State of the Art Review: Brachial-Ankle PWV

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The brachial-ankle pulse wave velocity (brachial-ankle PWV), which is measured simply by wrapping pressure cuffs around the four extremities, is a simple marker to assess the stiffness of the medium- to large- sized arteries. The accuracy and reproducibility of its measurement have been confirmed to be acceptable. Risk factors for cardiovascular disease, especially advanced age and high blood pressure, are reported to be associated with an increase of the arterial stiffness. Furthermore, arterial stiffness might be involved in a vicious cycle with the development/progression of hypertension, diabetes mellitus and chronic kidney disease. Increase in the arterial stiffness is thought to contribute to the development of cardiovascular disease via pathophysiological abnormalities induced in the heart, brain, kidney, and also the arteries themselves. A recent independent participant data meta-analysis conducted in Japan demonstrated that the brachial-ankle PWV is a useful marker to predict future cardiovascular events in Japanese subjects without a previous history of cardiovascular disease, independent of the conventional model for the risk assessment. The cutoff point may be 16.0 m/s in individuals with a low risk of cardiovascular disease (CVD), and 18.0 m/s in individuals with a high risk of CVD and subjects with hypertension. In addition, the method of measurement of the brachial-ankle PWV can also be used to calculate the inter-arm systolic blood pressure difference and ankle-brachial pressure index, which are also useful markers for cardiovascular risk assessment.

1. Introduction

Much evidence has been accumulated to suggest that the pulse wave velocity (PWV), a measure of the arterial stiffness, is an independent marker of future cardiovascular events, and that measurement of this marker is simple enough to allow it to be measured in clinical practice in the management of patients with risk factors for or suffering from cardiovascular disease (CVD)[1-4]. We published our previous review on brachial-ankle PWV, entitled "Brachial-Ankle PWV: Current Status and Future Directions as a Useful Marker in the Management of Cardiovascular Disease and/or Cardiovascular Risk Factors," in 2016[1]. We discuss the more recent findings related to the brachial-ankle PWV in the current review.

2. What is Brachial-Ankle PWV?

2-1: Arterial Stiffness and Arterial Medial Layer

First, we would like to briefly describe the changes in the arterial medial layer that occur in association with atherosclerotic vascular damage, affecting the arterial stiffness[5-8]. The arterial medial layer plays an essential role in increase of the arterial stiffness. The major components of the medial layer are the vascular smooth muscle cells and connective tissue elements such as elastin and collagen. Consecutive proliferation and migration of vascular smooth muscle cells and abnormalities of the connective tissue elements (i.e., degeneration of elastin and increased deposition of collagen) in the vessel wall, results not only in neo-intimal thickening and plaque formation, but also in increase of the arterial stiffness[5-8]. In addition, a high vascular smooth muscle tone and blood pressure play important roles in functional arterial stiffening[2].
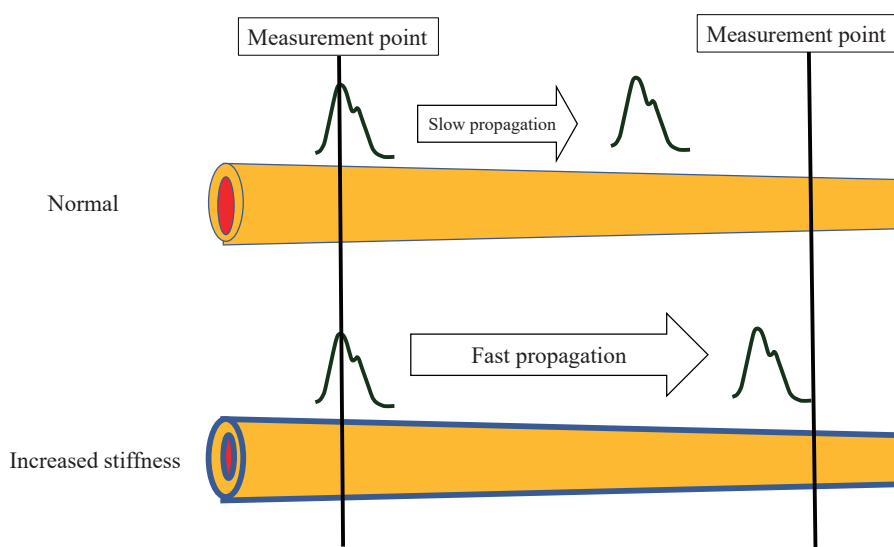
Fig. 1. Propagation of the pressure wave on the arterial wall in cases with/without increased arterial stiffness

2-2: The Concept of Brachial-Ankle PWV

PWV reflects segmental arterial elasticity[1, 2, 8-12]. The pulse wave, generated by cardiac contraction, is propagated throughout the arterial tree. PWV is calculated as the distance traveled by the pulse wave divided by the time taken for the pulse wave to travel this distance; increase in arterial stiffness is associated with accelerated propagation of the pulse wave, corresponding to an increase in the PWV (**Fig. 1**). In biomechanics, the Moens–Korteweg equation, shown below, describes the relationship of the PWV with vessel-related factors[1, 8-12]:

$$PWV^2 = E \cdot h/r \cdot p,$$

where E = elastic modulus, h = vessel wall thickness, r = vessel radius, and p = blood density. According to this equation, decrease in functional/structural elasticity, increase in the vessel wall thickness and/or the decrease in the vessel diameter can increase the PWV[1, 8-12].

The arterial tree can be simply classified into 3 levels: the elastic arteries (i.e., large-sized arteries), muscular arteries (i.e., medium-sized arteries), and arterioles[1, 2, 8-10]. In contrast to the carotid-femoral PWV, which is the parameter conventionally used to assess the stiffness of large-sized arteries, the brachial-ankle PWV is a marker of the stiffness of the large- to medium-sized arteries[11]. Brachial-ankle PWV is measured using a volume-plethysmographic apparatus (form PWV/ABI; OMRON Health Care, Co., Ltd., Kyoto, Japan). While measurement of the carotid-femoral PWV involves more effort and the need for probes to detect the arterial pulse waveform, the method of measurement of the brachial-ankle PWV is much simpler, and only involves wrapping of pressure cuffs around all four extremities[1, 2, 11]. The method of measurement of the brachial-ankle PWV is reported in detail in our previous review[1, 2, 11, 12]. The device simultaneously records the PWV, blood pressure in the four extremities (i.e., the ankle-brachial pressure index (ABI) and inter-arm blood pressure difference (IAD) can also be calculated), an electrocardiogram, and the heart sounds[11, 12]. The pulse volume waveforms are recorded using a semiconductor pressure sensor (the sample acquisition frequency for PWV is set at 1,200 Hz).

Diminished reliability of the brachial-ankle PWV measurement is reported in subjects with atrial fibrillation, frequent arrhythmias, and/or inaccurate pulse waveform recordings because of arterial stenosis (e.g., when the ankle-brachial pressure index is <0.95)[11-13]. The absolute values of the brachial-ankle PWV have been reported to be substantially higher than other measures of the PWV[14]. Sugawara *et al.* reported that the height-based formulas used to estimate the arterial path length grossly overestimate the actual path length, leading to overestimation of the brachial-ankle PWV[15]. Acceptable accuracy and reproducibility of measurement of the brachial-ankle PWV have been confirmed in previous studies[11].

3. Factors that Increase the Brachial-Ankle PWV

The significances of the effects of the conventional risk factors for CVD on the arterial stiffness are summarized as follows;

3-1: Age, Blood Pressure, and Heart Rate

Based on the results of a meta-analysis, Cecerja et al. reported that age and blood pressure are major determinants of the arterial stiffness[16]. A recent cross-sectional study reported that the brachial-ankle PWV is associated more closely with the home blood pressure than with the office blood pressure[17], and prospective observational studies have reported that high blood pressure, and also high heart rate, are associated with accelerated increase of the brachial-ankle PWV[18-21].

3-2: Diabetes Mellitus/Glucose Intolerance

Several studies have reported that abnormal glucose metabolism, even in its early stages, is associated with and increase in the arterial stiffness and also with accelerated increase of the arterial stiffness[18, 22, 23].

3-3: Lipid Metabolism

Conflicting results have been reported on the association of hypercholesterolemia with arterial stiffness, but a recent meta-analysis revealed that hypercholesterolemia is associated with the carotid intima-media thickness rather than with the PWV[24]. Some studies have reported an association of the serum triglyceride level, but not of the serum cholesterol level, with the brachial-ankle PWV[25-28]. Based on these findings, as compared to high blood pressure and/or abnormal glucose metabolism, dyslipidemia may not contribute directly to increase of the arterial stiffness.

3-4: Smoking

Dose-dependent association of smoking with the progression of arterial stiffening has been reported[29, 30].

3-5: Uric Acid

While it still remains to be clearly concluded if serum uric acid is an independent risk factor for CVD[31], recent studies have reported a significant association of the serum uric acid levels with arterial stiffness and the progression of arterial stiffening[32, 33].

3-6: Obesity/Metabolic Syndrome/Sleep Apnea

Metabolic syndrome and obstructive sleep apnea act to increase the arterial stiffness[34-38]. In addition, nonalcoholic fatty liver disease has also been reported to be associated with increase of the brachial-ankle PWV[39]. Under these conditions, inflammation and/or an activated sympathetic nervous system are thought to have some roles in increasing the arterial stiffness[34-39]. On the other hand, Tang *et al.* reported that arterial stiffness, as measured by the brachial-ankle PWV, increased with the body mass index (BMI), however, this association was no longer observed after adjustments for all other cardiovascular risk factors[40]. In addition to metabolic syndrome and sleep apnea, obesity is often associated with many risk factors for CVD, and therefore, the significance of the effect of obesity itself on the arterial stiffness has not yet been fully clarified.

3-7: Chronic Kidney Disease (CKD)

Risk factors for CKD, such as hypertension and diabetes mellitus, act directly to increase the arterial stiffness[18, 19, 22, 23], and in some studies, the PWV was higher in subjects with diabetic CKD than in those with non-diabetic CKD[41]. Even so, increased arterial stiffness has been observed even in the early stages of CKD[42-45], and vascular calcification related to advanced CKD may augment this increase in arterial stiffness[45]. Recently, the ARIC study reported that the estimated glomerular filtration rate is more closely associated with the carotid-femoral PWV than with the brachial-ankle/heart-ankle PWV[46]. Thus, stiffness of the large arteries may have an essential role in the initiation/progression of CKD.

3-8: Mechanisms of Increase of the Arterial Stiffness

Arteries have three wall layers, and pathophysiological abnormalities caused by risk factors for CVD, which affect components in all the three layers, increase the arterial stiffness. The tissue components that could be affected include: endothelium (endothelial dysfunction); media (elastin degradation, collagen deposition, cross-linking of collagen, vascular smooth muscle cell hypertrophy and proliferation, calcification, and deposition of advanced glycation end products); adventitia (collagen deposition and cross-linking of collagen)[1, 2, 6-8]. For example, aging and hypertension cause thinning, splitting, fraying and fragmentation of the elastic fibers[47]. Vascular inflammation and oxidative stress related to those risk factors cause endothelial dysfunction, degradation of collagen and elastin, changes in the proteoglycan composition and hydration status, and medial calcification[48-50]. Elevated blood pressure and vascular inflammation cause vascular smooth muscle cell hypertrophy[48-50]. Diabetes increases the accumulation of advanced glycation end products on collagen and elastin[23, 51], and chronic kidney disease increases arterial stiffness via arterial calcification[49, 50]. Clinical studies have reported significant associations of the brachial-ankle PWV with markers of inflammation or oxidative stress[33, 52]. On the other hand, high blood pressure, high heart rate, and high sympathetic tone increase functional arterial stiffness[1, 2, 18-21]. Recently, several molecular targets involved in arterial stiffening have been identified, and considering these mechanisms, establishment of de-stiffening approaches that will not affect the arterial
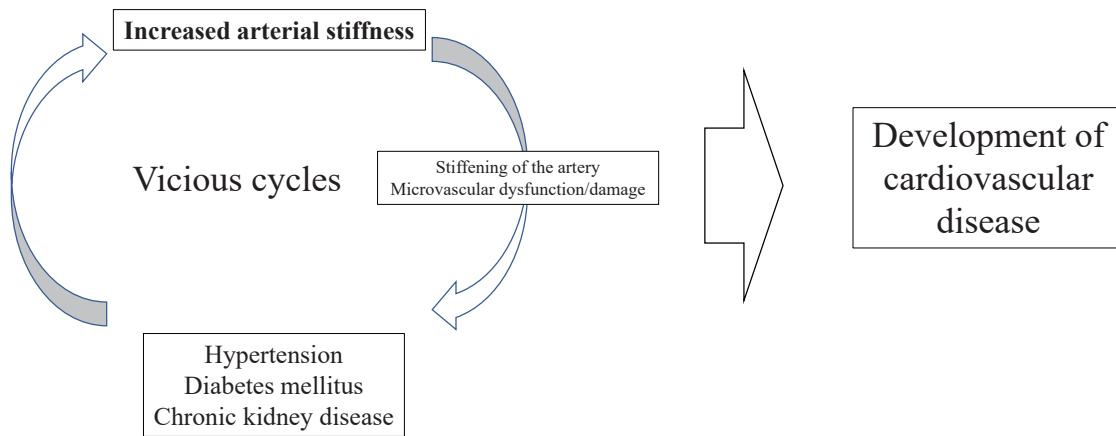
Fig. 2. Vicious cycles among arterial stiffness and hypertension/diabetes mellitus/chronic kidney disease
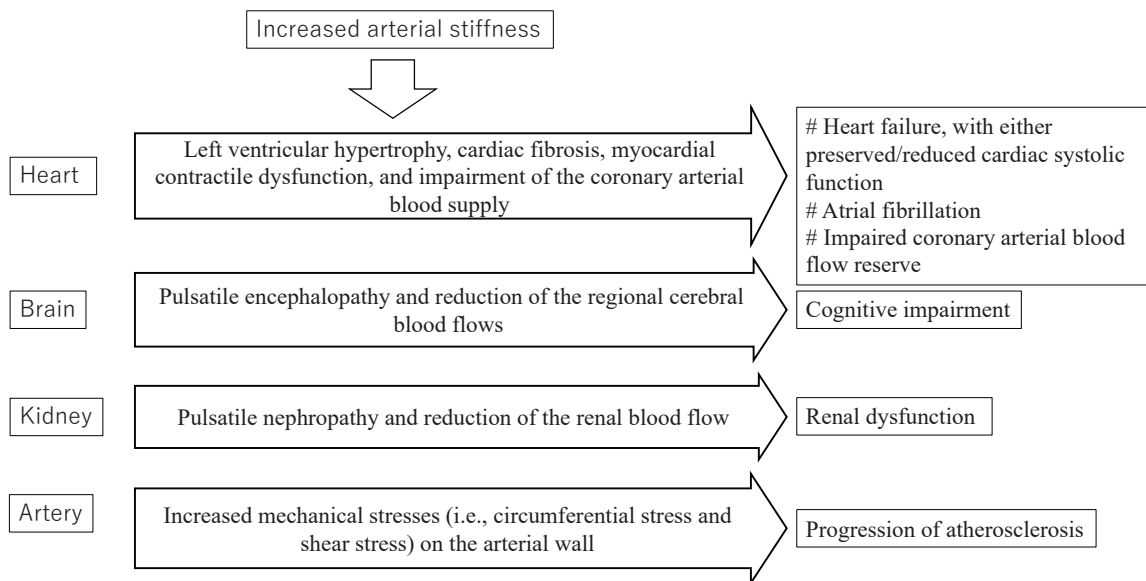

Fig. 3. Pathophysiological abnormalities associated with increased arterial stiffness which contribute to the development of cardio-vascular disease

strength or remodeling is proposed[53-55].

4. Mechanisms of Initiation and Progression of Cardiovascular Disease

4-1: PWV and Progression of the Cardiovascular Risk

Increased arterial stiffness increases the amplitude of the forward pressure wave and also causes microvascular damage in the peripheral resistance arteries and in the kidney, which cause the development of hypertension, diabetes mellitus, and/or CKD[56-62]. Details of the underlying mechanisms are described in section 4-2. Conversely, hypertension, diabetes mellitus and CKD also contribute to the progression of arterial stiffening[16-19, 22, 23, 41-45], thus forming a vicious cycle[63, 64], which may exacerbate the risk status for CVD (**Fig. 2**).

4-2: PWV and Pathophysiological Abnormalities in the Cerebro-Cardiovascular Systems

In the presence of atherosclerotic disease burdens, plaque rupture has a pivotal role in the onset of CVD. On the other hand, arterial stiffness is thought to reflect diffuse functional and structural changes of the arterial wall rather than the extent of focal plaque lesions[48-50]. Even so, increased arterial stiffness is an independent risk factor affecting the prognosis[3, 4]. The plausible mechanisms are summarized in **Fig. 3**; it would appear that both functional and structural arte-
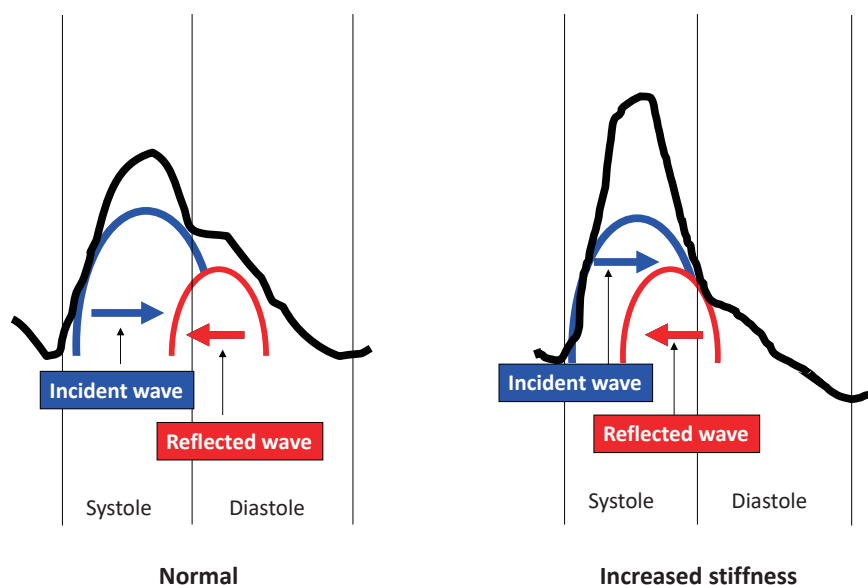
Fig. 4. Central hemodynamics in cases with/without increased arterial stiffness

rial stiffness are important[1, 2, 5-8, 64-66].

Firstly, the conduit arteries have a dominant role in cushioning against and dampening the pressure oscillations associated with intermittent ventricular ejection (i.e., the windkessel effect) and transforming the pulsatile flow into a steady flow for supplying oxygen to the tissues[1, 2, 5-8, 64-66]. This elasticity of the conduit arteries has beneficial effects on the cerebro-cardiovascular system, such as it facilitates organ blood supply during diastole, especially to the heart, reducing the cardiac afterload, and/or protects the arterial wall and microvasculature from the mechanical stresses generated by cardiac contractions[1, 2, 5-8, 64-66]. Impairment of conduit arterial function could have several harmful effects on the cerebro-cardiovascular systems (**Fig. 3**).

4-2-1: Heart

Increased arterial stiffness directly increases the cardiac afterload. It increases the speed of travel of the pressure wave in the arteries, and a summation of the forward pressure wave and reflected pressure wave in the aorta is observed during cardiac systole[2, 8, 66] (**Fig. 4**). This phenomenon is thought to further increase the cardiac afterload[2, 8, 66]. The increased cardiac afterload causes left ventricular hypertrophy and cardiac fibrosis, and finally myocardial contractile dysfunction[67, 68]. Coronary arteries are mostly perfused during cardiac diastole[2, 8, 66]; increased arterial stiffness causes both a reduction of the stock volume of blood in the aorta and acceleration of the speed of return of the reflected pressure wave to the aorta during systole

(**Fig. 4**), potentially contributing to impairment of the coronary arterial blood supply to the heart. The above-mentioned pathophysiological abnormalities could cause heart failure, both with preserved/reduced cardiac systolic function[69-71], atrial fibrillation[72] and impaired coronary arterial flow reserve[73].

4-2-2: Brain and Kidney (Pulsatile Nephropathy and Encephalopathy)

Attenuation of the cushioning effect of the elastic arteries amplifies the pressure pulsatility and increases the transmission of pulsatile energy to the peripheral microcirculation (**Fig. 5**). Exposure of small vessels to high pressure and high flow levels results in microvascular damage, especially, in high-blood flow organs such as the brain and kidney[1, 2, 5-8, 64, 65, 66] (the so-called pulsatile nephropathy and encephalopathy)[65]. Recently, Jefferson et al. demonstrated that increased stiffness of the central arteries could contribute to reductions in regional cerebral blood flows[74] and also of the renal blood flow[75]. These phenomena may cause cognitive impairment and renal dysfunction, respectively[60-62, 76, 77].

4-2-3: Arterial Remodeling and Atherogenic Actions

The arterial wall is exposed to two mechanical stresses; circumferential stress (stretch) and shear stress. Increased arterial stiffness is associated with abnormalities of both stresses owing to fluctuations of the pressure and speed of the blood flow in the arterial lumen[78]. These stresses trigger signaling cascades in the arterial wall contributing to vascular growth, such

Normal

Increased stiffness

Cushioning effect

Pulsatile energy generated by the heart

Attenuated cushioning effect

Pulsatile energy generated by the heart

Microvascular damage

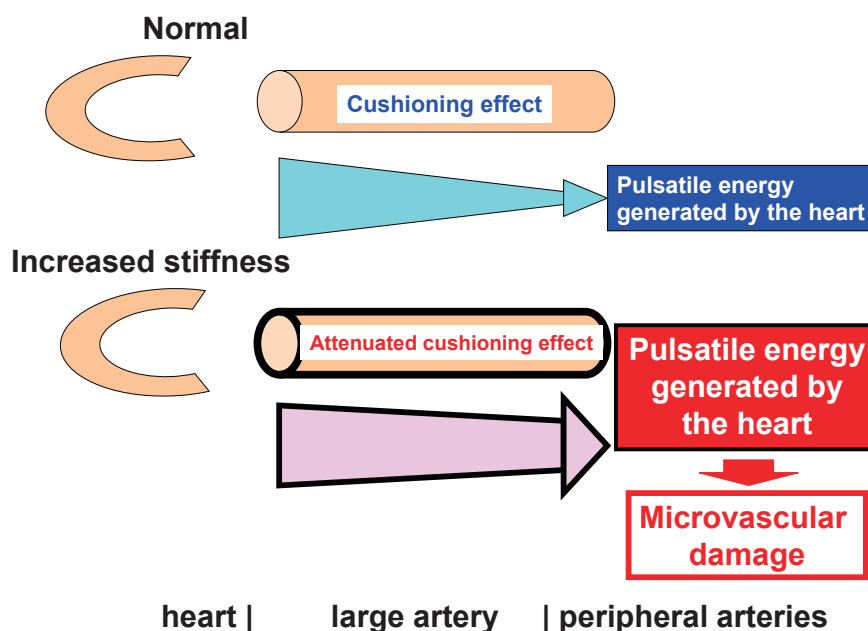heart |　　large artery　　| peripheral arteries

Fig. 5. Cushioning effect of the large arteries on the pulsatile energy generated by the heart
In the case of attenuation of the cushioning effect, the pulsatile energy causes peripheral vascular damage

as tyrosine kinase, phosphatidyl inositol-3-kinase, protein kinase C, epithelial sodium channel, and/or nicotinamide adenine dinucleotide phosphate oxidase signalings, and activations of these signaling cascades are thought to contribute to the initiation/progression of atherosclerosis and also to arterial wall thickening[79, 80]. In addition, local arterial stiffness may affect the arterial vulnerability to plaque formation[81], and an association has been reported between arterial stiffness and carotid atherosclerosis[68, 82]. Recently, we reported from the FMD-J multicenter prospective observational study conducted in subjects with hypertension (FMD-J study B), that increased arterial stiffness rather than endothelial dysfunction may be more closely associated with the progression of carotid atherosclerosis[83]. Furthermore, in this study, endothelial dysfunction was associated with the progression of arterial stiffening[83], and therefore, endothelial dysfunction may affect the progression of atherosclerosis via, at least in part, increasing arterial stiffness.

5. Is Brachial-Ankle PWV Useful for Cardiovascular Risk Stratification? (Value as a Predictor of the Prognosis, Independent of Other Established Markers)

5-1: Brachial-Ankle PWV, Cardiovascular Events, and Cutoff Value

Several prospective studies have suggested that brachial-ankle PWV is an independent predictor of

the risk of cardiovascular disease. When the terms brachial-ankle PWV and cardiovascular events/prognosis were entered as key words in PubMED, a total of 55 studies examining the usefulness of the brachial-ankle PWV as a marker to predict future cardiovascular events or prognosis were found. Among these, 22 had been conducted in subjects without a history of CVD and 23 had been conducted in subjects with CVD (including CKD) (i.e., 11 studies on CKD, 14 studies on coronary artery disease, 3 studies on heart failure, and 6 studies on cerebrovascular disease)[69, 70, 84-136]. These studies confirmed the usefulness of brachial-ankle PWV as a predictor of the risk of cardiovascular disease. The results of most of these studies are summarized in Table 2 in Reference 1[1].

J-BAVEL (Japan Brachial-Ankle Pulse Wave Velocity Individual Participant Data (IPD) Meta-Analysis of Prospective Studies) is an IPD meta-analysis of cohort studies that investigated the association of the brachial-ankle PWV with the all-cause mortality and risk of CVD that was conducted by the brachial-ankle PWV IPD meta-analysis study group[3]. This collaborative study included the data from 14 cohort studies conducted in Japan (9 published and 5 unpublished studies). A total of 14,673 Japanese participants without a history of CVD were included for the analyses. During the average follow-up period of 6.4 years, 687 participants died and 735 developed cardiovascular events. A higher brachial-ankle PWV was significantly associated with a higher risk of CVD,
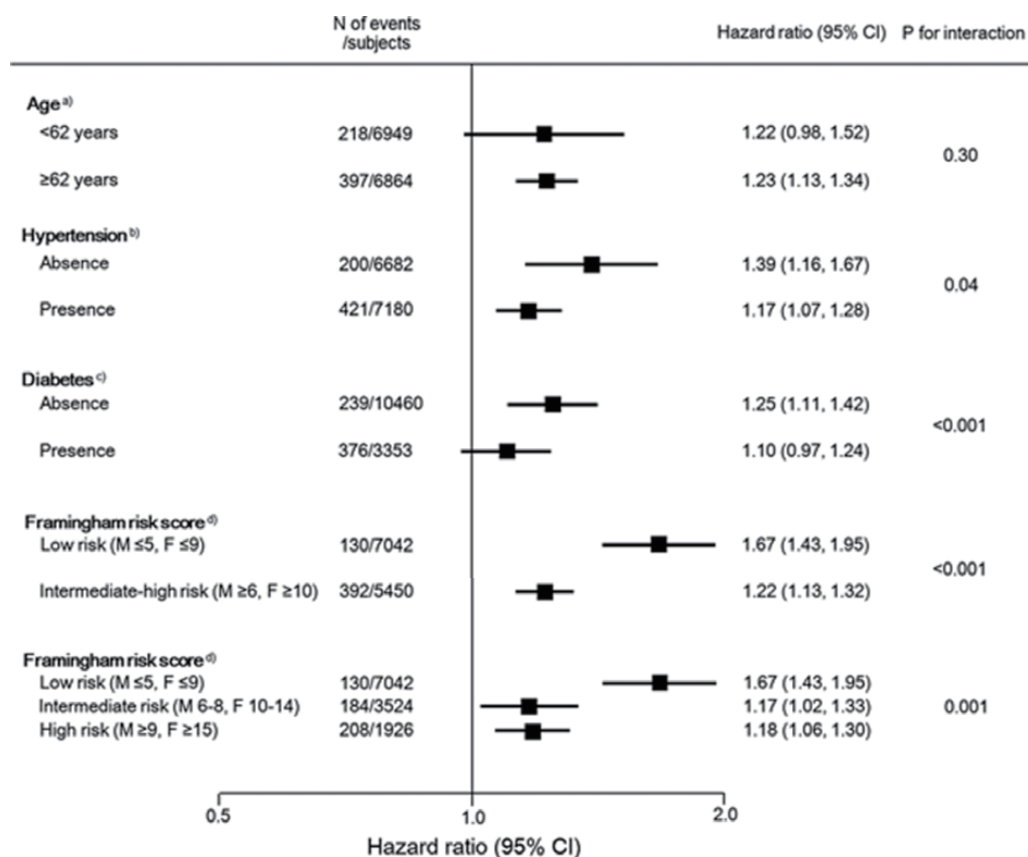
Fig. 6. Results of an individual participant data meta-analysis conducted to examine the significance of the brachial-ankle pulse wave velocity as a predictor of future cardiovascular events in patient sub-groups

even after adjustments for conventional risk factors (*P* for trend < 0.001).

The important findings of this study were as follows; 1) Every one standard deviation unit higher brachial-ankle PWV was associated with a 1.2-fold (95% CI, 1.13–1.30) higher risk of CVD; 2) Addition of brachial-ankle PWV to the model incorporating the Framingham risk score (FRS) significantly improved the accuracy of the risk assessment for CVD; 3) With regard to the risk status for CVD defined by the FRS, the association of the brachial-ankle PWV was stronger in the subjects classified as being at low risk as compared with that in the subjects classified as being at intermediate-high risk (*P* for interaction < 0.001), although the hazard ratio for CVD was significantly higher in subjects with higher brachial-ankle PWV in both subgroups (**Fig. 6**)[3]; 4) The point on the receiver operating characteristic curve that was closest to yield-

ing the ideal of 100% sensitivity and 100% specificity was 15.9 m/s in the total study population (mean age = 60 ± 12 years old, mean blood pressure = 134 ± 21/79 ± 11 mmHg). In subjects with hypertension, the optimal cutoff value of the brachial-ankle PWV for predicting future CVD was 18.3 cm/s[137].

While carotid-femoral PWV is thought to be applicable in subjects with a high risk of CVD risk in the conventional risk assessment[4, 138], brachial-ankle PWV may be applicable even in those with a low risk of CVD[3]. The J-VABEL study reported the usefulness of the brachial-ankle PWV for predicting future CV events in subjects without a history of CVD. Furthermore, its usefulness has also been reported for predicting the CVD risk in subjects with CKD[106-111], coronary artery disease[117-130], heart failure[69, 70, 131] and cerebrovascular disease[132-136].

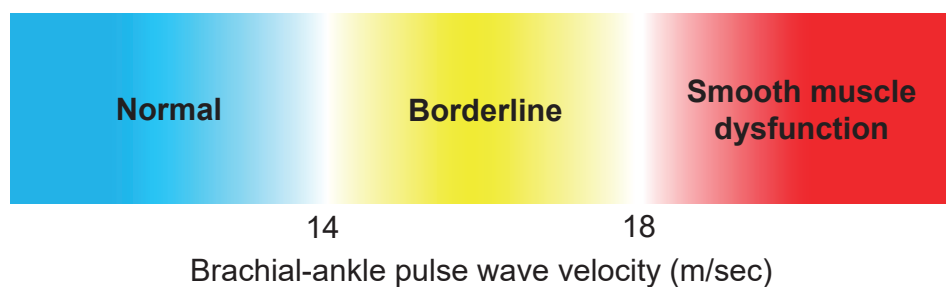The J-VABEL study proposed a cutoff value of

Fig. 7. Cutoff range of the brachial-ankle pulse wave velocity
Modified Hypertension. 2018 Nov; 72(5): 1060-1071

the brachial-ankle PWV for assessment of the CVD risk, but its value changed depending on the patients' clinical characteristics. The risk factors for CVD, especially advanced age and high blood pressure, act to increase the PWV[16]; therefore, two cutoff points of 16.0 m/s in patients with a low risk of CVD and 18.0 m/s in patients with a high risk of CVD and those with hypertension have been proposed[3, 5, 137]. The Physiological Diagnosis Criteria for Vascular Failure Committee proposed a cut-off value with its border zone has been proposed (**Fig. 7**)[5].

Flow-mediated vasodilatation (FMD), a marker of endothelial function, is also known as an independent predictor of future CV events[139]. Recently, the FMD-J multicenter prospective study (FMD-J study A) conducted in Japanese subjects with coronary artery disease showed that both FMD and brachial-ankle PWV were independent predictors of the risk of the patients[125]. Thus, while the FMD-J study, conducted in subjects with hypertension, proposed that endothelial dysfunction may contribute, at least in part, to the progression of arterial stiffness (FMD-J study B)[83], arterial stiffness may have a pivotal role in the development of CVD, independent of endothelial dysfunction.

The pathophysiological abnormalities related to increase of the arterial stiffness of the large-sized rather than the medium-sized arteries are thought to be the key underlying the increased cardiovascular risk[1, 2, 5-8, 64-66]; therefore, the carotid-femoral PWV has been suggested as a better and more direct measure of the arterial stiffness[8, 138]. The ARIC study reported that in elderly subjects, the significance of differences in the cumulative incidence of CVD among patients divided into quartiles according to the values of the markers was the highest for the carotid-femoral PWV, followed by that for the brachial-ankle PWV and then the cardio-ankle vascular index (CAVI)[105]. Even so, there are two issues with measurement of the carotid-femoral PWV (i.e., exposure of the inguinal region and need a probe to detect the pulse wave). On the other hand,

the brachial-ankle PWV is measured simply by wrapping pressure cuffs around the four extremities, so that the examiner does not have to have any special training or experience[1, 2, 11]. In addition, stiffness index β transformation of the brachial-ankle PWV, such as CAVI, may attenuate the significance of the brachial-ankle PWV as a risk marker for the development of pathophysiological abnormalities related to CVD[140]. Therefore, brachial-ankle PWV, not adjusted for the blood pressure, is quite applicable to cardiovascular risk assessment in daily practice.

5-2: Steno-Stiffness Approach in Clinical Practice

Measurement of the brachial-ankle PWV allows calculation of three markers, namely, brachial-ankle PWV, ABI, and IAD. ABI is a marker for the detection of peripheral arterial disease and IAD is a marker for the diagnosis of carotid artery stenosis, subclavian artery stenosis and vertebral artery stenosis. The J-VABEL study also demonstrated that lower (< 0.90) and higher ABI (≥ 1.30) values are significantly associated with an increased risk of CVD[141] and all-cause mortality, and IAD ≥ 15 mmHg is a reliable predictor of future stroke in Japanese subjects without a past history of CVD[142].

Based on above mentioned results of the J-VABEL studies, we propose that in daily practice, the use of the steno-stiffness approach (i.e., IAD, ABI, and brachial-ankle PWV) for CVD risk assessment in primary prevention may be efficient (**Fig. 8**)[143]. Firstly, we have to pay attention to the shape of the pressure waveform recorded to confirm the accuracy of the recording (dumping of the pressure waveform means inaccurate recording). IAD ≥ 15 mmHg is a simply measured useful physiological marker of the risk of stroke, and ABI < 0.90 or ≥ 1.30 is also a risk marker for the development of CVD. Finally, we can assess the extent of arterial stiffness based on the value of the brachial-ankle PWV. **Table 1** describes the approach to manage patients with abnormal findings
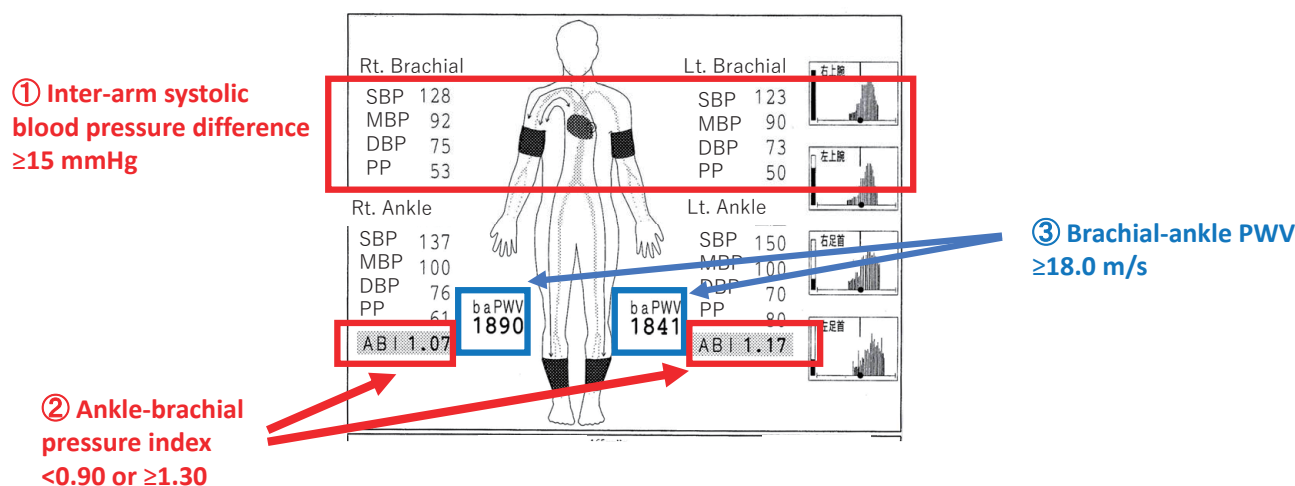
① Inter-arm systolic blood pressure difference ≥15 mmHg

③ Brachial-ankle PWV ≥18.0 m/s

② Ankle-brachial pressure index <0.90 or ≥1.30

Fig. 8. Schema of the steno-stiffness approach for the management of subjects with atherosclerotic cardiovascular diseases and/or cardiovascular risk factors

Abbreviations: Rt.=right; Lt.=left; SBP=systolic blood pressure; MBP=mean blood pressure; DBP=diastolic blood pressure; PP=pulse pressure

Table 1. Approach to patients with a high risk of cardiovascular disease

Re-confirmation of the status of control of the risk factors for cardiovascular disease.
Screening for subclinical cardiovascular disease (interview, physical examination [abdominal aneurysm, edema, heart enlargement, abnormal heart sounds, heart murmur, vascular bruit]).
Routine examinations (blood biochemical examination, electrocardiogram, chest X-ray).
Consider consulting a specialist, such as a cardiologist, neurologist or other specialists.
Other necessary examinations.

in the steno-stiffness approach.

6. Does Brachial-Ankle PWV Serve as a Surrogate Endpoint for Intervention? (Therapeutic Regression and Its Relation to Improvement of the Prognosis)

Several studies have reported that medical treatments for cardiovascular risk factors (i.e., hypertension, diabetes mellitus and hypercholesterolemia)[144-151] and lifestyle modifications (i.e., exercise, smoking cessation, and weight reduction)[29, 152, 153] lead to improvement of the brachial-ankle PWV. Recently, while sacubitril-valsartan was found to be more effective for the management of heart failure than enalapril[154], sacubitril-valsartan, as compared to enalapril, did not significantly reduce central aortic stiffness[155]. Thus, management and treatment of risk factors for CVD provide beneficial effects on the arterial stiffness, but the effect might be limited[156]. Therefore, further studies are needed to clarify whether arterial stiffness is a useful marker for assessing the effects of interventions for reducing the risk of cardiovascular disease.

7. Conclusion

Brachial-ankle PWV is a simple and useful marker for cardiovascular risk assessment, especially in subjects with a low risk of cardiovascular disease. The cutoff value for the risk assessment might be 16.0 m/s in subjects with a low risk of CVD, and 18.0 m/s in subjects with a high risk of CVD and or those with hypertension.

Conflict of Interest Statement

Hirofumi Tomiyama and Kazuki Shiina received funds from Omron Health Care company, Asahi Calpis Wellness company, and Teijin Pharma company.

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