Cut-Off Value of the Ankle-Brachial Pressure Index at Which the Accuracy of Brachial-Ankle Pulse Wave Velocity Measurement is Diminished

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Background The present study was conducted to establish the cutoff value of the ankle–brachial pressure index (ABI) at which the accuracy of brachial–ankle pulse wave velocity (baPWV) measurement is diminished.
Methods and Results The baPWV and ABI were measured in 1,361 patients with an atherosclerosis-related disease and 7,889 subjects without any atherosclerotic risk factors, in order to determine the percent difference of the brachial–ankle PWV (%baPWV), the angle of the rise of the anacrotic limb (%angle) and of the amplitude of the entire waveform (%amplitude) in both sides. The %angle and %amplitude were significantly higher in subjects whose %baPWV was ≥19% than in those subjects whose %baPWV was <19% (19% was the mean value+3SD of 7,889 healthy subjects). The %baPWV ≥19% was defined as the abnormal discrepancy of baPWV caused by arterial stenosis in both sides. The receiver operator characteristic curve discriminated the abnormal discrepancy of baPWV by ABI because the area under the curve was 0.86. The highest discriminating sensitivity and specificity were 91% and 75% at ABI=0.95.
Conclusion An ABI <0.95 seems to be the marker of diminished baPWV accuracy. (*Circ J* 2005; **69:** 55–60)

Key Words: Accuracy; Ankle–brachial pressure index; Arterial stenosis; Pulse wave velocity

Pulse wave velocity (PWV) is used in the management of atherosclerotic cardiovascular disease as a validated marker of disease severity and a predictor of future events[1–4] Recently, the use of brachial–ankle PWV, which can be obtained by simply wrapping the 4 extremities with blood pressure cuffs, was validated[5–7] and the technique is quite simple it is thus useful for screening the general population; in addition, the ankle–brachial blood pressure index (ABI) can also be simultaneously obtained[5–7] For accurate PWV measurement, a clear recording of the pulse waves is very important, but in cases of severe atherosclerosis, the stenosis of the arteries affects the recording and it is not sufficiently clear[8,9] ABI is a simple marker of peripheral arterial stenosis[10–15] and can provide information about the prevalence of arterial stenosis in subjects who are undergoing a brachial–ankle PWV recording. However, the cut-off value for ABI at which the accuracy of brachial–ankle PWV measurements is diminished because of arterial stenosis has not been established. Therefore, we proposed and evaluated the following hypothesis. At the site of arterial stenosis, the serial changes in the waveform obscure the foot of the waveform and delay the calculated PWV[9] The discrepancy in brachial–ankle PWV (abnormal difference) between the 2 sides of the body reflects the lack of accuracy of the brachial–ankle PWV measurement on the delayed side because of arterial stenosis. Therefore, we examined the ABI on the side of the delayed brachial–ankle PWV as a marker of the lack of brachial–ankle PWV accuracy in patients with a discrepancy in their brachial–ankle PWV values (abnormal difference).

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Methods

Subjects

Of the patients who visited the outpatient clinic of the Second Department of Internal Medicine of Tokyo Medical University Hospital or were admitted to the department for the diagnosis or treatment of cardiovascular disease between April 2001 and August 2003, patients who underwent a brachial–ankle PWV recording and gave their informed consent were enrolled in the study. Subjects with a plasma creatinine concentration of greater than 176.8 μmol/L, with an aortic graft, and those with atrial fibrillation, were excluded. The total number of subjects was 1,361 (60±12 years old). Atherosclerotic cardiovascular diseases were classified according to the criteria of the International Classification of Diseases (10th version) for coronary heart disease, cerebrovascular disease, and peripheral arterial disease. Hypertension, dyslipidemia and diabetes mellitus were diagnosed according to the guidelines of the Japanese Society of Hypertension[16] the Japan Atherosclerosis Society[17] and the Japan Diabetes Society[18] The study's protocol was approved by the ethical committee of Tokyo Medical University.

Table 1 Characteristics of the Subjects With an Atherosclerosis-Related Disease

Number	*1,361*
No of subjects with concomitant disease	
Hypertension	*800*
Diabetes mellitus	*726*
Dyslipidemia	*677*
Ischemic heart disease	*503*
Cerebrovascular disease	*110*
Smoker	*752*
TC (mg/dl)	*206±67*
HDL (mg/dl)	*53±21*
TG (mg/dl)	*151±124*
Blood sugar (mg/dl)	*143±70*
Age (years)	*59±12*
BMI	*24±9*
SBP (mmHg)	*130±21*
DPB (mmHg)	*75±13*
baPWV (cm/s)	*1,573±401*
ABI	*1.10±0.12*

TC, total cholesterol; HDL, high-density lipoprotein cholesterol; TG, trigycerides; BMI, body mass index; SBP, systolic blood pressure; DPB, diastolic blood pressure; baPWV, brachial-ankle pulse wave velocity; ABI, ankle-brachial pressure index.

Measurement of PWV and ABI

Brachial–ankle PWV was measured using a volume-plethysmograph (Form/ABI, Colin, Co Ltd, Komaki, Aichi, Japan). Details of the methodology have been previously described[6,7] The brachial–ankle PWV measurement was conducted while the patient's condition was stable and all recordings were made while the patients were taking their normal medication; none of the patients received intravenous medication. The subjects were examined while resting supine. Electrocardiographic electrodes were placed on both wrists, and cuffs were wrapped around both brachia and ankles. Pulse volume waveforms at the brachium and ankle were recorded using a semiconductor pressure sensor. The brachial–ankle PWV was measured after the subject had rested for at least 5 min. Validation of this method has been previously reported[6,7]

Brachial and ankle blood pressures were obtained on the left and right sides using an oscillometric method simultaneously with the brachial–ankle PWV recording, and the ABI was calculated for both sides. The lower of the 2 ABI values was determined (lowABI) and used in subsequent statistic analyses.

Difference in the PWV of Both Sides

The percent difference in the brachial–ankle PWV measured on the 2 sides of the patient was represented as follows:

| right brachial–ankle PWV – left brachial–ankle PWV | ×100/right or left larger value of brachial–ankle PWV

Previously, we reported age-related changes in the brachial–ankle PWV of 7,889 subjects without any atherosclerotic risk factors[7] The percent difference in the brachial–ankle PWV between the 2 sides was 4±5% in that group. We divided the current subjects (n=1,361) into 4 groups according to the of mean and SD values of the

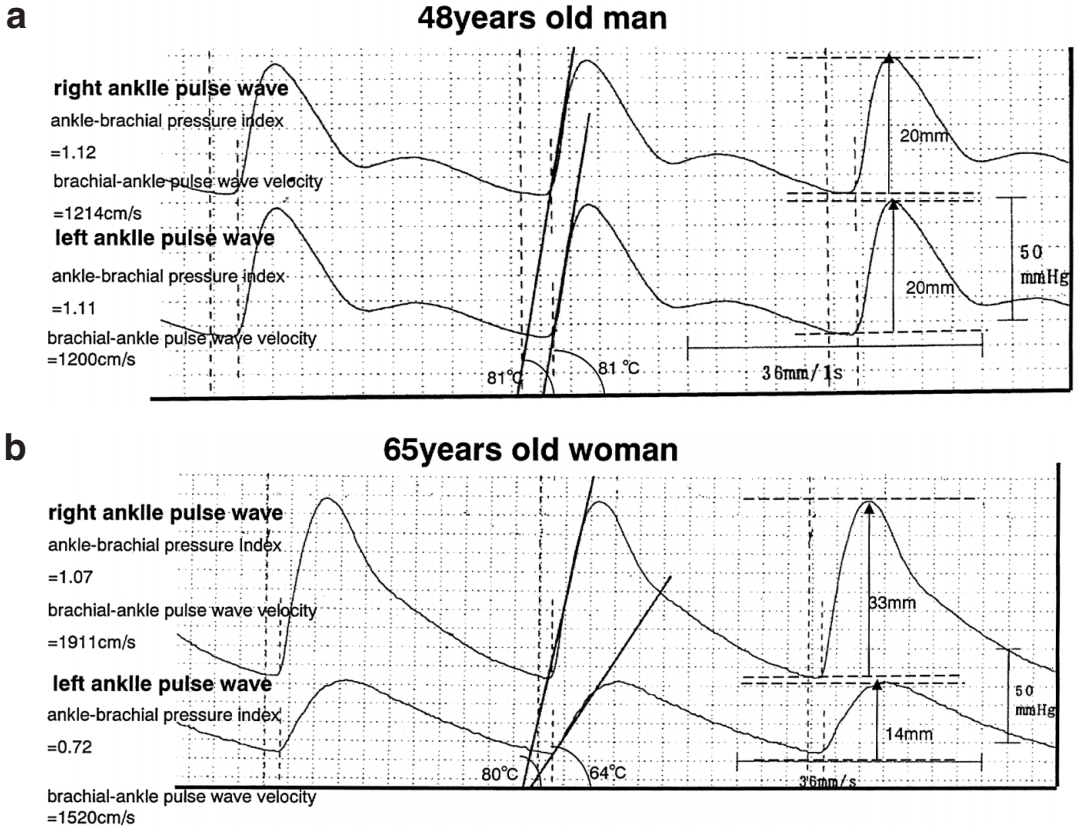

Fig 1. Demography of the measurement of the angle of the rise of the anacrotic limb and the amplitude of the entire waveform in both sides in a subject whose percent difference in the brachial–ankle pulse wave velocity (PWV) was 4% (a) and another in whom the percent difference in the brachial–ankle PWV was 20% (b).

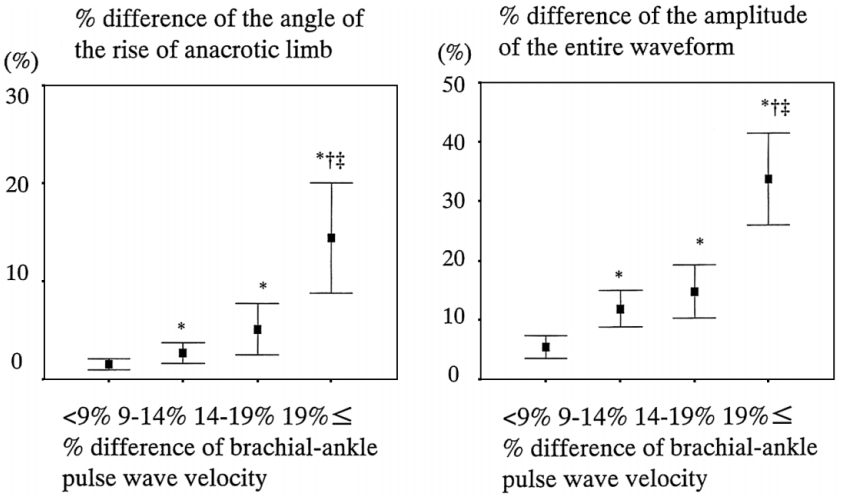

Fig 2. Percent difference of the angle of the rise of the anacrotic limb and that of the amplitude of the entire waveform in both sides among subjects whose percent difference of brachial–ankle pulse wave velocity (PWV) was <9%, 9–14%, 14–19%, and ≥19%. *p< 0.01 vs subjects with <9%, †p<0.01 vs subjects with 9–14%, ‡p<0.01 vs subjects with 14–19%.

percent difference of brachial–ankle PWV between the 2 sides of the 7,889 healthy subjects (less than mean+1SD, from mean+1SD to mean+2SD, from mean+2SD to mean+3SD, and over mean+3SD). The percent difference in the brachial–ankle PWV between the 2 sides was <9% in 1,155 subjects, 9–14 in 129 subjects, 14–19 in 44 subjects, and ≥19% in 33 subjects. We measured the percent difference of the angle of the rise of the anacrotic limb and that of the amplitude of the entire waveform from both sides (Fig 1) and compared the differences among the 4 groups.

We performed an additional experiment to support our hypothesis. In 7,889 healthy subjects, the mean ABI was 1.11±0.07, and an ABI >1.04 (mean–1SD) suggested nonstenosis in the measured artery. On the other hand, ankle blood pressure is usually greater than brachial blood pressure, and therefore it is possible that ABI <1.00 reflects stenosis in the measured artery. We selected subjects whose ABI in the higher side was >1.04 and in the lower side was <1.0 (n=99) as those with possible unilateral arterial stenosis. The percent difference of the brachial–ankle PWV, of the angle of the rise in the anacrotic limb, and that of the amplitude of the entire waveform was measured. The changes in these parameters were assessed according to the changes in the ABI of the lower side.

Laboratory Measurements

Plasma total cholesterol, high-density lipoprotein cholesterol, and blood sugar were measured enzymatically. All blood samples were obtained in the morning after an overnight fast.

Statistics

Data are expressed as the mean value±SD. The statistical analysis was performed using the SPSS software package (SPSS, Chicago, IL, USA). For 2 groups' comparison, Wilcoxon's t-test was used. For more than 3 groups' comparison, a one-way analysis of variance with Bonferroni's adjustment was used. The receiver operating characteristic (ROC) curve was used to compare the sensitivity and specificity of ABI for discriminating abnormal discrepancy of brachial–ankle PWV of both sides. A p value of less than 0.05 was considered to indicate statistical significance.

Results

Table 1 shows the clinical characteristics of the patients

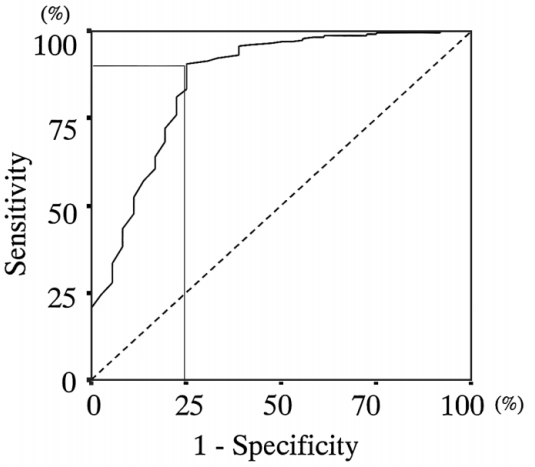

Fig 3. Receiver operating characteristic curve between ankle–brachial pressure index and the prevalence of abnormal discrepancy of brachial–ankle pulse wave velocity.

with atherosclerosis-related diseases. Fig 1 depicts the demography of the measurement of the angle of the rise of the anacrotic limb and the amplitude of the entire waveform in both sides in a subject in whom the percent difference in the brachial–ankle PWV was 4% (Fig 1a) and one in whom the percent difference in the brachial–ankle PWV was 20% (Fig 1b). Fig 2 shows the percent differences of the angle of the rise of the anacrotic limb and the amplitude of the entire waveform in both sides among the 4 groups. The values of these 2 parameters were abruptly increased in the group in which the percent difference of brachial–ankle PWV in both sides was ≥19% as compared with the other 3 groups. Thus, in subjects in whom the percent difference of brachial–ankle PWV was ≥19%, the records of pulse waveform were definitely obscured in the side with the lower brachial–ankle PWV. Therefore, we defined the abnormal discrepancy in the brachial–ankle PWV of both sides as ≥19% (mean+3SD of the values of the 7,889 subjects without any atherosclerotic risk factors)7. The ROC curve demonstrated that the area under curve was 0.86 and the highest discriminating sensitivity and specificity were 91% and 75% at ABI=0.95 (Fig 3).

Fig 4 shows the distribution of the percent difference of brachial–ankle PWV in both sides according to the changes

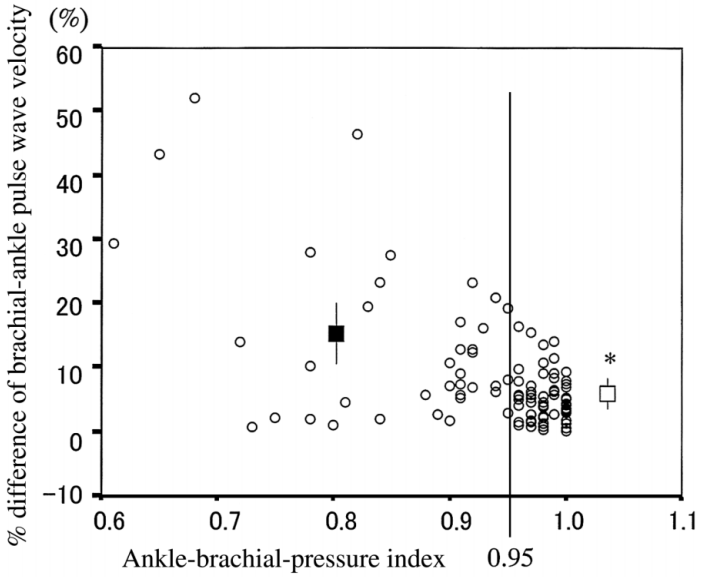

Fig 4. Distribution of the percent difference of brachial–ankle pulse wave velocity in both sides according to the changes in the lower ankle–brachial pressure index in subjects whose ankle–brachial pressure index in the higher side was >1.04 and in the lower side was <1.0. (Closed square)=Mean value of the percent difference of brachial–ankle pulse wave velocity in both sides in subjects whose lower ankle–brachial pressure index was <0.95. (Open square)=Mean value of the percent difference of brachial–ankle pulse wave velocity in both sides in subjects whose lower ankle–brachial pressure index was ≥0.95. *p<0.01 vs subjects whose lower ankle–brachial pressure index was <0.95.

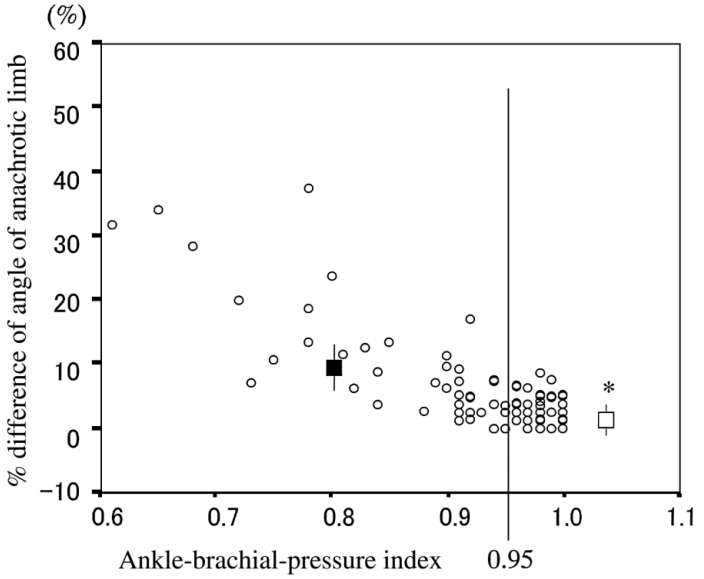

Fig 5. Distribution of the percent difference of the angle of the rise of the anacrotic limb in both sides according to the changes in the lower ankle–brachial pressure index in subjects whose ankle–brachial pressure index in the higher side was >1.04 and in the lower side was <1.0. (Closed square)=Mean value of the angle of the rise of the anacrotic limb in both sides in subjects whose lower ankle–brachial pressure index was <0.95. (Open square)=Mean value of the angle of the rise of the anacrotic limb in both sides in subjects whose lower ankle–brachial pressure index was ≥0.95. *p<0.01 vs subjects whose lower ankle–brachial pressure index was <0.95.

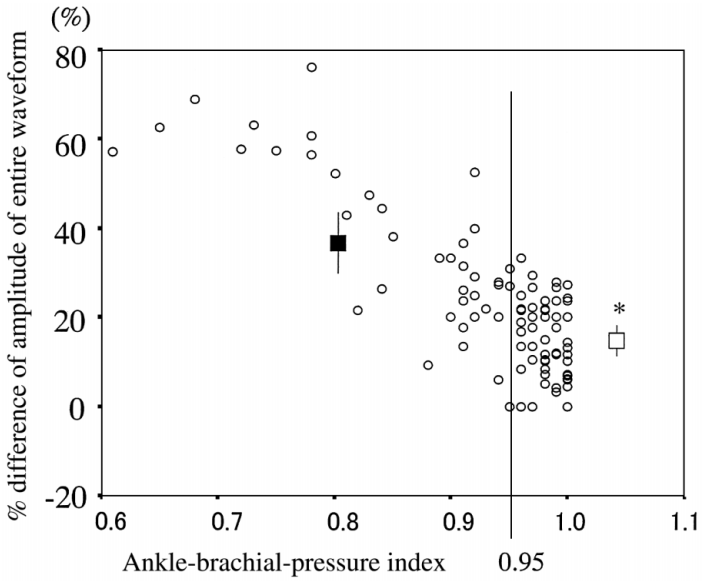

Fig 6. Distribution of the percent difference of the amplitude of the entire waveform in both sides according to the changes in the lower ankle–brachial pressure index in subjects whose ankle–brachial pressure index in the higher side was >1.04 and in the lower side was <1.0. (Closed square)=Mean value of the amplitude of the entire waveform in both sides in subjects whose lower ankle–brachial pressure index was <0.95. (Open square)=Mean value of the amplitude of the entire waveform in both sides in subjects whose lower ankle–brachial pressure index was ≥0.95. *p<0.01 vs subjects whose lower ankle–brachial pressure index was <0.95.

in the lower ABI in subjects whose ABI in the higher side was >1.04 and in the lower side was <1.0. This difference was higher in subjects whose lower ABI was <0.95 than in subjects whose lower ABI was ≥ 0.95.

Figs 5 and 6 show the distributions of the percent difference of the angle of the rise of the anacrotic limb and of the amplitude of the entire waveform in both sides according to the changes in the lower ABI in subjects whose ABI in the higher side was >1.04 and in the lower side was <1.0. These differences were higher in subjects whose lower ABI was <0.95 than in subjects whose lower ABI ≥0.95.

Discussion

Kempczinski demonstrated serial changes in pressure pulse waveforms according to the severity of arterial stenosis: loss of the reflected diastolic wave; a decrease in the rate of fall of the catacrotic limb, with a delayed arrival and rounding of the pulse crest; and a further delay in the rise of the anacrotic limb, with a continued decrease in the amplitude of the entire waveform.[9] Carter clearly demonstrated a delay in the foot of the waveform in patients with arterial occlusive disease, compared with normal subjects.[10] PWV is calculated from the distance between 2 recording points of the waveform and the time delay of the waveform between these 2 points and usually, the characteristic point of the waveform is determined as the foot of the waveform.[8] The delay in the rise of the anacrotic limb and a decrease in the amplitude of the entire waveform as a result of arterial stenosis obscure the foot of the waveform and delay the calculated PWV.[9] The present study demonstrated that the percent difference of the angle of the rise of the anacrotic limb and of the amplitude of the entire waveform in both sides were both increased abruptly in subjects whose percent difference of brachial–ankle PWV in both sides was ≥19%. Thus, a percent difference of brachial–ankle PWV in both sides ≥19% seems to relate to the delay in the calculated brachial–ankle PWV caused by arterial stenosis, and we defined this value as the abnormal discrepancy of brachial–ankle PWV.

The ROC curve demonstrated that ABI=0.95 is the best cut-off value for discriminating this abnormal discrepancy of the brachial–ankle PWV of both sides. Conventionally, an ABI=0.9 is used as a marker to discriminate atherosclerosis obliterans (ASO),[15,19] and this value is thought to be the cut-off value for eliminating subjects in whom there is diminished accuracy of the brachial–ankle PWV. However, our results suggest that ABI=0.95 is the best marker.

The additional experiment was performed in subjects who had possible unilateral arterial stenosis (their ABI in the higher side was >1.04 and in the lower side was <1.0). The parameters related to the delayed brachial–ankle PWV caused by arterial stenosis (the percent differences of brachial–ankle PWV, of the angle of the rise of the anacrotic limb, and of the amplitude of the entire waveform, in both sides) were higher in subjects whose lower ABI was <0.95 than in subjects whose lower ABI ≥0.95. These results support the validity of ABI <0.95 as the cut-off value of diminished brachial–ankle PWV accuracy.

An examination of the relationship between ABI and the difference in brachial–ankle PWV measurements on the stenotic and non-stenotic sides of patients with unilateral ASO might determine whether this ABI cut-off value is a marker of diminished brachial–ankle PWV accuracy. Carter reported that the ABI was >1.0 in all of the control subjects, <0.80 in all of the patients with arterial obstruction, and also <0.80 in more than 50% of the patients with arterial stenosis.[10] The results of that previous study show the difficulty in obtaining patients with unilateral ASO and a range of ABI. Furthermore, the rigidity of the artery (such as arterial calcification) that elevates the blood pressure in the lower leg, the severity of the arterial stenosis, and the extent of the collateral blood flow to the site distal to the stenotic artery may independently influence either brachial–ankle PWV or ABI. These influences may obscure the association between the accuracy of brachial–ankle PWV and ABI. Therefore, evaluating the cut-off value of ABI to be used as a marker of diminished brachial–ankle PWV accuracy in patients with unilateral ASO has some difficulties.

Using an in silica circulating simulation experimental system that enabled the stepwise generation of stenosis, the pressure and pulse waveforms at the center or periphery could be simultaneously recorded, enabling the pressure ratio for the central and peripheral sides to be obtained at the point at which a change in the waveform occurs at the periphery. This model could be used to obtain the peripheral/central blood pressure ratio at the point when the above-mentioned changes occur, according to the level of graded stenosis.[20] In vivo, however, the waveform reflects peripheral influences on systolic blood pressure,[21] and the peripheral systolic blood pressure is usually higher than the central systolic blood pressure.[22] Therefore, the normal peripheral/central pressure ratio is >1.0 in vivo and 1.0 in the in silica model; thus, the peripheral/central blood pressure ratio that impairs the recording of the waveform in this in vitro model cannot be applied in vivo.

Study Limitations

Although Doppler measurements are the standard method of obtaining ABI, we used the oscillometric method in this study and its precision for systolic blood pressure measurements of the lower extremities is still uncertain.[23] However, Cortez-Cooper et al demonstrated the accuracy of systolic blood pressure measurements in the lower extremities using the present method, compared with the Doppler technique, in normal subjects.[24] Furthermore, the accuracy of this method in patients with arterial stenosis has also been confirmed by us.[25] We recognize that the present study was a surrogate study for determining the ABI cut-off value marking the diminished accuracy of the brachial–ankle PWV because of the difficulty in accruing patients with unilateral ASO, which was another limitation of this study.

In conclusion, in the application of brachial–ankle PWV for the management of pathophysiological conditions related to atherosclerosis, the ABI value, which is simultaneously obtained, requires attention to the confirmation of its accuracy. The present study proposes that an ABI <0.95 is to be a marker of diminished brachial–ankle PWV accuracy.

Acknowledgments

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