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Association between Systolic Blood Pressure Difference ≥10 mm Hg and Ankle-Brachial Index

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Abstract

Background: In new outpatients, blood pressure should be measured in both arms. A previous study reported that an inter-arm systolic blood pressure difference (ΔSBP) of ≥10 mm Hg is associated with an increased risk of mortality. Aim: The aim was to identify the associations with absolute values of ΔSBP (|ΔSBP|) ≥10 mm Hg. Subjects and Methods: This study included 2481 patients. Patients with a body mass index ≥25 kg/m^2 were defined as obese. The group of A was defined as following: ankle-brachial index (ABI) was <0.9 or ≥1.3. ΔSBP was expressed as right arm BP minus left arm BP. |ΔSBP| ≥10 mm Hg were analyzed using multivariate logistic analysis. Results: |ΔSBP| ≥10 mm Hg was found in 6.0% of patients and |ΔSBP| < 5 mm Hg in 80.4%. In multivariate analysis, the odds ratios (ORs) of the associations with |ΔSBP| ≥10 mm Hg were significantly associated with abnormal ABI and obesity regardless of sex and age. Moreover, the OR of the combined effects of abnormal ABI and obesity was higher than that of abnormal ABI and obesity alone. Conclusion: |ΔSBP| ≥10 mm Hg was associated with abnormal ABI and obesity. In a primary care setting, blood pressure should be actively measured in both arms. This study suggests that the associations with |ΔSBP| ≥10 mm Hg may be a useful part of screening for abnormal ABI.

Keywords

Systolic Blood Pressure Difference, Ankle-Brachial Index, Obesity, Odds Ratio, Combined Effects

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1. Introduction

Blood pressure difference (ΔBP) was recently reported to be a predictor of peripheral artery disease (PAD) [1], atherosclerosis, vascular mortality, and all-cause mortality [1]-[5]. Several studies have focused on the frequency of significant ΔBP (≥10 mm Hg) [1] [2] [5] and the correlation of ΔBP with systolic BP (SBP) [6] [7]. In a longitudinal study, primary care patients with absolute values of ΔSBP (|ΔSBP|) ≥10 mm Hg who were receiving antihypertensive medication had an increased risk of mortality [8]. Two types of patient positions have been used to evaluate ΔSBP: seated [2] [4]-[8] and supine [1]. However, many previous studies have included less than 500 subjects [4]-[7] [9] [10].

Using the Form ABI/PWV (Form PWV/ABI®, OMRON Colin Co. Ltd., Komaki, Japan) device to examine 2481 patients, the first aim was to identify the associations with |ΔSBP| ≥10 mm Hg when BP was calculated in the supine position. The second aim was to investigate combined effects, such as abnormal ABI and obesity, on |ΔSBP| ≥10 mm Hg.

2. Study Patients and Methods

This cross-sectional study was performed based on the research from the Department of Outpatients in Urban population about Blood pressure differences and Laid out Effect by Harasanshin-hospital Analysis for Non-acute Diseases-3 (DOUBLE HAND-3) study in Fukuoka, Japan, from August 2004 to November 2010. First, we conducted 4971 examinations by using Form ABI/PWV. Of these 4971 examinations on patients who participated in a medical check-up for arteriosclerosis, 2410 examinations of the same patients who enrolled at the second and subsequent examinations (48.8%) were excluded, and a further 80 were excluded due to lack of information (1.6%). Thus, data from 2481 (1578 men and 903 women) outpatients who registered for the first examination only were analyzed. Informed consent was obtained from each patient before the examination, and the study was conducted in accordance with the principles of the Declaration of Helsinki and institutional procedures.

2.1. Definitions

ΔSBP was defined as the difference between the SBP of the right arm and that of the left arm, and was calculated as right arm BP minus left arm BP. Significant |ΔSBP| included values of ≥10 mm Hg. Obesity was defined as a body mass index (BMI) ≥25 kg/m^2. Ankle-brachial index (ABI) was classified into 3 groups: 0.9 ≤ ABI < 1.3 (group I); ABI < 0.9 (group II); and ABI ≥ 1.3 (group III). It was also classified into 2 groups: 0.9 ≤ ABI < 1.3 (group I) and ABI < 0.9 or ABI ≥ 1.3 (group IV) [11] [12]. The combined effects of |ΔSBP| ≥10 mm Hg according to obesity and ABI were classified into 4 groups: non-obesity + group I (Group A); obesity + group I (Group B); non-obesity + group IV (Group C); and obesity + group IV (Group D). The patients were categorized according to age into 2 general groups (young and middle-aged group (<65 years old) and elderly group (≥65 years old)) and into 6 specific groups (<40 years, 40 - 49 years, 50 - 59 years, 60 - 69 years, 70 - 79 years, and ≥80 years). The patients who smoked were defined as current smokers.

2.2. Blood Pressure Measurement

With patients in a supine position, the BP in all 4 limbs was recorded simultaneously by using an automatic device (Form PWV/ABI) with 4 cuffs wrapped on the upper arms and the ankles. This device, whose accuracy has been previously validated [1] [13], measures the electrocardiogram signal, phonocardiogram signal, and ABI, as well as BP, by using the cuff-oscillometric method.

2.3. Statistical Analyses

Comparison of continuous variables between groups was performed with *t*-tests. Categorical variables were compared using Fisher's exact two-tailed test. Differences for |ΔSBP| ≥10 mm Hg among the 6 groups of age were tested with a two-way analysis of variance. There were summarized as associations between the percentages of |ΔSBP| ≥10 mm Hg according to sex and age. Trend analysis was carried out by chi-square calculations for linear trends. Stepwise multivariate logistic regression analysis was used to identify the associations that might be associated with |ΔSBP| ≥10 mm Hg. The explanatory variables were sex, age, obesity, and the combined effects of obesity and abnormal ABI. A two-sided P value of <0.05 was considered statistically significant. All the statistical analyses were performed using SPSS software version 16.0.2 (SPSS Inc., Chicago, IL, USA) and Stata/MP® version 14.1 (Stata Corp., College Station, TX, USA).

3. Results

3.1. Patient Characteristics

|ΔSBP| was <5 mm Hg in 80.4% (n = 1994) of the patients in this study. The SBP on the left arm was lower than that on the right in 54.6% (n = 1354) of patients, higher than that on the right in 35.7% (n = 885) of patients, and same as that on the right in 9.7% (n = 242) of patients (**Figure 1**). The percentage of total patients, male patients, and female patients who had |ΔSBP| >10 mm Hg was 6.0%, 6.1%, and 5.9%, respectively. On comparing patients with |ΔSBP| ≥10 mm Hg and those with |ΔSBP| <10 mm Hg, significant differences were found in the BMI, SBP, and percentage of obesity in men, while in women and for the total group, significant differences were found in the BMI, SBP, and percentage of obesity (**Table 1**).

3.2. Relationship between the Percentage of Patients with |ΔSBP| ≥10 mm Hg, Abnormal ABI, and Obesity, According to Sex and Age

In men, the percentage of patients with |ΔSBP| ≥10 mm Hg showed no significant change with increasing age (P = 0.42), but a significant increase and decrease was seen with abnormal ABI (P < 0.001) and obesity (P < 0.001), respectively (**Figure 2(a)**). In women, the percentage of patients with |ΔSBP| ≥10 mm Hg showed no significant change with increasing age (P = 0.46) and with obesity (P = 0.31), but a significant increase was seen with abnormal ABI (P = 0.007, **Figure 2(b)**).

3.3. Logistic Regression Analysis

The odds ratios (ORs) of total patients, male patients, and female patients for associations with |ΔSBP| ≥10 mm Hg are shown in **Table 2**. Although the OR of the combined effects of obesity and abnormal ABI were higher than that of obesity alone, it was similar to that of abnormal ABI alone (**Table 2**). The OR of total patients, male patients, and female patients of |ΔSBP| ≥10 mmHg was not significantly associated with sex and age in all logistic analyses.

4. Discussion

4.1. Causes of |ΔSBP| ≥10 mm Hg, and Sample Size Calculated as the Prevalence in Previous Studies

The differences in aortic systolic pressure wave reflections between the arms could have resulted from at least 3

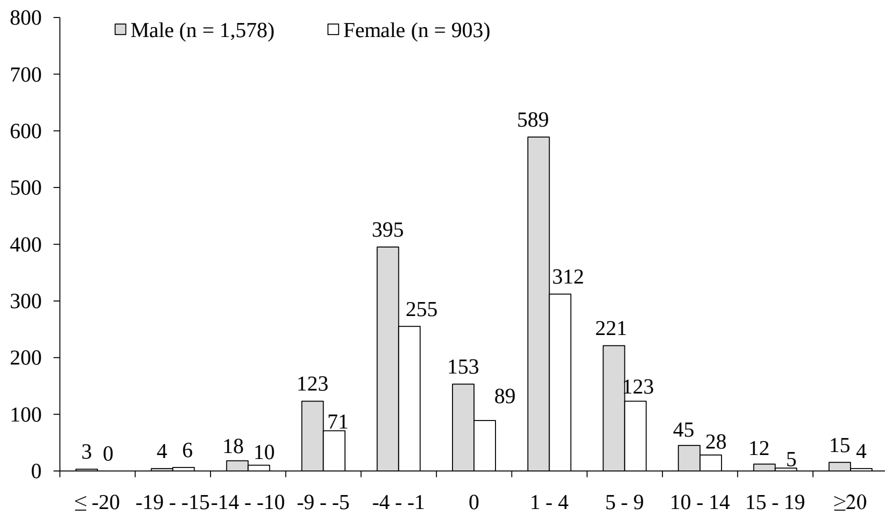

Figure 1. Systolic blood pressure: right arm (R)-left arm (L) (mm Hg) according to sex. The graph shows the distribution of ΔSBP divided into groups of 3 mm Hg in 2481 patients.

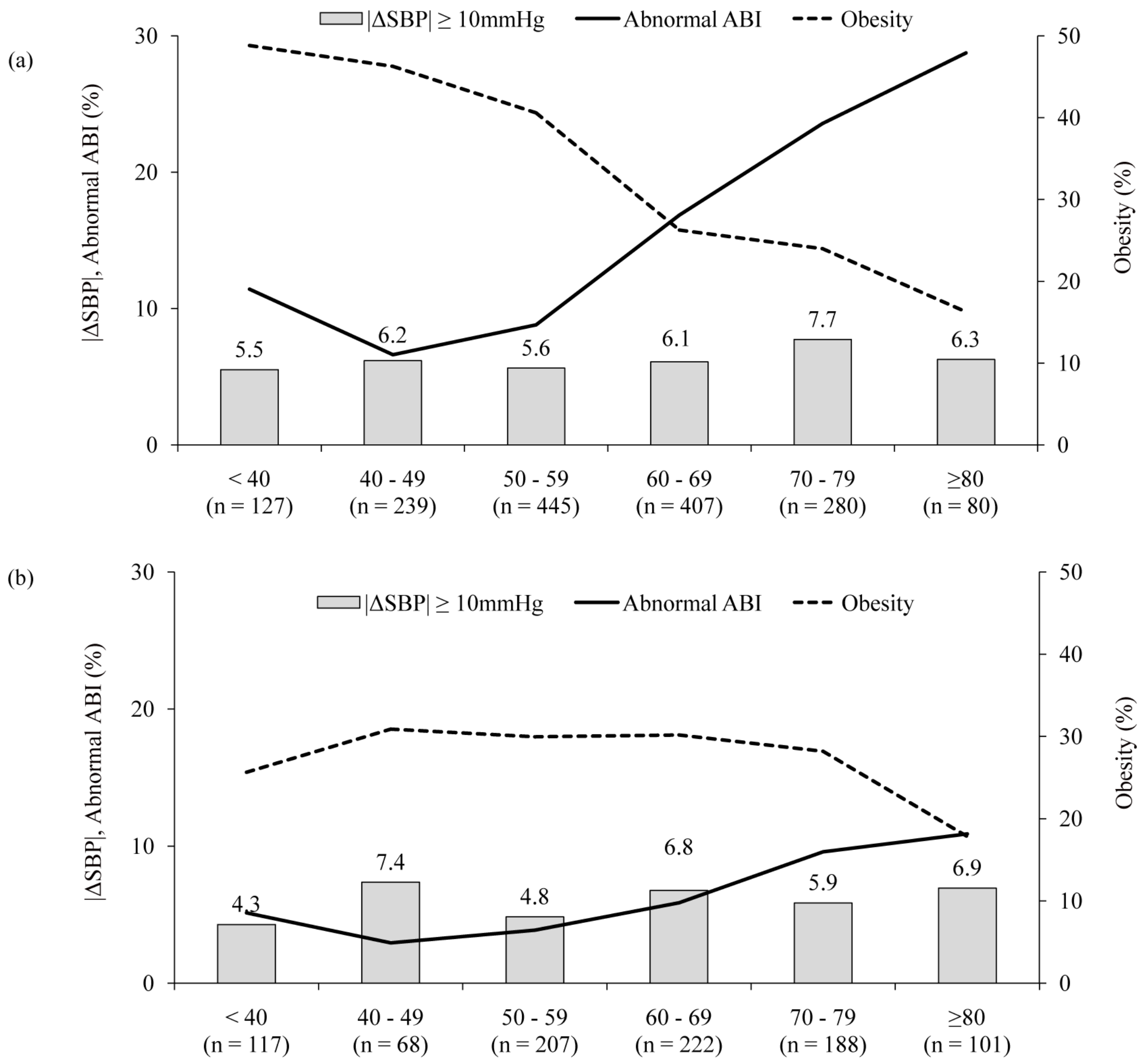

Figure 2. (a) The associations between ΔSBP, abnormal ABI, and obesity according to sex and age in men. When analyzing the trends for 6 age groups, the percentage of patients with |ΔSBP| ≥10 mm Hg showed no significant change with increasing age ($P = 0.42$), but a significant increase and decrease was seen with abnormal ABI ($P < 0.001$) and obesity ($P < 0.001$), respectively; (b) The associations between ΔSBP, abnormal ABI, and obesity according to sex and age in women. When analyzed for 6 age groups, the percentage of patients with |ΔSBP| ≥10 mm Hg showed no significant change with increasing age ($P = 0.46$) and with obesity ($P = 0.31$), but a significant increase was seen with abnormal ABI ($P = 0.007$).

mechanisms: 1) differences in arterial pulse wave velocity; 2) differences in pressure wave reflection; and 3) differences in the timing of systolic ejection [14]. Some studies reported that an increased carotid—the intima-media thickness (IMT) in the left carotid artery [15] [16]. A previous study suggested that the cause of |ΔSBP| ≥10 mm Hg was pathologic rather than physiologic [17]. In addition to anatomical evidence for |ΔSBP| ≥10 mm Hg, aortic dissections, aortitis, infraclavicular arterial occlusion, and arterial embolism may be attributed to a thrombus complicated by atrial fibrillation, congenital coarctation of the aorta, or higher BP in the left arm, compared with the right arm [18] [19].

In this study, the percentage of patients with |ΔSBP| ≥10 mm Hg (6.0%) was similar to that found in previous studies. The sample size was calculated as a one-sample comparison of the proportion to the hypothesized value (from 3.5%, as referred to in previous studies, to 33%) [1] [3]-[9] [17] [20] [21]: the number of study patients that were required for a power of 90% at a two-sided alpha of 0.01 to detect a |ΔSBP| ≥10 mm Hg of 6.0% ranged from 21 to 1149 patients, meeting the eligibility criteria. Power analysis could be calculated the minimum

Table 1. (a) Basic clinical characteristics in total patients; (b) Basic clinical characteristics in male; (c) Basic clinical characteristics in female.

(a)

	Total (n =2481)		|ΔSBP| ≥10 mmHg (n =150, 6.0%)		|ΔSBP| <10 mmHg (n =2331, 94.0%)		
Total	mean	(SD)	mean	(SD)	mean	(SD)	P-value
Sex, male, n, %	1578	63.6	97	64.7	1481	63.5	0.78
Age	60.8	(13.2)	61.8	(13.3)	60.7	(13.2)	0.32
Age ≥65years, n, %	982	39.6	64	42.7	918	39.4	0.43
BMI	23.9	(4.0)	25.5	(4.7)	23.7	(3.9)	<0.001
Obesity ≥25kg/m^2, n, %	813	32.8	73	48.7	740	31.7	<0.001
SBP	133.5	(20.3)	144.2	(23.2)	132.8	(19.9)	<0.001
Group I, yes, n, %	2201	88.7	112	74.6	2,089	89.6	
Group II, yes, n, %	125	5.0	16	10.7	109	4.7	0.001
Group III, yes, n, %	155	6.3	22	14.7	133	5.7	

(b)

	Men (n =1578)		|ΔSBP| ≥10 mmHg (n= 97, 6.1%)		|ΔSBP| <10 mmHg (n =1,481, 93.9%)		
Men	mean	(SD)	mean	(SD)	mean	(SD)	*P*-value
Age	59.0	(13.0)	59.8	(13.2)	58.9	(13.0)	0.51
Age ≥65years, n, %	542	34.3	35	36.1	507	34.2	0.71
BMI	24.2	(3.9)	25.7	(4.4)	24.1	(3.9)	<0.001
Obesity ≥25kg/m^2, n, %	562	35.6	50	51.5	512	34.6	0.001
SBP	133.4	(19.5)	143.7	(25.3)	132.7	(18.9)	<0.001
Group I, yes, n, %	1,356	85.9	72	74.2	1,284	86.7	
Group II, yes, n, %	100	6.4	9	9.3	91	6.1	0.013
Group III, yes, n, %	122	7.7	16	16.5	1106	7.2	

(c)

	Women (n =903)		|ΔSBP| ≥10 mmHg (n = 53, 5.9%)		|ΔSBP| <10 mmHg (n = 850, 94.1%)		
Women	mean	(SD)	mean	(SD)	mean	(SD)	*P*-value
Age	63.9	(12.9)	65.4	(12.9)	63.8	(13.0)	0.37
Age ≥65years, n, %	440	48.7	29	54.7	411	48.4	0.37
BMI	23.2	(4.0)	25.1	(5.2)	23.1	(3.9)	0.001
Obesity ≥25kg/m^2, n, %	251	27.8	23	43.4	228	26.8	0.009
SBP	133.8	(21.7)	145.0	(18.9)	133.1	(21.6)	<0.001
Group I, yes, n, %	845	93.6	40	75.5	805	94.7	
Group II, yes, n, %	25	2.8	7	13.2	18	2.1	0.001
Group III, yes, n, %	33	3.6	6	11.3	27	3.2	

Abbreviations were body mass index, BMI; systolic blood pressure, SBP; ankle-brachial index, ABI; ABI from 0.9 to 1.3, Group I; ABI < 0.9, Group II; ABI ≥ 1.3, Group III. Comparison between |ΔSBP| ≥10 mmHg and |ΔSBP| <10 mmHg.

sample size required so that one can reasonably detect an effect of a given size, and then this study documented that sample size was enough to detect.

4.2. Association of BMI with Abdomen, Atherosclerosis, and Vascular Event

Previous studies have reported relations between BMI and abdominal circumference [22], abdominal circum-

Table 2. Association of both variables and combined effects with |ΔSBP| ≥10 mmHg, using logistic regression, in the studied patients (n = 2481).

		Total (n = 2481)				Men (n = 1578)				Women (n = 903)			
	Reference	Odds ratio	95% C.I. Lower	95% C.I. Upper	P-value	Odds ratio	95% C.I. Lower	95% C.I. Upper	P-value	Odds ratio	95% C.I. Lower	95% C.I. Upper	P-value
Men	Women	0.88	0.61	1.26	0.47	—	—	—	—	—	—	—	—
Age	< 65 years	1.11	0.78	1.59	0.55	1.11	0.71	1.75	0.65	1.15	0.65	2.06	0.63
Group B	Group A	2.64	1.79	3.90	< 0.001	2.62	1.60	4.28	< 0.001	2.57	1.35	4.87	0.004
Group C	Group A	4.42	2.64	7.38	< 0.001	3.33	1.77	6.25	< 0.001	8.86	3.70	21.23	< 0.001
Group D	Group A	4.51	2.30	8.84	< 0.001	3.75	1.65	8.55	0.002	6.49	2.00	21.07	0.002

Abbreviations were confidence interval, C.I.; obesity, OB; ankle-brachial index, ABI. Normal ABI means ABI from 0.9 to 1.3, Abnormal ABI means ABI < 0.9 or ≥1.3. group A, non-obesity + normal ABI; group B, obesity + normal ABI; group C, non-obesity + abnormal ABI; group D, obesity + abnormal ABI

ference and visceral fat area [23] [24], BMI and stroke [25], and visceral fat and peripheral artery disease [13]. This study also showed that |ΔSBP| ≥10 mm Hg was associated with BMI and abnormal ABI. However, it was unclear whether there is association of |ΔSBP| ≥10 mm Hg in seated position with obesity, abdominal circumference, visceral fat area, and abnormal ABI. Although it is possible that the associations with |ΔSBP| ≥10 mm Hg are different for supine and seated positions, we suggest that outpatients with |ΔSBP| ≥10 mm Hg in seated position should be actively distinguished from abnormal ABI in primary care.

4.3. Association of |ΔSBP| ≥10 mm Hg with Traditional Makers

It is recommended by the Japanese hypertension treatment guidelines and by the American Heart Association that the blood pressure in both arms of new outpatients be measured routinely [26]-[28]. A number of research studies reported no associations with ΔBP and age [1] [6] [8]. This study found no association of the percentage of |ΔSBP| ≥10 mm Hg with age (men, P = 0.51; women, P = 0.37; and total, P = 0.78). Similarly, the percentage of patients with |ΔSBP| ≥10 mm Hg had no association with sex, as was shown in previous studies [1] [6] [8] [29]. Therefore, association with |ΔSBP| ≥10 mm Hg was also suggested to be pathological rather than physiological.

With regard to the OR of |ΔSBP| ≥10 mm Hg for obesity, there has been a report of an association with ΔBP and obesity [1]; the OR of 2.64 in all the patients in the present study is similar to that of 1.90 reported in a study in Ohasama, Japan [1]. Moreover, this study, which includes both sexes, showed that the OR of |ΔSBP| ≥10 mm Hg increased with an increase in obesity.

4.4. Association of |ΔSBP| ≥10 mm Hg with Development of Abnormal ABI and Vascular Events

The hypertensive state is related to progression to more advanced atherosclerosis [30]-[32], calcification of atherosclerosis [32]-[34]. Previous studies using carotid ultrasonography have reported conflicting results with regard to significant differences in IMT of the right and left side: some studies reported a significant difference [16] [17], while others studies reported no significant difference [2] [35] [36]. Moreover, it has been reported that ΔBP is related to the development of PAD, cardiovascular events [1] [5] [9] [20], vascular mortality, and all-cause mortality in meta-analyses [9] [21].

This study demonstrated the ORs of |ΔSBP| ≥10 mm Hg for the separate and combined effects of obesity and abnormal ABI, regardless of sex and age (**Table 2**). The OR of |ΔSBP| ≥10 mm Hg for abnormal ABI in all patients with obesity increased from 2.64 to 4.51, whereas in male patients with obesity, it increased from 2.62 to 3.75, and in female patients with obesity, it increased from 2.57 to 8.86. Similarly, abnormal ABI developed due to the vascular endothelial function disorder associated with aging [13]. This study suggested that abnormal ABI was potentially present in patients with |ΔSBP| ≥10 mm Hg in the supine position. Thus, in common practice, outpatients with |ΔSBP| ≥10 mm Hg in the sitting position should be assessed for the differential diagnosis of abnormal ABI.

This study has several limitations. First, the study was only characteristics such as BMI, sex, SBP, DBP, and ABI, therefore, it should be considered those characteristics necessarily not to reflect the associations with |ΔSBP| ≥10 mm Hg and ABI because there was not atherosclerotic risk markers for such as life-related diseases, smoking, and history of vascular events. Second, this study was unclear that confirmed diagnosis based on the patients with abnormal ABI such as diseases of aortitis syndrome, peripheral artery disease, and excessive calcified intima of the aorta. This study was not measured the arm circumference which SBP was influenced, it was possible for |ΔSBP| ≥10 mm Hg to be reported in obese individuals when an inappropriate size of cuff was used. Third, it was unclear whether the percentage of patients with abnormal ABI detected using the |ΔSBP| ≥10 mm Hg calculated in the supine position yielded results similar to those obtained in the sitting position. However, the predictive markers of |ΔSBP| ≥10 mm Hg in a seated position in primary care may be a useful part of abnormal ABI screening, and thus, requires future research.

5. Conclusion

In conclusion, this study suggested that the association of various markers with |ΔSBP| ≥10 mm Hg is pathological rather than physiological. The OR of |ΔSBP| ≥10 mm Hg was significantly associated with both obesity and abnormal ABI, regardless of sex and age. The OR of the combined effects of abnormal ABI and obesity was higher than that of abnormal ABI and obesity alone.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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