Association of 4-limb systolic blood pressure heterogeneity with peripheral artery disease and left ventricular mass index

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Abstract

A large interarm and interleg systolic blood pressure (SBP) difference and ankle-brachial index (ABI) <0.9 were associated with peripheral artery disease and left ventricular hypertrophy. These 3 parameters were derived from 4-limb SBP data. However, there is no study to assess clinical significance of SBP heterogeneity in 4 limbs. The aim of this study was to evaluate the association of 4-limb SBP standard deviation (SD) with peripheral vascular parameters and echocardiographic data in patients with or without clinical findings of peripheral artery disease.

A total of 1240 patients were included, of whom 1020 had no clinical evidence of overt peripheral artery disease. The 4-limb blood pressures, brachial-ankle pulse wave velocity, and ABI were measured simultaneously by an ABI-form device.

In the multivariable linear regression analysis, increased left ventricular mass index (LVMI), ABI < 0.9, interarm SBP difference >10 mm Hg, and interleg SBP difference >15 mm Hg ($P \leq .030$) were associated with increased 4-limb SBP SD. Additionally, a subgroup multivariable linear regression analysis in 1020 patients without ABI < 0.9, interarm SBP difference >10 mm Hg, and interleg SBP difference >15 mm Hg found 4-limb SBP SD still had a positive correlation with LVMI ($P < .001$).

In addition to significant association with ABI < 0.9, interarm SBP difference >10 mm Hg, and interleg SBP difference >15 mm Hg, 4-limb SBP SD was positively correlated with LVMI in the multivariable linear regression analysis in all study patients. Furthermore, in the subgroup of patients without clinical evidence of peripheral artery disease, 4-limb SBP SD still had a positive correlation with LVMI. Hence, assessment of 4-limb SBP heterogeneity is useful in identification of high-risk group of peripheral artery disease and/or increased LVMI, irrespective of the presence of overt peripheral artery disease.

Abbreviations: ABI = ankle-brachial index, baPWV = brachial-ankle pulse wave velocity, DBP = diastolic blood pressure, E = transmitral E wave velocity, Ea = early diastolic mitral velocity, LVEF = left ventricular ejection fraction, LVH = left ventricular hypertrophy, LVMI = left ventricular mass index, PAOD = peripheral artery occlusive disease, SBP = systolic blood pressure, SD = standard deviation.

Keywords: ankle-brachial index, four-limb systolic blood pressure, interarm systolic blood pressure difference, interleg systolic blood pressure difference, left ventricular mass index

1. Introduction

An interarm systolic blood pressure (SBP) difference >10 mm Hg was demonstrated to be significantly correlated to subclavian stenosis, peripheral vascular disease, coronary artery disease, and increased cardiovascular and overall mortality.[1–3] Additionally, an interleg SBP difference >15 mm Hg was also reported to be associated with increased cardiovascular and overall mortality in patients with hemodialysis[4] and in elderly Chinese population.[5]

The ankle-brachial index (ABI) is an easily-obtained and reliable diagnostic tool for peripheral artery occlusive disease (PAOD) and an ABI < 0.9 has been frequently used to confirm

this diagnosis of PAOD.[6] Furthermore, abnormally high and low ABI was found to be associated with increased left ventricular mass index (LVMI)[7] and increased mortality.[8,9]

SBP difference between arms and legs and the value of ABI were all derived from 4-limb SBP data. Present technology makes simultaneous blood pressure measurement in 4 limbs possible,[10] which can offer a complete evaluation of blood pressure and generate a reliable value of blood pressure differences among 4 limbs. However, there is no study to assess clinical significance of SBP heterogeneity in 4 limbs. In the present study, we evaluate the association of SBP standard deviation (SD) among 4 limbs with peripheral vascular parameters and echocardiographic data and see whether there is a significant correlation between 4-limb SBP heterogeneity and cardiovascular function.

2. Methods

2.1. Study population

Study subjects were randomly included from a group of patients who arranged for echocardiographic examinations at Kaohsiung Municipal Siaogang Hospital. Patients with significant aortic or mitral valve disease, atrial fibrillation, acute illness such as infection, or inadequate image visualization were excluded. We did not include all patients consecutively because brachial-ankle pulse wave velocity (baPWV), ABI, and blood pressures must begin to be measured within 5 minutes after the completion of echocardiographic examination. A total of 1240 patients were included.

The study protocol was approved by the institutional review board of the Kaohsiung Medical University Hospital (KMUH-IRB-20130151). Informed consents have been obtained in written form from patients and all clinical investigation was conducted according to the principles expressed in the declaration of Helsinki. The patients gave consent for the publication of the clinical details.

2.2. Evaluation of cardiac structure and function

The echocardiographic examination was performed by one experienced cardiologist with a VIVID 7 (General Electric Medical Systems, Horten, Norway), with the participant breathing quietly in the left decubitus position. The cardiologist was blind to the other data. Two-dimensional and 2-dimensionally guided M-mode images were recorded from the standardized views. The Doppler sample volume was placed at the tips of the mitral leaflets to obtain the left ventricular inflow waveforms from the apical 4-chamber view. All sample volumes were positioned with ultrasonic beam alignment to flow. Pulsed tissue Doppler imaging was obtained with the sample volume placed at the lateral corner of the mitral annulus from the apical 4-chamber view. The wall filter settings were adjusted to exclude high-frequency signals and the gain was minimized. The echocardiographic measurements included left ventricular internal diameter in diastole (LVIDd), left ventricular posterior wall thickness in diastole (LVPWTd), interventricular septal wall thickness in diastole (IVSTd), E-wave deceleration time, transmitral E wave velocity (E), transmitral A wave velocity, and early diastolic mitral velocity (Ea). Left ventricular systolic function was assessed by left ventricular ejection fraction (LVEF). Left ventricular mass was calculated using Devereux-modified method, that is, left ventricular mass = 1.04 × ([IVSTd + LVIDd + LVPWTd]^3 – LVIDd^3) – 13.6 g.[11] LVMI was calculated

by dividing left ventricular mass by body surface area. Left ventricular hypertrophy (LVH) was defined as suggested by the 2007 European Society of Hypertension/European Society of Cardiology guidelines.[12] Left ventricular relative wall thickness (LVRWT) was calculated as the ratio of 2 × LVPWTd/LVIDd. Cardiac remodeling was defined as LVRWT more than 0.45 without LVH. Concentric LVH was defined as LVMI more than 125 g/m^2 in men and more than 110 g/m^2 in women, with LVRWT more than 0.45; eccentric LVH was defined as LVMI more than 125 g/m^2 in men and more than 110 g/m^2 in women, with LVRWT less than 0.45. The raw ultrasonic data were recorded and analyzed offline by a cardiologist, blinded to the other data, using EchoPAC software (GE Medical Systems).

2.3. Assessment of ABI and baPWV

The values of ABI and baPWV were measured by using an ABI-form device (VP1000; Colin Co. Ltd., Komaki, Japan), which automatically and simultaneously measures blood pressures in both arms and ankles using an oscillometric method.[13] ABI was calculated by the ratio of the ankle SBP divided by the arm SBP and the lower value of the ankle SBP was used for the calculation. For measuring baPWV, pulse waves obtained from the brachial and tibial arteries were recorded simultaneously and the transmission time, which was defined as the time interval between the initial increase in brachial and tibial waveforms, was determined. The transmission distance from the arm to each ankle was calculated according to body height. The baPWV value was automatically computed as the transmission distance divided by the transmission time. After obtaining bilateral baPWV values, the higher 1 was used as representative for each subject. The ABI and baPWV measurements were done once in each patient. The validation of this automatic device and its reproducibility have been previously published.[13]

2.4. Assessment of blood pressures

To prevent overestimation and observer bias, 4 limb blood pressures should be measured simultaneously with 1 or 2 automated devices.[14] In our study, the 4 limb blood pressure measurements were done simultaneously and automatically using the ABI-form device. The SBP and diastolic blood pressure (DBP) were measured by an appropriate cuff. After obtaining 4 limb blood pressures, we calculated the average of SBP and DBP of bilateral arms, interarm SBP difference, interleg SBP difference for later analysis. In addition, 4-limb SBP SD was calculated as the square root of the average value of (each limb SBP – mean value of 4-limb SBP).[2]

2.5. Collection of demographic, medical, and laboratory data

Demographic and medical data including age, gender, smoking history, and comorbid conditions were obtained from medical records or interviews with patients. Study subjects were defined as having hypertension if their SBP was ≥140 mm Hg or DBP ≥90 mm Hg, or antihypertensive medications were prescribed irrespective of blood pressure. Laboratory data were measured from fasting blood samples using an autoanalyzer (Roche Diagnostics GmbH, D-68298 Mannheim COBAS Integra 400). Blood samples were obtained within 1 month of enrollment.

2.6. Statistical analysis

Statistical analysis was performed using SPSS 22.0 for windows (SPSS Inc. Chicago). Data are expressed as percentages or mean ± SD. We compared categorical and continuous variables between 2 groups by using the Chi-square test and independent samples t test respectively and investigated any relationship between 2 variables by using the Pearson correlation method. Significant variables in the univariable linear regression analysis were selected for multivariable linear regression analysis. A difference was considered significant if the P value was less than .05.

3. Results

The mean age of the 1240 patients was 61 ± 14 years. The median value of 4-limb SBP SD was 12.40 mm Hg. The differences between patients with 4-limb SBP SD < 12.40 mm Hg and ≥12.40 mm Hg are shown in Table 1. Compared with patients with a 4-limb SBP SD < 12.40 mm Hg, patients with a 4-limb SBP SD ≥12.40 mm Hg were found to be older, higher percentage of male gender, higher prevalence of hypertension and cerebrovascular disease, higher SBP and DBP, lower heart rate, higher baPWV, higher prevalence of ABI < 0.9, interarm SBP difference

>10 mm Hg, and interleg SBP difference >15 mm Hg, lower triglyceride, total cholesterol, and hemoglobin, higher LVMI, lower prevalence of normal left ventricular geometry, and higher prevalence of concentric and eccentric LVH, higher LVEF, and lower Ea.

Table 2 shows the determinants of 4-limb SBP SD in the Pearson correlation analysis. The 4-limb SBP SD was significantly associated with age, gender, the presence of hypertension, and cerebrovascular disease, SBP, DBP, heart rate, triglyceride, total cholesterol, hemoglobin, baPWV, ABI < 0.9, interarm SBP difference >10 mm Hg, interleg SBP difference >15 mm Hg, LVMI, the presence of LVH, LVEF, Ea, and E/Ea.

Table 3 shows the multivariable linear regression analysis. In order to examine separately vascular and echocardiographic parameters in association with 4-limb SBP SD because 4-limb SBP SD would definitely be linked to SBP difference between arms, legs, and arms and legs, we performed 2 multivariable linear regression analyses. Variables in the basic model (age, sex, hypertension, cerebrovascular disease, SBP, diastolic blood pressure, heart rate, triglyceride, total cholesterol, hemoglobin) included significant variables in the univariable linear regression analysis except vascular and echocardiographic parameters. In

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Table 1

Comparison of baseline characteristics between patients with 4-limb SBP SD < 12.40 mm Hg and ≥12.40 mm Hg (median value).

Characteristics	All patients (n=1240)	4-limb SBP SD < 12.40 mmHg (n=619)	4-limb SBP SD ≥ 12.40 mmHg (n=621)
SBP SD (mm Hg)	12.91 ± 5.83	8.49 ± 2.79	17.35 ± 4.57[**]
Age, yr	61 ± 14	59 ± 15	63 ± 13[**]
Male gender (%)	56	52	60[*]
Smoking history (%)	15	15	15
Diabetes mellitus (%)	28	27	29
Hypertension (%)	69	60	79[**]
Coronary artery disease (%)	19	19	18
Cerebrovascular disease (%)	6	4	8[*]
SBP (mm Hg)	136 ± 21	130 ± 20	142 ± 21[**]
Diastolic blood pressure (mm Hg)	77 ± 12	76 ± 11	79 ± 13[**]
Heart rate (beats/min)	70 ± 13	71 ± 13	69 ± 11[*]
baPWV, cm/s	1765 ± 462	1690 ± 433	1840 ± 478[**]
ABI<0.9 (%)	6.0	4.0	7.9[*]
Interarm SBP difference >10 mm Hg (%)	5.4	3.7	7.1[*]
Interleg SBP difference >15 mm Hg (%)	11.9	6.1	17.6[**]
Laboratory parameters			
Albumin (g/dL)	4.1 ± 0.5	4.1 ± 0.4	4.1 ± 0.5
Fasting glucose (mg/dL)	115 ± 42	115 ± 44	114 ± 41
Triglyceride (mg/dL)	157 ± 154	168 ± 196	148 ± 99[*]
Total cholesterol (mg/dL)	192 ± 44	195 ± 48	188 ± 39[*]
Hemoglobin (g/dL)	13.4 ± 2.1	13.6 ± 1.9	13.2 ± 2.2[*]
Uric acid (mg/dL)	6.8 ± 2.0	6.8 ± 2.1	6.8 ± 2.0
Echocardiographic data			
LVMI (g/m^2)	135 ± 44	127 ± 43	142 ± 44[**]
LV geometry			
Normal (%)	35	42	27[**]
Concentric remodeling (%)	6	7	6
Eccentric LVH (%)	43	38	49[**]
Concentric LVH (%)	16	13	18[*]
LVH (%)	59	51	67[**]
LVEF (%)	63 ± 13	62 ± 15	64 ± 12[*]
Ea (cm/s)	8.6 ± 3.4	9.0 ± 3.6	8.2 ± 3.0[**]
E/Ea	9.8 ± 5.1	9.5 ± 5.3	10.0 ± 5.0

ABI = ankle-brachial index, baPWV = brachial-ankle pulse wave velocity, E = transmitral E wave velocity, Ea = early diastolic mitral velocity, LAVI = left atrial volume index, LV = left ventricular, LVEF = left ventricular ejection fraction, LVH = left ventricular hypertrophy, LVMI = left ventricular mass index, SBP = systolic blood pressure, SD = standard deviation.

[*] $P < .05$.

[**] $P < .001$ compared patients with SBP SD < 12.40 mm Hg.

Table 2

Determinants of 4-limb SBP SD in Pearson correlation analysis.

Parameter	Univariable	
	r	P
Age, yr	0.147	<.001
Female gender	−0.091	.001
Smoking history	0.032	.316
Diabetes mellitus	0.041	.147
Hypertension	0.182	<.001
Coronary artery disease	−0.005	.860
Cerebrovascular disease	0.092	.004
SBP (mm Hg)	0.319	<.001
Diastolic blood pressure (mm Hg)	0.166	<.001
Heart rate (beats/min)	−0.108	<.001
Laboratory parameters		
Albumin (g/dL)	−0.042	.359
Fasting glucose (mg/dL)	−0.020	.550
Triglyceride (mg/dL)	−0.066	.039
Total cholesterol (mg/dL)	−0.080	.012
Hemoglobin (g/dL)	−0.150	<.001
Uric acid (mg/dL)	0.035	.312
baPWV (cm/s)	0.170	<.001
ABI<0.9	0.202	<.001
Interarm SBP difference >10 mm Hg	0.137	<.001
Interleg SBP difference >15 mm Hg	0.272	<.001
Echocardiographic data		
LVMI, g/m^2	0.230	<.001
LVEF	0.084	.003
Ea, cm/s	−0.160	<.001
E/Ea	0.099	.001

ABI = ankle-brachial index, baPWV = brachial-ankle pulse wave velocity, E = transmitral E wave velocity, Ea = early diastolic mitral velocity, LAVI = left atrial volume index, LV = left ventricular, LVEF = left ventricular ejection fraction, LVH = left ventricular hypertrophy, LVMI = left ventricular mass index, SBP = systolic blood pressure, SD = standard deviation.

Table 3

Determinants of 4-limb SBP SD in the multivariable linear regression analysis.

Parameter	Multivariable: Model 1		Multivariable: Model 2	
	β	P	β	P
Age, yr	0.015	.768	0.030	.539
Female gender	−0.129	.004	−0.111	.007
Hypertension	0.025	.520	0.044	.227
Cerebrovascular disease	0.011	.781	0.005	.901
SBP (mmHg)	0.277	<.001	0.253	<.001
Diastolic blood pressure (mmHg)	−0.032	.664	0.025	.716
Heart rate (beats/min)	−0.053	.193	−0.102	.012
Laboratory parameters				
Triglyceride (mg/dL)	−0.008	.837	−0.018	.627
Total cholesterol (mg/dL)	−0.041	.312	−0.078	.042
Hemoglobin (g/dL)	−0.073	.116	−0.067	.122
baPWV (cm/s)	−	−	−0.059	.265
ABI <0.9	−	−	0.098	.023
Interarm SBP difference >10 mm Hg	−	−	0.129	<.001
Interleg SBP difference >15 mm Hg	−	−	0.134	.001
Echocardiographic data				
LVMI, g/m^2	0.103	.030	−	−
LVEF	0.061	.155	−	−
Ea, cm/s	−0.032	.572	−	−
E/Ea	0.008	.882	−	−

ABI = ankle-brachial index, β = standardized coefficient, baPWV = brachial-ankle pulse wave velocity, E = transmitral E wave velocity, Ea = early diastolic mitral velocity, LAVI = left atrial volume index, LV = left ventricular, LVEF = left ventricular ejection fraction, LVH = left ventricular hypertrophy, LVMI = left ventricular mass index, SBP = systolic blood pressure, SD = standard deviation.
Variables in the basic model (age, sex, hypertension, cerebrovascular disease, SBP, diastolic blood pressure, heart rate, triglyceride, total cholesterol, hemoglobin) included significant variables in the univariable linear regression analysis except vascular and echocardiographic parameters. Covariates in the model 1 included variables in the basic model + LVMI, LVEF, Ea, E/Ea. Covariates in the model 2 included variables in the basic model + baPWV, ABI < 0.9, interarm SBP difference >10 mm Hg, interleg SBP difference >15 mm Hg.

4. Discussion

In the present study, using a simultaneous 4-limb blood pressure measurement technique, we found that increased LVMI, ABI< 0.9, interarm SBP difference >10 mm Hg, and interleg SBP difference >15 mm Hg were independently associated with an increased 4-limb SBP SD in the multivariable linear regression analysis. In addition, a subgroup multivariable linear regression analysis in 1020 patients without ABI< 0.9, interarm SBP difference >10 mm Hg, and interleg SBP difference >15 mm Hg found 4-limb SBP SD still had a positive correlation with LVMI. Hence, assessment of 4-limb SBP heterogeneity may provide a simple method of identifying patients at increased risk of the presence of peripheral artery disease and LVH. Even in patients without evidence of overt peripheral artery disease, 4-limb SBP heterogeneity is still helpful in identifying patients with increased LVMI. Additionally, although echocardiography can be successfully used in community screening, it is still slightly expensive, operator-dependent, a little time-consuming, and not available in many communities. In contrast, 4-limb blood pressure measurement is simpler, cheaper, and less operator-dependent. Thus, it may be helpful for large-volume screening.

Atherosclerosis was reported to be correlated with the interlimb SBP difference and LVH.[2,15,16] Atherosclerosis directly resulted in a decrease in blood perfusion in the affected limbs and thus increased interlimb SBP difference.[2,17–19] Hence,

the first multivariable linear regression analysis (model1: covariates included variables in the basic model, LVMI, LVEF, Ea, and E/Ea), male gender, high SBP, and increased LVMI were significantly associated with increased 4-limb SBP SD. In the second multivariable linear regression analysis (model 2: covariates included variables in the basic model, baPWV, ABI< 0.9, interarm SBP difference >10 mm Hg, and interleg SBP difference >15 mm Hg), male gender, high SBP, low heart rate, low total cholesterol, ABI< 0.9, interarm SBP difference >10 mm Hg, and interleg SBP difference >15 mm Hg were significantly associated with increased 4-limb SBP SD.

Table 4 shows a subgroup analysis in 1020 patients without anyone of the followings: ABI< 0.9, interarm SBP difference >10 mm Hg, and interleg SBP difference >15 mm Hg. We found increased 4-limb SBP SD still had a significant correlation with increased LVMI in the multivariable linear regression analysis. The LVMI was lower in the 1020 patients without anyone of the above 3 parameters than in the 220 patients with at least one of the above 3 parameters (131±43 vs 150±48 g/m^2, P<.001). In addition, in 189 patients without diabetes, hypertension, coronary artery disease, and cerebrovascular disease, 4-limb SBP SD still had a positive correlation with LVMI (r=0.203, P=.005).

Using the receiver operating characteristic curve, we calculated the sensitivity and specificity of 4-limb SBP SD in prediction of LVH. We found the area under the curve was 0.607 (P<.001) and the sensitivity and specificity of 4-limb SBP SD >11.80 mm Hg in prediction of LVH were 61% and 56%, respectively.

Table 4

Determinants of 4-limb SBP SD in 1020 patients without anyone of the followings: ABI < 0.9, interarm SBP difference >10 mm Hg, and interleg SBP difference >15 mm Hg.

	Univariable linear regression analysis		Multivariable linear regression analysis	
Parameter	r	P	β	P
Age, yr	0.101	.001	0.040	.127
Female gender	−0.080	.011	−0.150	.001
Smoking history	0.002	.966		
Diabetes mellitus	0.018	.568		
Hypertension	0.187	<.001	0.046	.246
Coronary artery disease	−0.038	.224		
Cerebrovascular disease	0.030	.402		
SBP, mm Hg	0.251	<.001	0.081	.260
Diastolic blood pressure, mm Hg	0.140	<.001	0.173	.019
Heart rate, beats/min	−0.124	<.001	−0.137	.002
Laboratory parameters				
Albumin, g/dL	0.023	.655		
Fasting glucose, mg/dL	−0.050	.166		
Triglyceride, mg/dL	−0.075	.031	−0.025	.525
Total cholesterol, mg/dL	−0.065	.062		
Hemoglobin, g/dL	−0.078	.037	−0.132	.004
Uric acid, mg/dL	0.001	.986		
Echocardiographic data				
LVMI, g/m^2	0.178	<.001	0.185	<.001
LVEF	0.093	.003	0.115	.009
Ea, cm/s	−0.097	.002	0.044	.370
E/Ea	0.051	.108		

ABI = ankle-brachial index, β = standardized coefficient, baPWV = brachial-ankle pulse wave velocity, E = transmitral E wave velocity, Ea = early diastolic mitral velocity, LAVI = left atrial volume index, LV = left ventricular, LVEF = left ventricular ejection fraction, LVH = left ventricular hypertrophy, LVMI = left ventricular mass index, SBP = systolic blood pressure, SD = standard deviation.

patients with increased 4-limb SBP SD should have some significant atherosclerosis over affected limbs. Significant atherosclerosis might contribute to LVH[18,19] through the mechanism of arterial pressure waveform change and arterial stiffness increase.[18,20] Our present study really found patients with increased 4-limb SBP SD had a high LVMI. In addition, previous studies evidently showed that interarm SBP difference >10 mm Hg and interleg SBP difference >15 mm Hg were significantly associated with increased LVMI.[3,21,22] Abnormal ABI was also reported to be associated with high LVMI.[16,23] Patients with ABI < 0.9, interarm SBP difference >10 mm Hg, and interleg SBP difference >15 mm Hg had a large SBP difference between arm and leg, between arms, and between legs respectively, so we could easily realize why 4-limb SBP SD had a positive correlation with these 3 parameters in the present study. Because increased 4-limb SBP SD had a significant association with these 3 parameters and these 3 parameters were significantly correlated with increased LVMI, our present study showed that increased 4-limb SBP SD had a significant association with increased LVMI. Therefore, assessment of 4-limb SBP heterogeneity is helpful to identify the high risk group of peripheral artery disease and increased LVMI.

Previous studies have demonstrated the prevalence of ABI < 0.9,[23] interarm SBP difference >10 mm Hg,[5,24] and interleg SBP difference >15 mm Hg[25] were relatively low. In fact, in the present study, there were only 6.0%, 5.4%, and 11.9% patients with ABI < 0.9, interarm SBP difference >10 mm Hg, and interleg SBP difference >15 mm Hg, respectively. Most of our patients (82.3%) had none of these 3 parameters. Hence, it was important to find a parameter to identify patients with high LVMI in patients without these 3 parameters. The present study actually showed 4-limb SBP SD was positively correlated with LVMI in patients without the 3 parameters. Therefore, 4-limb SBP SD was still useful in identifying high risk group of high LVMI in patients without ABI < 0.9, interarm SBP difference >10 mm Hg, and interleg SBP difference >15 mm Hg.

4.1. Study limitations

There were several limitations to this study. First, because this study was cross-sectional, the causal relationship and long-term clinical outcomes could not be confirmed. Future prospective studies were needed to assess the ability of 4-limb SBP SD in predication of adverse cardiovascular outcomes. Second, in the Pearson correlation analysis and multivariable linear regression analysis, we found 4-limb SBP SD had a positive correlation with SBP. Hence, antihypertensive medication might be useful in decreasing 4-limb SBP SD. However, the present study was just a cross-sectional one, so we could not confirm this viewpoint. Third, no studies had documented the reliable abnormal value of 4-limb SBP SD, we used 50 percentile of 4-limb SBP SD to classify our study patients. Fourth, because simultaneous 4-limb blood pressure measurement was not possible or allowed in some patients, such as those with limb amputation, severe wound over limbs, breast cancer, and arteriovenous shunt over limb for hemodialysis, 4-limb SBP SD could not be obtained in such patients. Fifth, low 4-limb SBP SD might reflect minimal insignificant atherosclerosis among 4 limbs or similar significant atherosclerosis among 4 limbs. We may need another useful parameter to differentiate these 2 situations. Finally, because the subjects of this study were already being evaluated for heart disease by echocardiography, it was susceptible to selection bias and making findings potentially less generalized.

5. Conclusions

In addition to significant association with ABI < 0.9, interarm SBP difference > 10 mm Hg, and interleg SBP difference > 15 mm Hg, 4-limb SBP SD was positively correlated with LVMI in the multivariable linear regression analysis. Furthermore, a subgroup multivariable linear regression analysis in 1020 patients without ABI < 0.9, interarm SBP difference > 10 mm Hg, and interleg SBP difference > 15 mm Hg found 4-limb SBP SD still had a positive correlation with LVMI. Hence, assessment of 4-limb SBP heterogeneity is useful in identification of high risk group of peripheral artery disease and increased LMVI. Additionally, even in patients without evidence of overt peripheral artery disease, 4-limb SBP heterogeneity is still helpful in identifying the patients with increased LVMI.

Author contributions

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