Original Article

Reproducibility of Masked Hypertension Determined from Morning and Evening Home Blood Pressure Measurements over a 6-Month Period

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Recently, the existence of so-called masked hypertension has attracted attention. In this study, the reproducibility of masked hypertension determined from morning and evening home blood pressure measurements was examined over a 6-month period. Home blood pressure measurements were taken consecutively for 7 days in volunteers at a company in 2002 and again in 2003. The 503 Japanese subjects (329 male, 174 female, mean age: 39.4 years), who were not taking antihypertensive drugs, were asked to measure their home blood pressure three times every morning and three times every evening. We defined casual blood pressure 140 (systolic) or 90 (diastolic) mmHg and home blood pressure 135 or 85 mmHg as hypertension. We also defined normotension as <140 and <90 mmHg in casual blood pressure and <135 and <85 mmHg in home blood pressure. We examined the reproducibility of four blood pressure categories (normotension, hypertension, white-coat hypertension, and masked hypertension) over a 6-month period. When measured in morning home blood pressure, the reproducibility of masked hypertension (59.1%) was significantly higher than that of white-coat hypertension (25.0%) and similar to that of hypertension (67.6%). However, the reproducibility of masked hypertension (23.5%) was similar to that of white-coat hypertension (32.0%) and significantly lower than that of hypertension (66.7%) when determined using evening home blood pressure. The concordances in the four blood pressure categories between the two periods were 0.582 (κ coefficient) and 0.463 when determined using morning and evening home blood pressure data, respectively. In conclusion, the reproducibility of masked hypertension over a 6-month period was moderate in an urban Japanese population when evaluated by morning home blood pressure. (*Hypertens Res* 2007; 30: 845–851)

Key Words: home blood pressure, masked hypertension, white-coat hypertension, reproducibility

Introduction

Recent studies have shown the importance of 24-h ambulatory blood pressure measurement or home blood pressure measurement, in addition to conventional casual blood pressure measurement in the clinic, for the diagnosis and management of hypertension (1–4). With the spread of these measurements, attention has focused on the existence of so-

called masked hypertension (5) or reverse white-coat hypertension (6, 7), in which casual blood pressure is normal but ambulatory or home blood pressure is elevated.

Concerning the influence of masked hypertension on target organ damage, many reports show a severity similar to that in true hypertension but greater than that in true normotension (8, 9). Moreover, the clinical importance of identifying patients with masked hypertension is growing, since home blood pressure measurement studies recently showed that the

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Received January 29, 2007; Accepted in revised form April 19, 2007.

prevalence of cardiovascular events in elderly patients treated with hypertensives who were considered to have masked hypertension was comparable to that in true hypertensive patients and obviously higher than that in true normotensive subjects (10). Recently, we reported data on the prevalence of masked hypertension determined by home blood pressure measurement (11). However, to our knowledge, the reproducibility of masked hypertension determined using home blood pressure has not been examined.

In this study, we evaluated the reproducibility of four blood pressure categories, including masked hypertension, in an urban Japanese population by measuring home blood pressure in the morning and evening under the same conditions over a period of 6 months.

Methods

Subjects

Home blood pressure was measured consecutively for 7 days in the fall of 2002 (1,036 volunteers; period 1) and the spring of 2003 (962 volunteers; period 2) among employees of a single company and their family members aged 20 years or older (20 to 84 years old), all of whom provided written informed consent. Of these, we selected 572 subjects, 384 male and 188 female, with a mean age of 41.2 years, for whom all data were obtained for both periods. In both periods, there was no use of antihypertensive drugs in 503 (329 male, 174 female; mean age 39.4 years) of the 572 subjects, and we used these 503 subjects without medication in this study. Shift workers were excluded from the subject group, as they were considered unfit as survey subjects. This study was approved by the Institutional Review Board of the Health Center of Keio University and by the participating company.

Blood Pressure Measurement

Home Blood Pressure Measurement

The first and second periods of home blood pressure measurement were October 16 to November 13, 2002, and April 1 to 23, 2003, respectively. The average temperature was similar in both periods (highest/lowest temperature 16.0/9.0°C in period 1; 17.6/9.4°C in period 2). A new semi-automatic device (HEM-759P, Omron Life Science Co. Ltd., Tokyo, Japan) based on the oscillometric principle was used by all subjects. To validate the device, simultaneous measurement using both arms was performed, where initially the auscultatory method was used on one side and the tested device on the other side (3). Then, each measurement was taken using the contralateral arm. In this study, the difference between the auscultatory method and the device was within 5 mmHg in 20 selected subjects. The subjects were requested to measure their blood pressure upon rising in the morning and before going to bed at night consecutively for 7 days including Saturday and Sunday. Measurement was performed within 1 h

Table 1. Background of Subjects

Number of subjects	503
Male/female	329/174
Age (years)	39.4±10.3
Height (cm)	167.0±8.3
Body weight (kg)	63.0±12.1
Body mass index (kg/m ²)	22.5±3.0
Period 1	
Casual blood pressure (mmHg)	118±14/73±11
Morning home blood pressure (mmHg)	116±14/73±10
Evening home blood pressure (mmHg)	115±13/69±10
Period 2	
Casual blood pressure (mmHg)	119±14/73±11
Morning home blood pressure (mmHg)	117±14/73±10
Evening home blood pressure (mmHg)	116±13/69±9
Drinking habit (%)	55.3
Smoking habit (%)	19.9
Hypertension without medication (%)	3.4

after rising in the morning, after urination and before breakfast. At night, it was performed at least 30 min after taking a bath. Blood pressure was measured three times in the morning and three times before going to bed, always while the subject was seated, and the data were printed by a printer attached to the semi-automatic sphygmomanometer. The print-outs were attached to the survey sheet. Measurement started on Tuesday, Wednesday, or Thursday, and we evaluated the mean of the second and third of each set of three values for 6 days (12 points in the morning and evening) and excluded all values measured on the first day.

Casual Blood Pressure Measurement

Casual blood pressure was measured by doctors with a mercury sphygmomanometer while the subjects were seated, after at least 2 min of rest. We repeated the measurement when the value of the first measurement was ≥ 140 mmHg (systolic) or ≥ 90 mmHg (diastolic). If more than two measurements were taken, the last blood pressure reading was used to define systolic blood pressure and diastolic blood pressure. The value measured within 1 month before or after the home blood pressure measurement period was adopted as casual blood pressure. The value measured at the time of a medical checkup was accepted as casual blood pressure.

Classification of Subjects

We divided the 503 subjects into four blood pressure categories, and evaluated the prevalence of each category in each period and the reproducibility of each category over a 6-month period: a normotension group, whose casual and home blood pressures were normal; a hypertension group, whose casual and home blood pressures were high; a white-coat hypertension group, whose casual blood pressure was high

Table 2. Prevalence of Four Blood Pressure Categories Determined from Casual Blood Pressure and Morning or Evening Home Blood Pressure in Period 1 and Period 2

	Period 1		Period 2	
	Morning	Evening	Morning	Evening
Normotension (%)	81.5	86.9	78.7	84.9
Hypertension (%)	7.4	4.8	8.4	5.4
White-coat hypertension (%)	2.4	5.0	2.6	5.6
Masked hypertension (%)	8.7	3.4	10.3	4.2

but whose home blood pressure was normal; and a masked hypertension group, whose casual blood pressure was normal but whose home blood pressure was high. Hypertension was defined as casual blood pressure ≥ 140 mmHg (systolic) or ≥ 90 mmHg (diastolic) and home blood pressure ≥ 135 mmHg (systolic) or ≥ 85 mmHg (diastolic) (12). Normotension was defined as casual blood pressure < 140 mmHg (systolic) and < 90 mmHg (diastolic) and home blood pressure < 135 mmHg (systolic) and < 85 mmHg (diastolic).

Data Analysis

Values are expressed as the mean $\pm$ SD. For casual and home blood pressures, the differences between the periods were determined by a two-tailed paired Student's *t*-test. Analysis of categorical data was carried out with the χ^2 test or, when appropriate, Fisher's exact test. Concordance of the four blood pressure categories in both periods was evaluated using the κ coefficient (13). The relationship between the periods for casual blood pressure and that for home blood pressure were analyzed by simple correlation. The significance of the simple correlation coefficients was assessed using Fisher's *Z* transformation. Values of $p < 0.05$ were considered to indicate statistical significance. All statistical analyses were performed using SPSS version 11.0J software (SPSS Inc., Chicago, USA).

Results

Background Factors

Table 1 shows the background characteristics of the 503 subjects. The subjects included more males than females, at a ratio of 2 to 1, with a mean age of 39.4 years. On average, no difference was observed between the two periods for either casual blood pressure measured in the outpatient clinic or home blood pressure. About half of the subjects had a drinking habit, and about 20% of subjects smoked. In addition, 3.4% of subjects had hypertension and were not taking anti-hypertensive medication.

Prevalence of Each Blood Pressure Category in Each Period

Table 2 shows the prevalence of normotension, hypertension, white-coat hypertension, and masked hypertension determined from casual blood pressure and home blood pressure measured in the morning and evening in each period. Using the morning home blood pressure, the prevalence of hypertension (7.4–8.4%) or masked hypertension (8.7–10.3%) was higher and that of normotension (78.7–81.5%) or white-coat hypertension (2.4–2.6%) was lower than that using the evening home blood pressure.

Relationship between Smoking Habit and Prevalence of Masked Hypertension

The prevalence of each blood pressure category determined from casual blood pressure and home blood pressure measured in the morning or evening was compared according to smoking status in each period. As shown in Table 3, masked hypertension, along with hypertension, was always more frequent in smokers.

Reproducibility of Each Blood Pressure Category

The reproducibility of each blood pressure category examined over a 6-month period is shown in Table 4 and Fig. 1. The reproducibility of masked hypertension using the morning home blood pressure (59.1%) was significantly better than that using the evening home blood pressure (23.5%) or that of white-coat hypertension using the morning home blood pressure (25.0%). Furthermore, this higher reproducibility of masked hypertension using the morning home blood pressure was similar to that of hypertension (67.6%). However, the reproducibility of masked hypertension (23.5%) was similar to that of white-coat hypertension (32.0%) and significantly lower than that of hypertension (66.7%) when determined using evening home blood pressure. The concordances of the four blood pressure categories in both periods were 0.582 (κ coefficient) and 0.463 when we used the morning and evening home blood pressures, respectively.

Table 3. Comparison of Prevalence of Four Blood Pressure Categories Determined by Casual Blood Pressure and Morning or Evening Home Blood Pressure According to Smoking Status in Both Periods

	Morning home blood pressure				Evening home blood pressure			
	Period 1		Period 2		Period 1		Period 2	
	Smoker (n=100)	Nonsmoker (n=403)	Smoker (n=99)	Nonsmoker (n=404)	Smoker (n=100)	Nonsmoker (n=403)	Smoker (n=99)	Nonsmoker (n=404)
Normotension (%)	75.0	83.1	71.7	80.4	80.0	88.6	76.8	87.1
Hypertension (%)	9.0	6.9	14.1	6.9	9.0	3.7	12.1	3.5
White-coat hypertension (%)	5.0	1.7	0	3.2	5.0	5.0	2.0	6.7
Masked hypertension (%)	11.0	8.2	14.1	9.4	6.0	2.7	9.1	2.7
<i>p</i> value	0.144		0.014		0.048		<0.001	

Table 4. Concordance of Four Blood Pressure Categories Determined from Casual Blood Pressure and Home Blood Pressure Measured in the Morning and Evening in Period 1 and Period 2

		Period 1				
		Normotension	Hypertension	White-coat hypertension	Masked hypertension	Total
A: Using morning home blood pressure	Period 2					
	Normotension	377	5	7	7	396
	Hypertension	6	25	1	10	42
	White-coat hypertension	7	2	3	1	13
	Masked hypertension	20	5	1	26	52
	Total	410	37	12	44	503
		κ coefficient=0.582				
B: Using evening home blood pressure	Period 2					
	Normotension	406	0	13	8	427
	Hypertension	5	16	3	3	27
	White-coat hypertension	14	4	8	2	28
	Masked hypertension	12	4	1	4	21
	Total	437	24	25	17	503
		κ coefficient=0.463				

Relationships between the Periods for Casual Blood Pressure and Home Blood Pressure

Compared to the strong correlation in home blood pressure between the periods ($r=0.914$ for morning systolic, $r=0.894$ for evening systolic, $r=0.898$ for morning diastolic, $r=0.867$ for evening diastolic), the correlation in casual blood pressure ($r=0.741$ for systolic, $r=0.724$ for diastolic) was apparently weak. In addition, the correlation in evening home blood pressure values, both systolic and diastolic, was slightly weaker than that in morning home blood pressure values.

Relationship between Drinking Habit and Reproducibility of Evening Home Blood Pressure

The reproducibility of evening home blood pressure was evaluated in 202 subjects who reported "no alcohol drinking" in both periods and 241 who reported "alcohol drinking" in both

periods. Compared to nondrinkers ($r=0.904$ for systolic, $r=0.877$ for diastolic), among drinkers evening home blood pressure, both systolic ($r=0.862$) and diastolic ($r=0.842$), were slightly less reproducible.

Discussion

This study provides a new observation that in an urban Japanese population, there was moderate concordance of the four blood pressure categories classified by casual blood pressure and home blood pressure measurement over a 6-month period. As evaluated by morning home blood pressure, the reproducibility of masked hypertension was higher than that of white-coat hypertension and similar to that of hypertension.

Recently, in addition to conventional casual blood pressure measurement, ambulatory blood pressure or home blood pressure measurement has been performed more often in general

Fig. 1. Reproducibility of normotension, hypertension, white-coat hypertension, and masked hypertension determined from casual and home blood pressure measured in the morning and evening in period 1 and period 2. □, using morning home blood pressure; ■, using evening home blood pressure. * $p < 0.05$, ** $p < 0.01$.

practice (1–4). Because the separation of normotension and hypertension can be assessed independently by either of the two methods, there is new complexity to the process of defining blood pressure status. Concerning white-coat hypertension, in which hypertension is shown by casual blood pressure but normotension is shown by ambulatory or home blood pressure, many reports have usually shown a relatively low severity of target organ damage and a low risk of cardiovascular morbidity (14, 15). Until recently, little attention has been given to the category showing masked hypertension—that is, normal blood pressure in casual blood pressure but high blood pressure in ambulatory or home blood pressure. If it is true that ambulatory blood pressure or home blood pressure gives a better classification of risk, it can be inferred that people with masked hypertension should be regarded as genuinely hypertensive. However, we have no data evaluating whether or not masked hypertension is reproducible on repeated testing.

In a study of 319 clinically normotensive volunteers, Selena *et al.* (9) found that 23% had masked hypertension, defined as daytime blood pressure $\geq 135/85$ mmHg. Belkic *et al.* (16) found that 36 of 267 men (13.5%) had masked hypertension, defined as daytime ambulatory diastolic blood pressure > 85 mmHg and clinic diastolic blood pressure < 85 mmHg. Two population-based studies have also described this phenomenon. In the Ohasama study, Imai *et al.* (17) reported that 10.2% of subjects with normal screening blood pressure had ambulatory blood pressure in the borderline hypertensive range (24-h average $> 133/78$ mmHg). The second was the PAMELA study (18), which found masked hypertension in 9% of subjects. Compared to these previous data obtained by ambulatory blood pressure measurement, the prevalence of masked hypertension in the present study,

determined from the morning home blood pressure (8.7–10.3%), was similar.

Originally, masked hypertension was defined as normal casual blood pressure but elevated ambulatory blood pressure. However, in this study, considering the present exclusion of health insurance coverage in Japan for ambulatory blood pressure measurement and the consequent burden on individuals, we used home rather than ambulatory blood pressure measurement to examine the reproducibility of masked hypertension in an urban Japanese population.

It is very conceivable that among the four blood pressure categories, the reproducibility of white-coat hypertension and masked hypertension, both of which are attributed to the difference between casual blood pressure measured in the outpatient clinic and home blood pressure, is lower than that of normotension and hypertension. In the results of our present study as well, such was the case with white-coat hypertension. Regarding masked hypertension, the reproducibility was as low as that of white-coat hypertension when evaluated by home blood pressure in the evening. However, it was similar to that of hypertension when evaluated by home blood pressure in the morning.

In this study, the prevalence of masked hypertension evaluated by morning home blood pressure was higher than that of white-coat hypertension, and its reproducibility was also better than that of white-coat hypertension. On the other hand, both the prevalence and reproducibility of white-coat hypertension were higher than those of masked hypertension when we evaluated them by the evening home blood pressure. Thus, although the results differed between morning and evening home blood pressure in our study, it was previously reported that home blood pressure values measured in the morning are more stable in the case of Japanese people (19). The reason for this is probably related to the Japanese lifestyle, and it is known that the nighttime bathing and drinking habits of many Japanese people would cause a decrease in evening home blood pressure (3, 20–23). Therefore, evening home blood pressure is lower than morning home blood pressure in many Japanese people (24, 25), and we can infer that the prevalence of white-coat hypertension evaluated by evening home blood pressure will be higher and the prevalence of masked hypertension lower than we expected. In addition, our evaluation of the relationship between alcohol drinking and the reproducibility of evening home blood pressure revealed that evening home blood pressure values were slightly less reproducible in drinkers than in nondrinkers.

Although it has been reported that target organ damage is more severe in masked hypertension than in true normotension (8, 18), the present study showed moderate reproducibility of masked hypertension determined by morning home blood pressure. Therefore, the discovery and treatment of masked hypertension will become a more serious issue in the future. In this study, a diagnosis of masked hypertension was based on morning and evening home blood pressure values. Masked hypertension is considered important because

patients with this condition are more likely to have morning hypertension, especially those with high morning home blood pressure, and because of the possibility of complications associated with hypertension in those patients. For early detection of this condition, it may be necessary to popularize the use of home blood pressure measurement in the future. In order to identify masked hypertension, we may need to measure ambulatory or home blood pressure even in normotensive subjects in the clinic. Under the present financial constraints on health care coverage in Japan, home blood pressure measurement would be a good step toward discovering masked hypertension efficiently, if it was carried out preponderantly in individuals with a strong family history of hypertension or in those who have many risk factors (7). The present study also showed that masked hypertension (determined by either morning or evening home blood pressure values) was more frequent in smokers, with whom an association of masked hypertension has been noted (7), than in nonsmokers. Therefore, smokers are considered to be candidates for proactive home blood pressure monitoring.

In interpreting the present results, several study limitations should be considered. First, we adopted only one value measured within 1 month before or after each period of home blood pressure measurement as casual blood pressure, since almost all subjects were healthy normotensive volunteers. Therefore, the white-coat effect may have been strong (26), and there is a possibility that more white-coat hypertension and hypertension existed in the present study. However, the correlation between the periods for casual blood pressure in this study was similar to that of a former report (27). Second, each home blood pressure measurement used in the present study was derived from a set of three readings. Since the first value was significantly higher than the second and third, the average of the latter two values was adopted as the home blood pressure value at each measurement point (24). Therefore, there is a possibility that our home blood pressure measurements were underestimated, since we discarded the higher first values. However, for home blood pressure measurement, the number of readings that should be taken on each occasion—and which reading should be used for analysis—remain controversial, and clear guidelines have not been provided. Therefore, the reproducibility of home blood pressure and masked hypertension determined by home blood pressure readings may vary depending on the analytical methods used to obtain home blood pressure readings. In a recent study, the prevalence of hypertension and that of normotension were determined by 7 days of home blood pressure monitoring using five measurements: the first value, the second value, an average of the first and second values, an average of the second and third values, and an average of all three values (28). As a result, when the average of measurements in the second to seventh days was used for evaluation, there was no significant difference among the five measurements. Therefore, as in this study, it is unlikely that any measurement used can greatly affect results as long as an average of 7 days of

measurements is used for evaluation.

In conclusion, the reproducibility of masked hypertension evaluated by morning home blood pressure was moderate and similar to the data obtained on hypertension in an urban Japanese population.

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