# Association of simultaneously measured limbs blood pressure differences with ankle-brachial index

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## Abstract

**Objects:** To investigate the association of simultaneously measured limbs blood pressures with Ankle-Brachial Index as the current non-invasive diagnosis method of peripheral artery disease in clinical primary care.

**Methods:** 228 subjects (61 males, mean age, 63.92±10.72 years; 167 females, mean age, 59.47±7.33 years) were enrolled. Limbs blood pressure measurements were simultaneously performed using a blood pressure and pulse monitor device in the supine position. Data were statistically analyzed with SPSS 15.0.

**Results:** The mean age of the 229 subjects was 60.66±8.58 years. Variance analysis presented that RABI and LABI have significant differences with inter-arm difference in SBP (≥10 mmHg VS < 10 mmHg,≥10 mmHg VS ≥15 mmHg and≥15 mmHg VS < 10 mmHg). RABI have significant differences with inter-ankle difference in DBP (≥15 mmHg VS < 10 and≥10 mmHg VS ≥15 mmHg). Multinomial logistic regression analysis presented that LABI (<0.9; OR, 10.028; CI, (1.109-90.682); P=0.040) was independently associated with inter-arm SBP difference ≥ 10mmHg; LABI (<0.9; OR, 15.469; CI, (1.776-134.773); P=0.013) and RABI (0.90-1.00; OR, 4.231; CI, (1.205-14.860); P=0.024) were independently associated with inter-arm SBP difference ≥ 15mmHg. RABI (<0.9; OR, 7.189; CI, (1.010-51.179); P=0.049) and RABI (0.90-1.00; OR, 6.273; CI, (1.783-22.077); P=0.004) were independently associated with inter-ankle SBP difference≥ 15mmHg. LABI (0.90-1.00; OR, 4.331; CI, (1.039-14.330); P=0.016) was independently associated with inter-ankle DBP difference of ≥ 10mmHg. After excluding 99 hypertension patients, LABI (<0.9; OR, 246.330; CI, (5.442-11191.384); P=0.005) was still independently associated with inter-arm SBP difference ≥ 15mmHg.

**Conclusion:** LABI <0.9 was independently associated with inter-arm SBP difference ≥ 15mmHg, while these differences still existed after excluding 99 hypertensive patients. In addition, the cut off (0.90-1.00) of ABI was independently associated with inter-arm SBP difference ≥ 15mmHg and inter-ankle DBP difference ≥ 10mmHg or ≥ 15mmHg. Hence, detection of limbs blood pressure difference with simultaneous measurement may provide an aid for the non-invasive diagnostic method of peripheral artery disease in clinical primary care.

**Key Words:** ankle-brachial index; non-invasive diagnosis; blood pressure; statistical analysis; peripheral artery disease

## Introduction

The Ankle-Brachial Index (ABI), i.e. the ratio of the blood pressure at the ankle to the blood pressure in the upper arm (brachium), is a simple, non-invasive, and well-documented diagnosis tool for Peripheral Artery Disease (PAD) in lower extremities. ABI<0.9 has been used to identify this condition in both clinical practice and epidemiologic studies [1-2]. Furthermore, the reduction of ABI is not only the independent risk factors of cardiovascular disease occurrence but also the potent predictors of cardiovascular disease mortality. Blanes et al.'s study reported that PAD (ABI<0.9) was associated with risk factors for inducing atherosclerosis, such as aging, male, diabetes, smoking, higher Systolic Blood Pressure (SBP) and coronary artery disease [3]. Thus, ABI is of important application value in clinical intervention treatment.

Recent study reported that a blood pressure difference between bilateral arms has been associated with subclavian stenosis, PAD, cardiovascular mortality and all-cause mortality [4-8]. Meanwhile, recent studies on inter-leg systolic blood pressure difference have added new evidence to this concept [9-11]. The meta-analysis reported by Singh [11] showed that inter-arm systolic blood pressure of 10 mmHg or more was associated with PAD (Risk Ratios(RR), 2.22; Confidence Interval (CI), 1.41–3.5; P =0.0006; sensitivity 16.6%; 6.7–35.4; specificity 91.9%; 83.1–96.3; 8 cohorts; 4774 subjects)， and inter-leg blood pressure difference of 15 mmHg or more was strong predictor of PAD (P =0 .0001).

Current technology has allowed to measure limbs blood pressure simultaneously [12], which could generate true blood pressure differences between four limbs, provide a better comprehensive evaluation of blood pressure [12, 14-15]. Inter-arm or inter-ankle blood pressure differences are known to be associated with low ABI, but little is known about the relationship between simultaneous limbs blood pressure differences and ABI.

Accordingly, this study aims to investigate the association of simultaneously measured limbs blood pressures with ABI as the current non-invasive diagnosis method of PAD in clinical primary care.

## Subjects and Methods

*Subjects*

This study was approved by the Ethics Committee of School Hospital in Beijing University of Technology, and College of Life Science and Bioengineering in Beijing University of Technology. All subjects gave written informed consent. From September 2015 to January 2016, staffs of Beijing University of technology took part in comprehensive examinations of cardiovascular disease and its risk evaluation. Subjects with limb disability, hemiplegia, congenital heart disease, heart failure, and the history of artery intervention were excluded. Finally, 228 subjects (61 males, mean age, 63.92±10.72 years; 167 females, mean age, 59.47±7.33 years) were enrolled in this study.

*ABI Measurements*

ABI was measured in an air-conditioned room at a temperature of 22–23℃ by using the VS-1500 blood pressure and pulse monitor device (Fukuda Company, Beijing, China), which simultaneously and automatically measured the supine blood pressure of four limbs. Trained technicians placed the blood pressure cuffs on both arms and both ankles, and performed the measurements, after each subject had bared four limbs and taken 10-minute rest in supine position. ABI was calculated by the ratio of the ankle SBP divided by the arm SBP and higher value of the arm systolic blood pressure was used for the calculation.

*Limbs Blood Pressure Measurements*

Limbs blood pressure was measured in the same condition in supine position. In our study, limbs blood pressures were simultaneously and automatically measured by using the ABI device.

Based on the systolic and diastolic blood pressure, we calculated the inter-arm and inter-ankle blood pressure differences as the absolute value of the blood pressure difference between the right and left arm and blood pressure between the right and left ankle, respectively. Pulse pressure (PP) was the absolute value of difference between systolic and diastolic blood pressure. Pulse pressure index (PPI) was calculated as the ratio of PP to systolic blood pressure. Mean arterial pressure (MAP) was two-thirds diastolic pressure plus one-third systolic pressure. Above mentioned data were used for later statistical analysis.

In addition, the observer also administered a standardized questionnaire to collect information of subjects on age, sex, height, weight, medical history, lifestyle, use of medications, drinking and smoking history. The Body Mass Index (BMI) was calculated as the ratio of weight in kilograms to the square of height in meters.

*Statistical Analysis*

Data were stored in Excel 2013 and statistical analysis was performed with SPSS 15.0. Data values were expressed as percentages and mean±SD. The differences of inter-arm and inter-ankle were divided into 3 groups (≤10, 10-14 and≥15), and ABI were divided into 3 groups (<0.9, 0.90-1.00, >1.0). The differences between groups were checked by the analysis of variance for continuous variables and by Chi-square test for categorical variable. The differences of ABI on gender, hypertension, smoking and drinking were performed by independent-samples T test. Multinomial logistic regression analysis was used to determine the relationship between ABI and limbs blood pressure. A difference was considered significant if the P value was <0.05.

**Results**

The mean age of the 228 subjects was 60.66±8.58 years, 8 subjects were younger than 45 years, 31 subjects between 45 and 54 years, 136 subjects between 55 and 64 years, 39 subjects between 65 and 74 years, and 14 subjects were aged 75 years or older.

## Table1. Baseline Characteristics of the Study Participants

| Characteristics | | Male(n=61) | Female(n=167) | P |
|---|---|---|---|---|
| Age,y | | 63.92±10.72 | 59.47±7.33 | 0.002 |
| Body mass index, kg/m$^2$ | | 24.54±3.15 | 25.75±3.70 | 0.023 |
| Hpertension | | 32(52.5 ) | 67(40.1) | 0.041 |
| Drinking | | 19(31.1) | 8(4.8) | 0.000 |
| Smoking | | 26(42.6 ) | 7(4.2) | 0.000 |
| **Simultaneous limbs BP measurement, mmHg** | | | | |
| Left arm | Systolic pressure (LArSBP) | 136.69±19.01 | 135.78±18.22 | 0.740 |
| | Diastolic pressure (LArDBP) | 82.50±10.96 | 81.02±10.28 | 0.342 |
| Right arm | Systolic pressure (RArSBP) | 136.89±18.47 | 135.78±18.58 | 0.688 |
| | Diastolic pressure (RArDBP) | 83.21±11.87 | 81.32±10.06 | 0.230 |
| Left ankle | Systolic pressure (LAnSBP) | 151.48±26.19 | 150.38±22.77 | 0.754 |
| | Diastolic pressure (LAnDBP) | 79.82±10.87 | 77.25±8.30 | 0.057 |
| Right ankle | Systolic pressure (RAnSBP) | 150.45±25.93 | 150.47±22.78 | 0.997 |
| | Diastolic pressure (RAnDBP) | 77.05±11.50 | 75.16±7.58 | 0.150 |
| **BP on the higher arm/ankle side of systolic pressure, mmHg** | | | | |
| Arm | Systolic pressure (HArSBP) | 140.27±18.79 | 139.03±18.44 | 0.652 |
| | Diastolic pressure (HArDBP) | 83.94±11.56 | 81.72±10.38 | 0.166 |
| | Pulse pressure (HArPP) | 56.34±14.19 | 57.31±10.38 | 0.647 |
| | Pulse pressure index | 0.40±0.06 | 0.41±0.06 | 0.299 |
| | Mean arterial pressure | 102.72±12.73 | 100.03±11.85 | 0.295 |
| Ankle | Systolic pressure (HAnSBP) | 154.50±25.99 | 153.79±22.51 | 0.839 |
| | Diastolic pressure (HAnDBP) | 80.02±11.81 | 77.11±8.50 | 0.041 |
| | Pulse pressure (HAnPP) | 74.48±18.27 | 76.68±17.93 | 0.414 |
| | Pulse pressure index | 0.48±0.07 | 0.49±0.06 | 0.046 |
| **Inter-arm BP difference, mmHg** | | | | |
| Systolic | mean±SD | 6.97±7.66 | 6.63±5.98 | 0.725 |
| Diastolic | mean±SD | 4.35±3.30 | 3.95±3.84 | 0.466 |
| Systolic | ≥10mmHg, n(%) | 9（14.8） | 23（13.7） | 0.013 |
| Systolic | ≥15mmHg, n(%) | 9（14.8） | 17（10.2） | 0.117 |
| Diastolic | ≥10mmHg, n(%) | 3（4.9） | 7（4.1） | 0.206 |
| Diastolic | ≥15mmHg, n(%) | 1（1.6） | 4（2.4） | 0.180 |
| **Inter-ankle BP difference, mmHg** | | | | |
| Systolic | mean±SD | 7.06±7.87 | 6.74±5.20 | 0.715 |
| Diastolic | mean±SD | 4.87±4.07 | 4.11±3.48 | 0.165 |
| Systolic | ≥10mmHg, n(%) | 5（8.2） | 26（15.6） | 0.000 |
| Systolic | ≥15mmHg, n(%) | 8（13.1） | 16（9.6） | 0.102 |
| Diastolic | ≥10mmHg, n(%) | 3（6.6） | 18（10.8） | 0.001 |
| Diastolic | ≥15mmHg, n(%) | 3（4.9） | 0（0） | —— |
| **Arm-ankle BP difference, mmHg** | | | | |
| L-ABI | mean±SD | 1.08±0.15 | 1.08±0.10 | 0.979 |
| R-ABI | mean±SD | 1.08±0.16 | 1.08±0.09 | 0.734 |
| L-ABI | <0.9, n(%) | 4(6.6) | 6(3.6) | 0.527 |
| | 0.9-1.00, n(%) | 7(11.5) | 32(19.2) | 0.000 |
| | >1.00, n(%) | 50(82.0) | 129(77.2) | 0.000 |
| R-ABI | <0.9, n(%) | 4(6.6) | 4(2.4) | 0.100 |
| | 0.9-1.00, n(%) | 9(14.8) | 28(16.8) | 0.002 |
| | >1.00, n(%) | 48(94.1) | 135(80.8) | 0.000 |

Table 1 presents the clinical characteristics of the subjects by gender. The mean of limbs blood pressure and ABI in male was higher than female, but there was no significant difference between them. The distribution of limbs blood pressure differences was shown Figure1. There were 11.35%, 4.37%, 10.92%, and 9.61% of subjects with inter-arm difference in systolic blood pressure of >15 mmHg, inter-arm difference in diastolic blood pressure of >10 mmHg, inter-ankle difference in systolic blood pressure of >15 mmHg and inter-ankle difference in diastolic blood pressure of >10 mmHg, respectively.

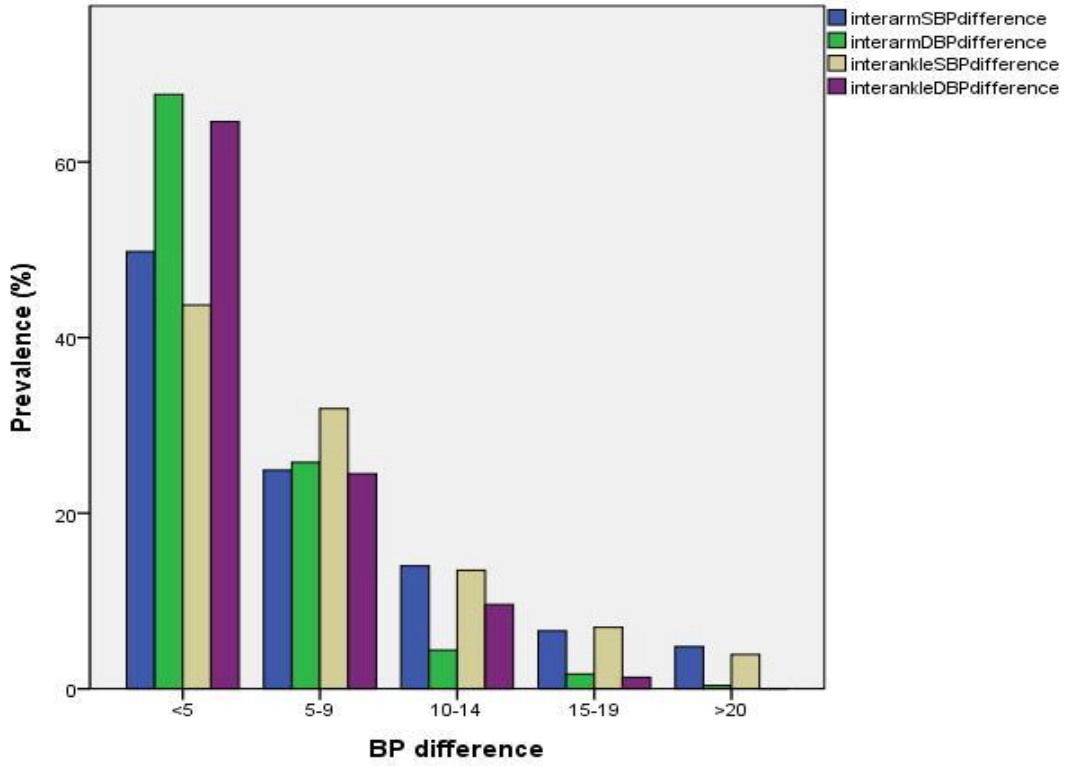


**Figure1. The distribution of limbs blood pressure difference in this study subject**

Variance analysis was performed to check the difference between limbs blood pressure differences(≤10, 10-14 and≥15) and ABI (<0.9, 0.90-1.00，>1.0), as shown in Figure 2. RABI and LABI have significant differences (P<0.05) with inter-arm difference in systolic blood pressure (≥10 mmHg VS < 10 mmHg, ≥10 mmHg VS ≥15 mmHg and ≥15 mmHg VS < 10 mmHg). RABI have significant differences (P<0.05) with inter-ankle difference in diastolic blood pressure (≥15 mmHg VS < 10 mmHg, ≥10 mmHg VS ≥15 mmHg). RABI and LABI have no significant differences (P>0.05) with inter-arm difference in diastolic blood pressure and inter-ankle difference in systolic blood pressure.

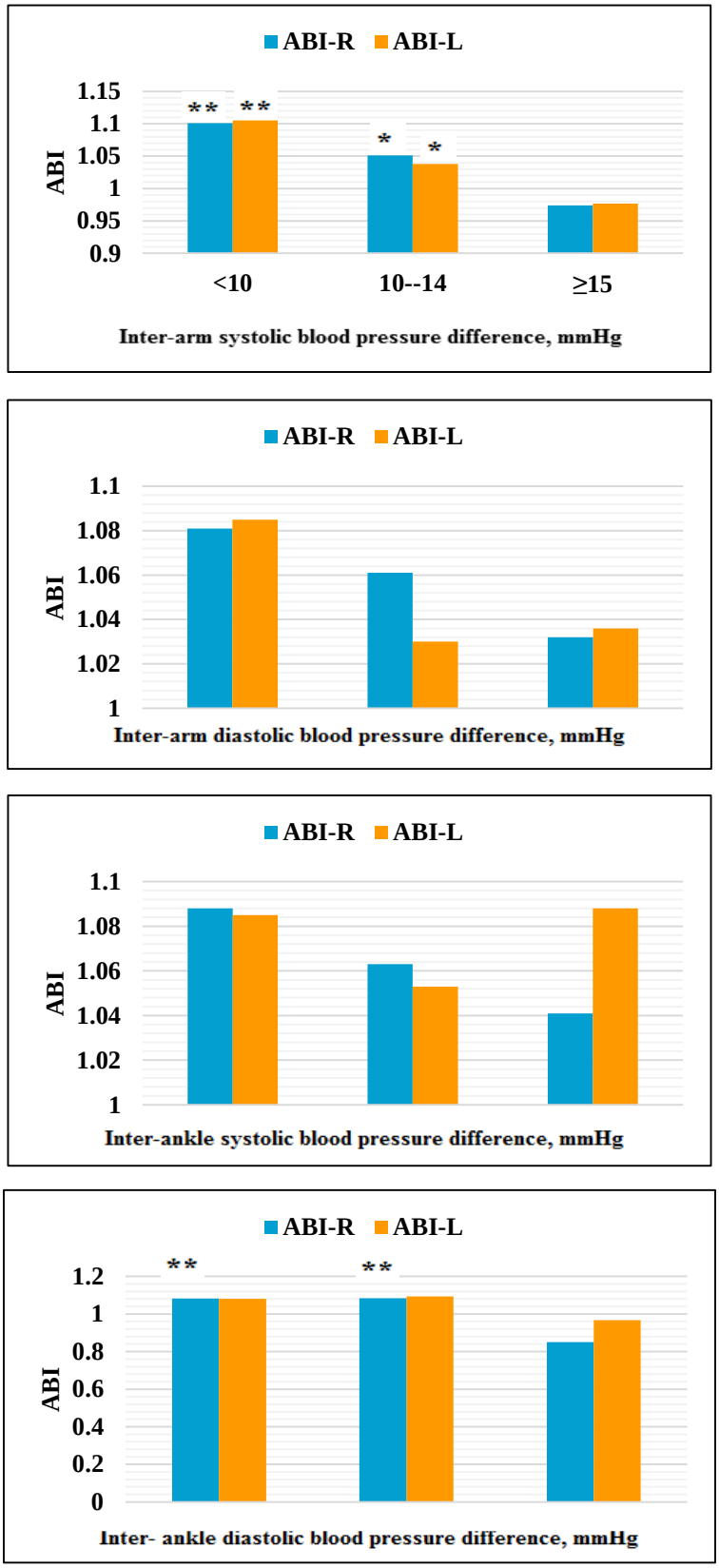


**Figure2. Variance analysis between limbs blood pressure differences and ABI**

*. The mean difference is significant at the 0.05 level.

**. The mean difference is significant at the 0.001 level.

The reference category is blood pressure difference ≥15 mmHg.

Multinomial logistic regression analysis presented the determinants of limbs blood pressure differences in all subjects, as shown in Table 2. BMI (Odds Ratio (OR), 1.151; 95% Confidence Interval (CI), (1.032-1.282); P=0.011), hypertension (OR, 0.350; CI, (0.152-0.807); P=0.014), and LABI (<0.9; OR, 10.028; CI, (1.109-90.682); P=0.040) were independently associated with inter-arm systolic blood pressure difference ≥ 10mmHg. Hypertension (OR, 0.236; CI, (0.080-0.695); P=0.009), LABI (<0.9; OR, 15.469; CI, (1.776-134.773); P=0.013) and RABI (0.90-1.00; OR, 4.231; CI, (1.205-14.860); P=0.024) were independently associated with inter-arm systolic blood pressure difference ≥ 15mmHg. RABI (<0.9; OR, 7.189; CI, (1.010-51.179); P=0.049) and (0.90-1.00; OR, 6.273; CI, (1.783-22.077); P=0.004) were independently associated with inter-ankle systolic blood pressure difference ≥ 15mmHg. LABI (0.90-1.00; OR, 4.331; CI, (1.039-14.330); P=0.016) was independently associated with inter-ankle diastolic blood pressure difference ≥ 10mmHg.
Since PAD has been associated with hypertension, we also performed a subgroup analysis after excluding 99 hypertension patients. After Multinomial logistic regression analysis in subgroup, we found that LABI (<0.9; OR, 246.330; CI, (5.442-11191.384); P=0.005) was still independently associated with inter-arm systolic blood pressure difference ≥ 15mmHg. In addition, ABI was not independently associated with inter-arm systolic blood pressure difference ≥ 10mmHg and inter-ankle systolic blood pressure difference ≥ 10mmHg or ≥ 15mmHg.

**Table2. Multinomial logistic regression analysis on limbs blood pressure differences**

| **≥10 mmHg** | | | **≥15 mmh** | | |
|---|---|---|---|---|---|
| **Parameter** | **OR(95% CI )** | **P** | **Parameter** | **OR(95% CI)** | **P** |
| **Inter-arm systolic blood pressure, mmHg** | | | | | |
| BMI | 1.151(1.032-1.282) | 0.011 | Hypertension | 0.236(0.080-0.69 | 0.009 |
| Hypertensio | 0.350(0.152-0.807) | 0.014 | LABI<0.9 | 15.469(1.776-134.7 | 0.013 |
| LABI<0.9 | 10.028(1.109-90.682) | 0.040 | RABI(0.90-1.00) | 4.231(1.205-14.860) | 0.024 |
| **Inter-arm diastolic blood pressure, mmHg** | | | | | |
| | —— | | | —— | |
| **Inter-ankle systolic blood pressure, mmHg** | | | | | |
| | —— | | RABI<0.9 | 7.189(1.010-51.179) | 0.049 |
| | | | RABI(0.90-1.00) | 6.273(1.783-22.077) | 0.004 |
| **Inter- ankle diastolic blood pressure, mmHg** | | | | | |
| LABI(0.90-1.00) | 4.331(1.039-14.330) | 0.016 | | —— | |

The reference category is blood pressure difference <10 mmHg.
Covariates in the Multinomial logistic regression model include age, BMI, hypertension, smoking, drinking, LABI (<0.9, 0.90-1.00 and >1) and RABI (<0.9, 0.90-1.00 and >1).

In addition, variance analysis was performed to check the ABI difference on age and BMI, the independent-samples T test was performed to check the ABI difference on hypertension, drinking and smoking, and the Pearson correlation analysis was performed to check the correlation degree between limbs blood pressures and ABI. The mean of RABI and LABI

with hypertension was higher than without hypertension, and there was significant difference between them in RABI. The mean of RABI and LABI in drinking was higher than not drinking, but there was no significant difference between them. The mean of RABI and LABI in smoking was higher than not smoking, but there was no significant difference between them. RABI decreased with age (45-75 years), while LABI presented the undulated change, but there was no significant difference between groups. RABI and LABI increased with BMI (18.5-32kg/$m^2$), but there was no significant difference between groups. RABI and LABI have significant differences ($P<0.05$) and a position correlation with systolic blood pressure, diastolic blood pressure, pulse pressure and pulse pressure index in the ankle.

**Discussion**

In this cross-sectional study, by using a simultaneous measurement technique, the association between limbs blood pressure differences and ABI was evaluated. Multinomial logistic regression analysis presented that LABI <0.9 was independently associated with inter-arm systolic blood pressure difference ≥ 10mmHg or ≥ 15mmHg; LABI (0.90-1.00) was independently associated with inter-ankle diastolic blood pressure difference ≥ 10mmHg; RABI (0.90-1.00) was independently associated with inter-arm systolic blood pressure difference ≥ 15mmHg and inter-ankle systolic blood pressure difference≥15mmHg. RABI<0.9 was independently associated with inter-ankle systolic blood pressure difference ≥ 15mmHg. However, inter-arm diastolic blood pressure difference ≥ 10mmHg or ≥ 15mmHg, inter-ankle systolic blood pressure difference ≥10mmHg and inter-ankle diastolic blood pressure difference≥15mmHg have no obvious correlation with ABI. LABI (<0.9; OR, 246.330; CI, (5.442-11191.384); P=0.005) was still independently associated with inter-arm systolic blood pressure difference ≥ 15mmHg after excluding 99 hypertension patients.

The values of ABI were good markers for PAD, and lower ABI was reported to be associated with generalized atherosclerosis [16]. Previous studies found that ABI<0.9 had a significant correlation with inter-arm systolic blood pressure difference≥ 15 mmHg or diastolic blood pressure ≥ 10 mmHg [6, 17-18]. Moreover, ABI<0.9 had a significant correlation with inter-ankle systolic blood pressure difference ≥ 15mmHg in hemodialysis patients [9]. This study also illustrated that ABI<0.9 was independently associated with inter-arm systolic blood pressure difference≥ 10mmHg or ≥ 15 mmHg and inter-ankle systolic blood pressure difference≥ 15mmHg. Hence, generalized atherosclerosis might be indicated by inter-arm/inter-ankle systolic blood pressure difference of ≥ 10mmHg or ≥ 15 mmHg.

Chen et al. reported that ABI<0.9 had a significant correlation with inter-ankle diastolic blood pressure difference ≥ 10 mmHg in hemodialysis patients [9]. Su et al. reported that ABI<0.9 had a significant correlation with inter-ankle difference in systolic blood pressure ≥ 15 mmHg [10]. However, this study found that inter-ankle systolic blood pressure difference ≥10 mmHg and inter-ankle diastolic blood pressure difference ≥ 15 mmHg have no obviously independent correlation with ABI. These results were different form previous studies. Verberk et al. reported that the prevalence of inter-arm difference in systolic blood pressure of 10 mmHg or more was roughly doubled when diagnosis measurements method used a sequential approach, or used manual approach rather than automated measurements approach [19].

In this study, by using a simultaneous measurement technique, the association between limbs blood pressure differences and ABI was evaluated. Therefore, the measurement technique of blood pressure might explain the difference or low prevalence between inter-ankle blood pressure difference and ABI in this study. In addition, inter-arm diastolic blood pressure difference ≥ 10mmHg or ≥ 15mmHg was not independent correlation with ABI in this study. Peninsula medical of University of Exeter in England followed 230 patients with hypertension for 10 years and found that inter-arm systolic blood pressure difference might lead to diseases such as heart disease, stroke, cerebral vascular disease and arterial stenosis or hardening, while inter-arm diastolic blood pressure difference might increase risk of death from heart disease, stroke and other diseases [20]. Therefore, the investigation of inter-arm systolic blood pressure difference is more important than inter-arm diastolic blood pressure difference.

The value of ABI from 0.90 to 1.00 is the critical value to estimate PAD. In this study, multinomial logistic regression analysis presents that LABI (0.90-1.00) was independently associated with inter-ankle diastolic blood pressure difference ≥ 10mmHg, and RABI (0.90-1.00) was independently associated with inter-arm systolic blood pressure difference ≥ 15mmHg and inter-ankle systolic blood pressure difference≥15mmHg. Ovbiagele reported that PAD (0.90≤ABI≤1.00) was independently associated with stroke [21]. Thus, this study suggests that further studies are necessary to clarify between ABI (0.90-1.00) and blood pressure differences of four limbs.

Previous studies found that inter-arm difference in systolic blood pressure was associated with risk factors for atherosclerosis, such as aging, hypertension, hypercholesterolemia, obesity, and low ABI [18]. In this study, hypertension, BMI and ABI<0.9 were correlated with inter-arm systolic blood pressure difference of 10 mmHg or 15 mmHg. In addition, gender was not a significant factor associated with inter-arm SBP difference [18]. Other studies showed that female gender was independent risk factor for inter-arm systolic blood pressure difference of 10 mmHg or more [10]. In this study, there was a difference between female and male in inter-arm systolic blood pressure difference ≥10 mmHg and inter-arm systolic/diastolic blood pressure difference ≥ 10 mmHg by Chi-square test, but the gender was not an independent risk factor for inter-arm systolic blood pressure difference. The large gap in sample size between male and female might be a cause of formation of the results in this study. Further studies are necessary to clarify the association between gender and inter-arm systolic blood pressure difference.

In this study, by using a simultaneous and noninvasive measurement technique, we measured four limbs blood pressures. But this technique was not a popular one to measure blood pressure in daily clinical practice. Hence, although four limbs blood pressure with simultaneous measurement could improve the predictive value for PAD, our results might be changed if daily clinical measurement was used. In addition, the subjects were mainly from retired people, whose health care consciousness is better than the serving officer. The factors of smoking, drinking, salting and movement have no significant difference with ABI of subjects in this study. Hence, the clinical utility of this study may be limited in community

people. Furthermore, follow-up data of subjects and enlarged sample size of subjects is necessary for future study.

## Conclusions

LABI <0.9 was independently associated with inter-arm SBP difference ≥ 15mmHg, while these differences still existed after excluding hypertensive patients. In addition, the cut off (0.90-1.00) of ABI was found to be independently associated with inter-arm SBP difference ≥ 15mmHg and inter-ankle DBP difference ≥ 10mmHg or ≥ 15mmHg. Hence, detection of limbs blood pressure difference with simultaneous measurement may provide an aid for the non-invasive diagnostic method of PAD in clinical primary care.

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