each tibial SBP} / \text{the higher brachial SBP}$.

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 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.¹³

Measurements of cfPWV

The principle 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). 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. 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-unilat-

eral 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. The cfPWV was calculated by the following equations: $cfPWV = L_f - L_c / \Delta T_{cf}$ (m/s).

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 (Fig. 1). 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.¹⁴ 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.¹⁵ 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.¹⁶ Current smoking was defined as having smoked a cigarette within 1 year prior to admission. Body mass index 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 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.

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) 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 concordance and discordance groups based on results of

both PWVs. The Fisher's exact test was conducted to investigate the association and frequency between findings of cPWV and those of baPWV. We carried out the Mann-Whitney test to compare each PWV between two subgroups in each bSBP, cSBP and a hypertension group. In addition to simple linear regression analysis which can estimate the relationship between a discordance group and each blood pressure-related variable, multiple linear regression analysis was performed to determine the independent influence of each variable on discordance. All statistical tests were two-tailed, and $p < 0.05$ was considered statistically significant.

RESULTS

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 pa-

tients 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. An accordance group defined that both results were normal or abnormal together, and the others were included into a discordance group except for an accordance group. 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 cPWV was 37.7% in total, and higher in the accordance group than the discordance group ($p < 0.001$). However, the percentage of an abnormal baPWV was 88.6% in total, and higher in the discordance

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 \pm 11.01	61.39 \pm 10.56	62.63 \pm 11.46	0.549
Body mass index (kg/m ²)	24.02 \pm 3.06	24.27 \pm 3.19	23.80 \pm 2.94	0.415
Brachial artery systolic blood pressure (mmHg)	140.40 \pm 21.00	145.50 \pm 22.1	135.80 \pm 19.0	0.013
Central artery systolic blood pressure (mmHg)	128.80 \pm 20.40	132.80 \pm 21.6	125.20 \pm 18.6	0.045
Brachial-ankle pulse wave velocity (m/s)	19.18 \pm 4.86	19.58 \pm 5.30	18.82 \pm 4.44	0.405
Carotid-femoral pulse wave velocity (m/s)	9.89 \pm 2.82	11.43 \pm 3.14	8.50 \pm 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 \pm 8.70	87.38 \pm 9.21	85.78 \pm 8.21	0.334
Total cholesterol (mg/dL)	176.47 \pm 42.30	174.95 \pm 47.12	177.83 \pm 37.80	0.718
LDL-cholesterol (mg/dL)	100.76 \pm 31.41	101.96 \pm 29.10	99.70 \pm 33.55	0.704
HDL-cholesterol (mg/dL)	43.35 \pm 12.67	43.13 \pm 14.25	43.55 \pm 11.22	0.862
Triglyceride (mg/dL)	130.69 \pm 78.23	127.15 \pm 72.61	133.75 \pm 83.29	0.658
HbA _{1c} (%)	6.56 \pm 1.19	6.64 \pm 1.24	6.50 \pm 1.15	0.538
Plasma glucose (mg/dL)	144.41 \pm 58.10	146.89 \pm 49.44	142.18 \pm 65.26	0.668
Carotid augmentation index (HR75) (%)	24.46 \pm 9.56	23.22 \pm 9.12	25.58 \pm 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 \pm standard deviation or number (%).

group ($p=0.001$). Fasting glucose, total cholesterol, triglyceride, HbA_{1c}, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol were not different between both groups.

Association between findings of cfPWV and those of baPWV

The total number of patients was 141. 71 patients (62.3%) showed normal finding and 43 patients (37.7%) showed abnormal finding in cfPWV. 13 patients (11.4%) showed normal finding and 101 patients (88.6%) showed abnormal finding in baPWV. Only one patient (2.3%) showed abnormal cfPWV and normal baPWV, but 59 patients (83.1%) showed normal cfPWV and abnormal baPWV in Table 2. It implied that the

discordance group was mostly composed of the patients (51.8% of all patients) who have both normal cfPWV and abnormal baPWV findings. The above results were shown to be statistically significant ($p=0.030$).

Association between pulse wave velocity and systolic blood pressure

The bSBP was categorized into two subgroups (<144 mmHg bSBP, and ≥ 144 mmHg bSBP) by 144 mmHg bSBP, which has been used as a criterion of hypertension in a study on ambulatory blood pressure in a rural Japanese community.¹⁷ The cSBP also was categorized into two subgroups (<133 mmHg cSBP, and ≥ 133 mmHg cSBP) by 133 mmHg. 133 mmHg cSBP was obtained by subtracting 11 mmHg, the mean value of differences between bSBP and cSBP of each patient, from 144 mmHg. Table 3 showed that both cfPWV and baPWV had increased bSBP and cSBPs in abnormal findings ($p<0.05$ in each group). Most patients with normal cfPWV had <144 mmHg bSBP and/or <133 mmHg cSBP ($p<0.001$ and $p=0.001$). Most patients with abnormal baPWV had <144 mmHg bSBP and/or <133 mmHg cSBP ($p=0.059$ and $p=0.011$).

Table 2. Association between the finding of cfPWV and that of baPWV

	cfPWV		<i>p</i> -value
	Normal (N = 71)	Abnormal (N = 43)	
baPWV			
Normal (N = 13)	12 (16.9)	1 (2.3)	0.030
Abnormal (N = 101)	59 (83.1)	42 (97.7)	

cfPWV, carotid-femoral pulse wave velocity; baPWV, brachial-ankle pulse wave velocity.

Table 3. Association between pulse wave velocity and systolic blood pressure

Variable	cfPWV			baPWV		
	Normal (N = 71)	Abnormal (N = 43)	<i>p</i> -value	Normal (N = 13)	Abnormal (N = 101)	<i>p</i> -value
Brachial artery systolic blood pressure (mmHg)	133.31±18.29	152.12±20.15	<0.001	127.77±18.80	142.03±20.82	0.021
Central artery systolic blood pressure (mmHg)	122.11±17.85	139.81±19.67	<0.001	114.46±18.32	130.63±19.98	0.007
<144 bSBP (mmHg)	53 (74.6)	16 (37.2)	<0.001	11 (84.6)	58 (57.4)	0.059
<133 cSBP (mmHg)	51 (71.8)	17 (39.5)	0.001	12 (92.3)	56 (55.4)	0.011

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

Table 4. Association between discordance of findings and blood pressure

Characteristic	Univariate			Multivariate		
	Odds ratio	Standard error	<i>p</i> -value	Odds ratio	Standard error	<i>p</i> -value
<144 bSBP (mmHg)	2.33	0.39	0.031 ^a	13.76	1.26	0.037 ^a
<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 ^a
cfPWV (m/s)	0.53	0.13	<0.001 ^b	0.39	0.19	<0.001 ^b

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

^a p -value <0.05

^b p -value <0.001

Association between discordance of PWV findings and SBP

Univariate analysis showed that <144 mmHg 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, <144 mmHg 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, <133 mmHg cSBP was not associated with the discordance of PWV findings (Table 4).

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 regardless of arterial stiffness.⁶ Therefore, it is difficult to determine whether the abnormal PWV finding actually means the progress of arteriosclerosis or that originates with 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, because peripheral arteries have less buffering effect than central arteries. These situations could cause discordance between the baPWV and cfPWV results in patients with about 140 mmHg bSBP, which is higher than normotensive. Our study demonstrated a significant association between the discordance of both PWV results 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 baPWV or cfPWV or both PWVs together to strictly evaluate arterial stiffness in various studies related to cardiovascular disease,^{8,18-21} 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 Shirai et al.⁷ 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. As mentioned earlier, Tanaka et al.⁴ conducted a study with a total of 2,287 adults (1,265 men and 1,022 women) in six different institutions in Japan and one in the USA to determine associations between cfPWV and baPWV. They reported that there was a significant positive relationship between cfPWV and baPWV, but baPWV results were approximately 20% higher than cfPWV results due to the stiffness of peripheral arteries in addition to central arteries. It might diminish the reliability of the prediction for cardiovascular diseases to include a peripheral component from the femoral artery to the posterior tibial artery in baPWV, because 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. Along with previous studies, we demonstrated that baPWV value was higher than cfPWV value in Table 1, and both PWV measures were positively correlated with SBP in Table 3. In addition, The abnormal baPWV findings were frequently observed in subjects with the normal cfPWV findings, and consequently led to the discordance between baPWV and cfPWV results. Our study newly confirmed that there was a significant association between the discordance of both PWV results and <144 mmHg bSBP, except for <133 mmHg cSBP. This fact implies that the higher the SBP is, the more the two PWV findings correspond with each other, given above results including Table 2. 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. The discordance might be more predominant in subjects adjacent to 140 mmHg bSBP, since baPWV varies with blood pressure more than cfPWV and consequently is prone to being abnormal in subjects with a slightly higher bSBP. However, we could not demonstrate whether there is a statistically significant association between the discordance and a subgroup among several subgroups randomly divided on the basis of 140 mmHg bSBP, on account of a small sample size. The cSBP was not related to the discordance between baPWV and cfPWV results in our study, because the cSBP only reflects conditions of central arteries and it may equally affect both PWV measures. In conclusion, this study suggest that the

result of cfPWV may be more useful for exactly estimating a patient's arterial stiffness by excluding a synergistic effect of elevated blood pressure in peripheral arteries, when patients undergo both PWV measures and then they have a slightly higher 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 <144 mmHg bSBP can be generalized to other populations. Second, the sample size of subjects is small when compared to preceding PWV related studies.^{3,4} 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, but we were unable to do so due to a small sample size. Therefore, the results of our study need to be reconfirmed with a larger number of participants. Finally, there have been no studies with subjects divided into normal and abnormal findings according to the intact measurement results on paper, thus many additional studies are needed to validate and strengthen the reliability of this study.

CONCLUSION

The baPWV measure was more affected by bSBP, and consequently resulted in an abnormal finding despite a normal cfPWV finding in the same person with <144 mmHg bSBP. However, <133 mmHg 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 a slightly higher bSBP.

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