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/m² 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/m². 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
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)

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 2481)</th>
<th>ΔSBP ≥10 mmHg (n = 150, 6.0%)</th>
<th>ΔSBP &lt;10 mmHg (n = 2331, 94.0%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male, n, %</td>
<td>1578 (63.6)</td>
<td>97 (64.7)</td>
<td>1481 (63.5)</td>
<td>0.78</td>
</tr>
<tr>
<td>Age</td>
<td>60.8 (13.2)</td>
<td>61.8 (13.3)</td>
<td>60.7 (13.2)</td>
<td>0.32</td>
</tr>
<tr>
<td>Age ≥65 years, n, %</td>
<td>982 (39.6)</td>
<td>64 (42.7)</td>
<td>918 (39.4)</td>
<td>0.43</td>
</tr>
<tr>
<td>BMI</td>
<td>23.9 (4.0)</td>
<td>25.5 (4.7)</td>
<td>23.7 (3.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obesity ≥25 kg/m², n, %</td>
<td>813 (32.8)</td>
<td>73 (48.7)</td>
<td>740 (31.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP</td>
<td>133.5 (20.3)</td>
<td>144.2 (23.2)</td>
<td>132.8 (19.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Group I, yes, n, %</td>
<td>2201 (88.7)</td>
<td>112 (74.6)</td>
<td>2089 (89.6)</td>
<td></td>
</tr>
<tr>
<td>Group II, yes, n, %</td>
<td>125 (5.0)</td>
<td>16 (10.7)</td>
<td>109 (4.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Group III, yes, n, %</td>
<td>155 (6.3)</td>
<td>22 (14.7)</td>
<td>133 (5.7)</td>
<td></td>
</tr>
</tbody>
</table>

(b)

<table>
<thead>
<tr>
<th></th>
<th>Men (n = 1578)</th>
<th>ΔSBP ≥10 mmHg (n = 97, 6.1%)</th>
<th>ΔSBP &lt;10 mmHg (n = 1481, 93.9%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>59.0 (13.0)</td>
<td>59.8 (13.2)</td>
<td>58.9 (13.0)</td>
<td>0.51</td>
</tr>
<tr>
<td>Age ≥65 years, n, %</td>
<td>542 (34.3)</td>
<td>35 (36.1)</td>
<td>507 (34.2)</td>
<td>0.71</td>
</tr>
<tr>
<td>BMI</td>
<td>24.2 (3.9)</td>
<td>25.7 (4.4)</td>
<td>24.1 (3.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obesity ≥25 kg/m², n, %</td>
<td>562 (35.6)</td>
<td>50 (51.5)</td>
<td>512 (34.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>SBP</td>
<td>133.4 (19.5)</td>
<td>143.7 (25.3)</td>
<td>132.7 (18.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Group I, yes, n, %</td>
<td>1356 (85.9)</td>
<td>72 (74.2)</td>
<td>1284 (86.7)</td>
<td></td>
</tr>
<tr>
<td>Group II, yes, n, %</td>
<td>100 (6.4)</td>
<td>9 (9.3)</td>
<td>91 (6.1)</td>
<td>0.013</td>
</tr>
<tr>
<td>Group III, yes, n, %</td>
<td>122 (7.7)</td>
<td>16 (16.5)</td>
<td>1106 (7.2)</td>
<td></td>
</tr>
</tbody>
</table>

(c)

<table>
<thead>
<tr>
<th></th>
<th>Women (n = 903)</th>
<th>ΔSBP ≥10 mmHg (n = 53, 5.9%)</th>
<th>ΔSBP &lt;10 mmHg (n = 850, 94.1%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63.9 (12.9)</td>
<td>65.4 (12.9)</td>
<td>63.8 (13.0)</td>
<td>0.37</td>
</tr>
<tr>
<td>Age ≥65 years, n, %</td>
<td>440 (48.7)</td>
<td>29 (54.7)</td>
<td>411 (48.4)</td>
<td>0.37</td>
</tr>
<tr>
<td>BMI</td>
<td>23.2 (4.0)</td>
<td>25.1 (5.2)</td>
<td>23.1 (3.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Obesity ≥25 kg/m², n, %</td>
<td>251 (27.8)</td>
<td>23 (43.4)</td>
<td>228 (26.8)</td>
<td>0.009</td>
</tr>
<tr>
<td>SBP</td>
<td>133.8 (21.7)</td>
<td>145.0 (18.9)</td>
<td>133.1 (21.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Group I, yes, n, %</td>
<td>845 (93.6)</td>
<td>40 (75.5)</td>
<td>805 (94.7)</td>
<td></td>
</tr>
<tr>
<td>Group II, yes, n, %</td>
<td>25 (2.8)</td>
<td>7 (13.2)</td>
<td>18 (2.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Group III, yes, n, %</td>
<td>33 (3.6)</td>
<td>6 (11.3)</td>
<td>27 (3.2)</td>
<td></td>
</tr>
</tbody>
</table>

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 $|\Delta SBP| \geq 10$ mmHg, using logistic regression, in the studied patients (n = 2481).

<table>
<thead>
<tr>
<th></th>
<th>Reference</th>
<th>Odds ratio (Men)</th>
<th>95% C.I. (Men)</th>
<th>P-value</th>
<th>Odds ratio (Women)</th>
<th>95% C.I. (Women)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>odds ratio</td>
<td>Lower</td>
<td>Upper</td>
<td>odds ratio</td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td></td>
<td></td>
<td>95% C.I.</td>
<td>P-value</td>
<td></td>
<td>95% C.I.</td>
<td>P-value</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.88</td>
<td>0.61</td>
<td>1.26</td>
<td>0.47</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>1.11</td>
<td>0.78</td>
<td>1.59</td>
<td>1.11</td>
<td>1.71</td>
<td>5.56</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>2.64</td>
<td>1.79</td>
<td>3.90</td>
<td>&lt; 0.001</td>
<td>2.62</td>
<td>1.60</td>
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<tr>
<td></td>
<td>Group C</td>
<td>4.42</td>
<td>2.64</td>
<td>7.38</td>
<td>&lt; 0.001</td>
<td>3.33</td>
<td>1.77</td>
</tr>
<tr>
<td></td>
<td>Group D</td>
<td>4.51</td>
<td>2.30</td>
<td>8.84</td>
<td>&lt; 0.001</td>
<td>3.75</td>
<td>1.65</td>
</tr>
</tbody>
</table>

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.

4.3. Association of $|\Delta SBP| \geq 10$ 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 $\Delta BP$ and age [1] [6] [8]. This study found no association of the percentage of $|\Delta SBP| \geq 10$ mm Hg with age (men, P = 0.51; women, P = 0.37; and total, P = 0.78). Similarly, the percentage of patients with $|\Delta SBP| \geq 10$ mm Hg had no association with sex, as was shown in previous studies [1] [6] [8] [29]. Therefore, association with $|\Delta SBP| \geq 10$ mm Hg was also suggested to be pathologic rather than physiological.

With regard to the OR of $|\Delta SBP| \geq 10$ mm Hg for obesity, there has been a report of an association with $\Delta BP$ 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 $|\Delta SBP| \geq 10$ mm Hg increased with an increase in obesity.

4.4. Association of $|\Delta SBP| \geq 10$ 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 $\Delta BP$ 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 $|\Delta SBP| \geq 10$ mm Hg for the separate and combined effects of obesity and abnormal ABI, regardless of sex and age (Table 2). The OR of $|\Delta SBP| \geq 10$ 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 $|\Delta SBP| \geq 10$ mm Hg in the supine position. Thus, in common practice, outpatients with $|\Delta SBP| \geq 10$ 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 $|\Delta\text{SBP}| \geq 10$ 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 $|\Delta\text{SBP}| \geq 10$ 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 $|\Delta\text{SBP}| \geq 10$ mm Hg calculated in the supine position yielded results similar to those obtained in the sitting position. However, the predictive markers of $|\Delta\text{SBP}| \geq 10$ 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 $|\Delta\text{SBP}| \geq 10$ mm Hg is pathological rather than physiological. The OR of $|\Delta\text{SBP}| \geq 10$ 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.

References


