Original Article


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To assess blood pressure control in the Japanese population, we analyzed previously obtained measurements of conventional, home and ambulatory blood pressures in 1,174 subjects aged ⩽ 40 in a Japanese community. On the basis of conventional blood pressure values and the use of antihypertensive medication, participants were classified as normotensive, untreated hypertensive and treated hypertensive subjects. When 140/90, 135/85 and 135/85 mmHg were used as the hypertension criteria for conventional, home and ambulatory blood pressure measurements, respectively, all three blood pressure values were higher in untreated and treated hypertensive subjects than in normotensive subjects. Among the treated hypertensive subjects, approximately half were classified as hypertensive not only by conventional blood pressure, but also by home or ambulatory measurements. Approximately 10% of the subjects defined as normotensive by conventional blood pressure measurement were classified as hypertensive by home or ambulatory measurements, whereas 60% of the untreated hypertensive subjects as defined by conventional blood pressure measurement had normal home or ambulatory blood pressure values. Therefore, we concluded that 1) the poor blood pressure control in treated hypertensive subjects was attributable not only to the white coat effect but also to inadequate control of blood pressure; and 2) a certain percentage of subjects were misclassified as hypertensive or normotensive by conventional blood pressure measurement. (Hypertens Res 2002; 25: 57–63)

Key Words: conventional blood pressure, home blood pressure, ambulatory blood pressure, blood pressure control, population based subjects

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This work was supported by Grants-in-Aid for Scientific Research (12877163, 13470085, 13671095, 10470102, and 01180) from the Ministry of Education, Science, Sports and Culture of Japan, *7 Ohasama Hospital, Iwate, Japan, and *8 Miyako Hospital, Iwate, Japan.

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Received September 3, 2001; Accepted in revised form October 15, 2001.
Introduction

It has been reported that only a small proportion of patients on antihypertensive medication have well controlled blood pressure (BP) (1–3), which finding is often attributed to poor compliance with antihypertensive medication (1, 4). However, it has been suggested that this apparently poor BP control is caused, at least in part, by the so-called white coat effect (WCE), since conventional casual BP (CBP) measurements taken in medical settings have been used in these studies.

Self-measurements of BP at home (HBP) and ambulatory BP (ABP) monitoring can be used to monitor BP in non-medical settings and can avoid the WCE (1, 5). Furthermore, these techniques have been reported to provide more reliable and reproducible BP information, since they allow multiple measurements and avoid observer bias as well as regression dilution biases (1, 5–8). ABP and HBP have also been reported to have better predictive power for the prognosis of hypertension than CBP (1, 5, 8–15). Therefore, these measurements may be suitable for the investigation of true BP control in the general population. However, only one, Italian, study has used HBP and ABP to investigate BP control in a general population (16, 17).

The objectives of our present study were 1) to clarify the proportion of subjects whose BP was well controlled in the general Japanese population; 2) to clarify whether poor BP control in treated hypertensive subjects was attributable to the WCE; and 3) to clarify the proportion of subjects who are misclassified as hypertensive or normotensive by the use of CBP.

Methods

Design

This report is part of a BP measurement project in Ohasama, Iwate Pref., Japan, begun in 1987. The socioeconomic and demographic characteristics of this region and the details of the study subjects have been described previously (9, 11, 18, 19).

The study protocol was approved by the Institutional Review Board of Tohoku University School of Medicine and by the Department of Health of the Ohasama Town Government.

Study Population

The selection of the study subjects has been described previously (9). In brief, of the total residents (N = 2,716) of Ohasama aged 40 years or older, 575 subjects were excluded because they worked out of town. This exclusion criterion was necessary because public health nurses visited subjects to attach the ABP monitoring devices during the workday. Of the remaining subjects, 121 hospitalized patients and 31 demented or bedridden subjects were excluded from participation. Thus, 1,989 individuals were eligible for the study. Of the eligible residents, 447 did not monitor ABP for various reasons. Of the remaining 1,542 subjects, 1,332 subjects completed the measurement of CBP. The representativeness of these study subjects has been fully reported previously (9). Among them, 158 (12%) subjects who did not measure morning HBP or evening HBP for more than 3 days were excluded from the study. This criterion was based on our previous observation that the average BP value obtained for the first 3 days was not significantly different from the values obtained for the entire study period (18). Thus, 1,174 subjects (88% of the representative population) were studied. No significant difference was observed in age, gender or socioeconomic status between those who measured HBP for more than 3 days and those who did not. Therefore, we considered that the 1,174 subjects (age, 61.7 ± 9.6 (SD) years; 32% male) could be treated as a representative sample of this population.

BP Measurements

CBP Measurement

CBP was measured twice by nurses or technicians while the subjects were seated and after at least 2 min rest. An automatic BP measuring device (USM700F; Ueda Electronic Work Co., Ltd., Tokyo, Japan) based on the microphone method was used.

ABP Measurement

ABP was monitored with the ABPM-630 device (Nippon Colin, Komaki, Japan), a fully automatic device preset to measure BP every 30 min. Although systolic and diastolic ABP were measured by both the cuff-oscillometric method and the microphone method, we used only data obtained by the cuff-oscillometric method for analysis.

HBP Measurement

In our study, we used the following procedure to ascertain the accuracy of home blood pressure. First, physicians and public health nurses conducted a health education class to inform the population about home BP recording and to teach them how to measure their own BP. Then, we checked whether or not they were able to measure their own BP correctly. Eighty percent of households in this town attended the class, and public health nurses visited all of the remaining households to provide instruction on home BP measurement and to check whether they were able to measure their own BP correctly. These procedures were also described in detail in our previous manuscript (18, 20). Subjects were asked to measure their BPs in the sitting position once every morning within 1 h after awaking and after more than 2 min of rest, and to record the measurements for 4 weeks. If individuals were taking antihypertensive drugs, BP was measured before taking the medication. Subjects were also asked to
measure their BP once every evening just before going to bed. HBP was measured with a semiautomatic BP measuring device (HEM401C; Omron Life Science, Kyoto, Japan) based on the cuff-oscillometric principle, which generates a digital display of systolic and diastolic BP.

The devices for measurement of CBP, HBP and ABP were calibrated before the study began. All devices met the criteria set by the Association for the Advancement of Medical Instrumentation (21). Differences (mean ± SD) between systolic BP/diastolic BP as measured by the auscultatory method and by these devices were 0.8 ± 5.2/ - 0.5 ± 7.3 mmHg (USM700F), - 0.8 ± 6.1/3.1 ± 6.9 mmHg (ABPM 630), and 1.6 ± 7.7/ - 2.4 ± 6.1 mmHg (HEM401C), respectively (20). Because the circumference of the arm was < 34 cm in most subjects, we used a standard arm cuff for all BP measurements.

Classification of Subjects

We classified the subjects into three groups according to their CBP values and their use of antihypertensive medications as follows: normotensive subjects (NT, subjects who had never taken antihypertensive medication and whose CBP was < 140 mmHg for systolic and < 90 mmHg for diastolic); untreated hypertensive subjects (UHT, subjects who were not taking antihypertensive medication and whose CBP was = 140 mmHg for systolic and/or ≥ 90 mmHg for diastolic); and treated hypertensive subjects (THT, subjects who were being treated with antihypertensive medication).

Criteria for Hypertension by HBP and ABP

We classified the subjects with morning HBP or 24-h ABP ≥ 135 mmHg (systolic) and/or ≥ 85 mmHg (diastolic) as home or ambulatory hypertensives. The cut-off level of 135/85 mmHg was based on JNC-VI criteria (1). Since the JNC-VI criteria were based on our previous prognostic criteria that were calculated by 24-h ABP (10) or morning HBP (11), we here used 24-h ABP or morning HBP for assessing hypertensive subjects.

Data Analysis

The CBP value of an individual was defined as the average of the two readings. The HBP value of an individual was defined as the mean of all measurements for that study subject (mean number of measurements: morning, 24 ± 6 days; evening, 24 ± 7 days). ABP data were included in the analysis if the monitoring period included more than 8 h of waking (daytime) and more than 4 h in bed (nighttime). These periods were estimated from the subjects’ diaries. If the 24-h ABP monitoring was not complete, the 24-h average ABP was calculated as follows: 24-h average ABP = (daytime average ÷ waking hours + night-time average ÷ sleeping hours) /24.

All data for CBP, HBP (morning and evening), and ABP (24-h, daytime, nighttime) are shown as the mean ± SD.

All statistical analyses were performed with SAS software (SAS Inst., Cary, USA) (22).

We also analyzed two age groups separately: middle-aged subjects (aged 40 to 64) and elderly subjects (aged 65 and older).

Results

BP Values in Each Group

Of the 1,174 participants, 625, 150 and 399 participants were classified as NT, UHT and THT on the basis of CBP measurement, respectively (Table 1). Mean CBP values in the THT subjects were significantly lower than those in the UHT subjects. In all three groups, mean HBP (morning and evening) and ABP (24-h, daytime, nighttime) values were lower than CBP values. HBP and ABP values in UHT and THT subjects were significantly higher than those in NT subjects. In THT subjects, HBP and ABP values were similar to those in UHT subjects. When we calculated the WCE as the difference between CBP and 24-h ABP, the systolic/diastolic WCE values were 23.8/8.4 mmHg, 9.4/2.7 mmHg and 3.0/0.3 mmHg for UHT, THT, and NT subjects, respectively (both p < 0.001). Similarly, when we calculated WCE as the difference between CBP and morning HBP (CBP - morning HBP), the systolic/diastolic WCE values were 21.5/5.8 mmHg, 4.2/ - 1.2 mmHg and 3.5/ - 1.8 mmHg for UHT, THT, and NT subjects, respectively (both p < 0.001).

Similar tendencies were observed in both the middle-aged (40 to 64 years) and the elderly (≥ 65 years) groups (Table 1). Mean systolic BP values were almost always higher in older than in younger subjects irrespective of the measurement method used.

BP Control in Each Group (Fig. 1)

CVP Measurement

Fifty-two percent, 42% and 42% of THT subjects in each of the whole, middle-aged and elderly groups, respectively, had CBP ≥ 140 mmHg for systolic and/or ≥ 90 mmHg for diastolic.

HBP Measurement

Forty-nine percent, 46% and 52% of THT subjects in the whole, middle-aged and elderly groups, respectively, were classified as hypertensive by HBP measurement. The remaining 51%, 54% and 48% of THT subjects in the respective groups were classified as normotensive by HBP measurement.

ABP Measurement

Similarly, 29%, 25% and 32% of subjects in the whole, mid-
### Table 1. Average BP Value (SD) in Each Group of Subjects Defined on the Basis of CBP Measurements

<table>
<thead>
<tr>
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<th>Conventional BP (mmHg)</th>
<th>Home BP (mmHg)</th>
<th>Ambulatory BP (mmHg)</th>
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<tbody>
<tr>
<td></td>
<td>Morning</td>
<td>Evening</td>
<td>24 h</td>
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<td>Daytime</td>
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<td>Whole subjects (N=1,174)</td>
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</tr>
<tr>
<td>UHT (N=150)</td>
<td>153.9 (15.1)**</td>
<td>132.7 (14.2)**</td>
<td>130.1 (12.7)**</td>
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<td></td>
<td>83.9 (11.3)**</td>
<td>78.0 (10.0)*</td>
<td>75.5 (8.2)*</td>
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<tr>
<td>THT (N=399)</td>
<td>137.3 (17.6)*</td>
<td>131.1 (14.0)*</td>
<td>127.9 (12.8)*</td>
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<tr>
<td></td>
<td>76.8 (12.0)*</td>
<td>76.1 (9.1)*</td>
<td>74.1 (7.8)*</td>
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<tr>
<td>NT (N=625)</td>
<td>121.3 (11.6)</td>
<td>117.8 (11.8)</td>
<td>118.4 (11.2)</td>
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<td>70.1 (8.5)</td>
<td>71.4 (9.0)</td>
<td>69.8 (6.9)</td>
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Aged 40–64 years (N=772)

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<thead>
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<th>Conventional BP (mmHg)</th>
<th>Home BP (mmHg)</th>
<th>Ambulatory BP (mmHg)</th>
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<td></td>
<td>Morning</td>
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<td>Daytime</td>
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<tr>
<td>UHT (N=93)</td>
<td>153.6 (15.5)**</td>
<td>130.0 (13.3)*</td>
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<td></td>
<td>85.1 (11.6)**</td>
<td>78.1 (9.9)*</td>
<td>76.0 (8.3)*</td>
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<td>THT (N=179)</td>
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<td></td>
<td>79.3 (11.7)*</td>
<td>79.9 (10.4)*</td>
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<td>NT (N=500)</td>
<td>120.7 (11.6)</td>
<td>116.6 (11.1)</td>
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<td>70.5 (8.6)</td>
<td>71.4 (9.2)</td>
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Aged 65 or over years (N=402)

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<tr>
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<th>Conventional BP (mmHg)</th>
<th>Home BP (mmHg)</th>
<th>Ambulatory BP (mmHg)</th>
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<tr>
<td></td>
<td>Morning</td>
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<td>24 h</td>
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<td></td>
<td></td>
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<td>Daytime</td>
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<tr>
<td>UHT (N=57)</td>
<td>154.2 (14.5)**</td>
<td>136.1 (14.9)*</td>
<td>132.2 (12.5)*</td>
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<td></td>
<td>81.8 (10.5)**</td>
<td>77.9 (10.2)*</td>
<td>74.8 (8.2)*</td>
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<td>74.8 (11.8)*</td>
<td>76.7 (9.8)*</td>
<td>73.0 (7.6)*</td>
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<tr>
<td>NT (N=125)</td>
<td>123.9 (10.9)</td>
<td>122.5 (13.2)</td>
<td>121.3 (11.0)</td>
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<td>68.8 (7.9)</td>
<td>71.3 (8.5)</td>
<td>69.9 (6.2)</td>
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</table>

*p < 0.05 vs. NT; ** p < 0.05 vs. NT and THT; BP, blood pressure; SBP, systolic BP; DBP, diastolic BP; CBP, conventional BP; N, number of subjects; UHT, untreated hypertensive subjects, subjects without antihypertensive medication and whose CBP higher than 140/90 mmHg. THT, treated hypertensive subjects, subjects with antihypertensive medication; NT, normotensives, subjects without antihypertensive medication and whose CBP lower than 140/90 mmHg.

**Discussion**

We demonstrated that the BP values of NT subjects were significantly lower than those of THT or UHT subjects, irrespective of the BP measurement method. ABP and HBP in THT subjects were similar to those in UHT subjects. These results suggest that BP control in THT subjects is not adequate in the Ohasama population. The CBP values in THT subjects were lower than those in UHT subjects, suggesting that the WCE in UHT subjects is larger than that in THT subjects. The difference between the WCE value of UHT subjects and THT subjects might be explained as follows: 1) since in Japan, white coat hypertension was known not to be treated, the proportion of subjects having large WCE values tended to be higher in UHT than that in THT; 2) subjects who were on antihypertensive medication might have been accustomed to the clinical environment, since such subjects frequently visit the outpatient clinics; 3) the timing of CBP measurement: CBP is usually measured during the daytime when the effects of antihypertensive drugs are strong. We also demonstrated that approximately half of the THT subjects
could be classified as hypertensive on the basis of our HBP and ABP criteria. In THT subjects, the prevalence of hypertension based on HBP or ABP was as high as that based on CBP. The finding that only a small proportion of THT subjects have well-controlled BP on the basis of CBP measurement was attributable not only to the WCE but also to inadequate control of BP despite antihypertensive medication. Among the subjects who did not take antihypertensive medication (UHT and NT subjects), the mean daytime BP value was higher than either the mean morning or the mean evening home BP. This was especially remarkable in younger subjects. These results suggest that home BP was not affected by mental or physical stressors in daily life. They may further indicate the differential characteristics of home BP and ambulatory BP measurements; i.e., ambulatory BP would reflect BP reactions throughout the day, while home BP would reflect BP in the absence of physical or mental stressors.

In the PAMELA study, an Italian population study, Mancia et al. (16) and Sega et al. (17) investigated the BP of middle-aged (< 65 years) and elderly (≥ 65 years) subjects in a general Italian population by using CBP, HBP and ABP. They demonstrated that HBP and 24-h ABP in THT subjects were as high as those in UHT subjects, and that these BP values in the THT subjects were higher than those in NT subjects. These results are consistent with ours. However, they also demonstrated that clinical BP values were similar between THT and UHT subjects. In our study, CBP in UHT subjects was significantly higher than that of THT subjects. These results suggest that the WCE in UHT subjects from the present Japanese population is higher than that in subjects from the general Italian population. We consider that this discrepancy might be attributable to the following: 1) the town of Ohasama is in a rural area, whereas the Italian population was selected from an urban area (Monza city); 2) in the PAMELA study, casual BP was measured by doctors using a conventional sphygmomanometer, while in our study casual BP was measured by nurses or technicians using automatic devices.

We demonstrated that approximately half of the THT subjects could be classified as hypertensive by both HBP and ABP measurements using JNC-VI criteria that were based on our prognostic criteria for HBP and ABP: 135 mmHg for systolic and/or 85 mmHg for diastolic. Matsubayashi et al. reported that 42% of the younger Japanese population (< 64 years) and 66% of the older Japanese population (≥ 65 years) could be classified as hypertensive by HBP measurement using the same criteria of 135 mmHg for systolic and/or 85 mmHg for diastolic. These data are similar to ours; i.e., 46% of younger subjects and 52% of elderly subjects could be classified as hypertensives by our HBP measurements. Furthermore, Mancia et al. reported that 64%
of the treated hypertensives in the PAMELA population were classified as hypertensives by ABP when they used their distribution criteria of 123 mmHg for systolic and/or 77 mmHg for diastolic (16). These data were also similar to ours; i.e., 64% of our THT subjects were classified as hypertensive or borderline hypertensive when we assessed ABP by their criteria (123 mmHg for systolic and 77 mmHg for diastolic). These results indicate that BP control in THT subjects is poor when assessed by ABP and HBP as well as by CBP in the general Italian and Japanese populations.

When we classified the NT subjects according to JNC-VI criteria for HBP and ABP, approximately 10% of the NT subjects as defined by CBP measurement were classified as hypertensive on the basis of ABP or HBP measurements. These subjects might be at a high risk for cardiovascular disease. If they are screened only by CBP, those who have hypertension on the basis of HBP and ABP, but not of CBP, would not be detected, would not be aware of their hypertension and would not be treated adequately, possibly leading to cardiovascular complications, target organ damage, a poor quality of life, and finally, unnecessary medical costs.

However, it is difficult to screen all subjects who have normal CBP value using ambulatory or HBP. Our previous report revealed that a number of factors—i.e., male sex, low casual pulse pressure, older age, a smoking habit, and use of antihypertensive medications—tended to result in a “reverse” white-coat effect (24). The mean systolic difference between CBP and HBP of the subjects who had all of the aforementioned factors was -9.5 mmHg; that is, the home systolic BP was 9.5 mmHg higher than the clinical systolic BP. We recommend that subjects who have several of these factors and are thus at high-risk for reverse WCE should measure their HBP or ABP even if they have a normal CBP value.

Similarly, approximately 60% of our UHT subjects as defined by CBP were classified as normotensive on the basis of HBP or ABP by JNC-VI criteria. If HBP or ABP had not been measured, these subjects would have received unnecessary medical treatment and may have experienced adverse effects from antihypertensive medication. In addition, unnecessary costs would be incurred by the health system.

Our study had some limitations. First, because HBP records were simply written down by the subjects, there may have been inaccuracies in the data, despite the fact that our nurses checked the accuracy of all subjects to measure their own BP. However, we previously demonstrated that HBP has better reproducibility and predictive value than CBP despite this source of misclassification (12). We therefore considered that the measurements reported by the patients were likely to be representative of the actual BP reading.

Second, we demonstrated that CBP measurement alone could cause many subjects to be misclassified as hypertensive or normotensive. We therefore recommended measuring HBP or ABP to diagnose hypertension. However, it has been reported that discrepancies between HBP- and ABP-based classifications of hypertension and indiscriminate use of self-BP and ABP monitoring in all hypertensives may result in confusion (25). This point needs to be taken into account.

Third, we used two consecutive measurements for CBP. To obtain a reasonable estimate of how WCE influences BP control, one should follow patients for a sufficiently long period of time using CBP. However, we consider that long-term, multiple CBP measurement is not feasible for screening of hypertension in the general population. Furthermore, we have already reported that the predictive power of the initial two measurements of HBP is better than that of the two consecutive measurements of CBP (12). Our data suggested that the superior predictive power of HBP over CBP may be related not only to the number of measurements but also to the lack of a WCE in HBP. Based on the present results, we therefore conclude that the use of dual CBP measurements from a single screening session may result in many subjects being misclassified as hypertensive or normotensive.

In summary, we demonstrated that 1) the poor BP control in subjects who are taking antihypertensive medication is attributable to the WCE as well as to inadequate control of BP by an antihypertensive regimen; and 2) many subjects are misclassified as hypertensive or normotensive on the basis of CBP readings.

References


