Original Article

The Importance of Home Blood Pressure Measurement for Preventing Stroke and Cardiovascular Disease in Hypertensive Patients: A Sub-Analysis of the Japan Hypertension Evaluation with Angiotensin II Antagonist Losartan Therapy (J-HEALTH) Study, a Prospective Nationwide Observational Study

Kazuyuki SHIMADA¹⁾, Toshiro FUJITA²⁾, Sadayoshi ITO³⁾, Hiroaki NARITOMI⁴⁾, Toshio OGIHARA⁵⁾, Kazuaki SHIMAMOTO⁶⁾, Heizo TANAKA⁷⁾, and Nobuo YOSHIKE⁸⁾

White-coat hypertension (HT) and masked HT can be identified by home blood pressure (BP) measurement. The prevalence of these subtypes and the associated risk of cardiovascular disease have not been fully investigated among Japanese hypertensive patients. The risk of cardiovascular events due to HT and its relationship with home BP measurement were examined among Japanese hypertensive patients receiving treatment in the Japan Hypertension Evaluation with Angiotensin II Antagonist Losartan Therapy (J-HEALTH) study, a nationwide prospective observational study. Both home and clinic BP were measured during treatment, and the occurrence of cardiovascular events was monitored in 4,596 Japanese patients (mean age of 60.8 years, 43.2% men, and mean follow-up period of 3.5 years). HT was defined as a systolic BP 140 mmHg for clinic BP and 135 mmHg for home BP while on treatment. The relative risk of all cardiovascular events and stroke increased along with higher clinic and home BP levels during treatment. The prevalence of white-coat HT, masked HT, well-controlled HT, and poorly controlled HT was 12.6%, 19.5%, 23.8%, and 44.1%, respectively. The relative risk of cardiovascular events was not significantly increased in the poorly controlled HT (relative risk [RR]: 2.05, 95% confidence interval [CI]: 0.77–5.45), white-coat HT (RR: 0.77, 95% CI: 0.15–3.96), and masked HT (RR: 2.00, 95% CI: 0.67–5.98) subgroups compared with the well-controlled-HT subgroup; however, the risk of masked HT was similar to that of poorly controlled HT. Monitoring both clinic and home BP is important to diagnose masked HT and to prevent cardiovascular disease in this subtype of HT. However, further investigation is required to fully characterize the cardiovascular risks associated with masked HT among Japanese patients receiving treatment. (*Hypertens Res* 2008; 31: 1903–1911)

Key Words: home blood pressure, cardiovascular disease, masked hypertension, losartan potassium, Japan Hypertension Evaluation with Angiotensin II Antagonist Losartan Therapy (J-HEALTH)

From the ¹⁾Jichi Medical University School of Medicine, Shimotsuke, Japan; ²⁾University of Tokyo, Graduate School of Medicine, Tokyo, Japan; ³⁾Tohoku University, Graduate School of Medicine, Sendai, Japan; ⁴⁾National Cardiovascular Center, Suita, Japan; ⁵⁾Osaka University, Graduate School of Medicine, Suita, Japan; ⁶⁾Sapporo Medical University School of Medicine, Sapporo, Japan; ⁷⁾Koshien University, Takarazuka, Japan; and ⁸⁾National Institute of Health and Nutrition, Tokyo, Japan.

This study was partly supported by a grant from Banyu Pharmaceutical Co., Ltd., Tokyo, Japan.

Address for Reprints: Kazuyuki Shimada, M.D., Jichi Medical University School of Medicine, 3311-1 Yakushiji, Shimotsuke 329-0498, Japan. E-mail: kazuyuki@jichi.ac.jp

Received April 10, 2007; Accepted in revised form August 6, 2008.

Introduction

The importance of blood pressure (BP) monitoring during antihypertensive therapy is widely accepted, and various studies have demonstrated that lowering BP reduces the risk of stroke and coronary events (1–3). In addition, multiple BP measurements in an individual have been shown to be superior to a few clinic BP measurements for estimating future cardiovascular morbidity and mortality (4–7). Numerous problems with clinic BP measurement have been identified, including the phenomenon of isolated clinic hypertension (HT), or so-called “white-coat hypertension” (8). Accordingly, ambulatory BP (ABP) monitoring and self-measurement at home are important tools for the optimal management of HT with respect to the assessment of cardiovascular risk (9). Another benefit of ABP and home BP measurement is the detection of isolated ambulatory/home HT, or “masked hypertension” (10). The potential impact of white-coat HT and masked HT on cardiovascular events is very important when considering therapeutic strategies for individual patients.

The Japan Hypertension Evaluation with Angiotensin II Antagonist Losartan Therapy (J-HEALTH) study was initiated in 2000 as a large-scale observational study of losartan therapy involving 30,000 patients. It has already demonstrated that losartan-based antihypertensive therapy is effective in controlling the BP in general practice in Japan (11).

Since a large-scale analysis of home BP data has not yet been conducted in Japan, direct evidence on the value of home BP measurement for predicting future cardiovascular events is still lacking (12). Although ABP data show better prognostic accuracy, the American Society of Hypertension (ASH) Ad Hoc Panel recommends the use of home BP information for screening. Self-measurement of BP at home has several advantages over ABP monitoring, such as the likelihood of obtaining a greater number of readings because of the ease of the procedure. In addition, self-measurement may increase compliance with antihypertensive therapy, and it is less expensive than ABP monitoring (13, 14). Self-measurement also enables patients to assess their own BP management (15, 16). In the J-HEALTH study, we obtained home BP data from 4,596 patients who agreed to perform self-measurement. We used their data to investigate the prevalence of white-coat HT and masked HT, as well as the relationship between clinic BP and home BP during treatment and cardiovascular events in the J-HEALTH cohort.

Methods

Patients

The eligible patients in this study were hypertensive men or women aged 20 years or older who had not taken any antihypertensive agents within the previous 1 month. Patients

who had previously been treated with losartan were excluded. Patients who had suffered a stroke or myocardial infarction (MI) within the previous month and patients who had severe hepatic disease, other severe diseases (malignancy or serious renal impairment), or serious viral infection were excluded. Pregnant or lactating women were also excluded. Any other patients who were judged by the investigators to be unsuitable for this study were also excluded. Each patient was informed of the purpose and methods of the study, as well as the measures employed for the protection of their privacy, before they were enrolled. Patients gave verbal informed consent and then underwent a complete review of their medical history, physical findings, and laboratory data. A total of 26,512 patients were used for analysis of the relationship between BP and cardiovascular events in the J-HEALTH study (17), and the 4,596 patients from that cohort who performed home BP monitoring during the study period were utilized for the present analysis. The design and methods of the J-HEALTH study, as well as the characteristics of the subjects, have been described in detail previously (17, 18).

Treatment

Patients were initially treated with the dosage of losartan approved in Japan, which is a single daily dose of 25–50 mg, usually in the morning. The dose was increased to a maximum of 100 mg once daily, if necessary. The addition of other antihypertensive agents was allowed beginning at 3 months after the start of losartan therapy, if required. A target BP value was not set in this study, and no restrictions were placed on the treatment of complications.

The clinic BP was measured every 3 months, and standard laboratory tests were performed every 6 months.

Clinic and Home Blood Pressure Measurements

Given that this study was conducted during daily medical practice, the clinic BP was measured according to the usual methods of each institution; no recommendations or training were provided with respect to measurement of the clinic BP. Clinic BP was measured a maximum of three times prior to starting losartan therapy, and all available data were used for the calculation of the mean baseline clinic BP. After the start of losartan therapy, the clinic BP was measured every 3 months, and a representative value was recorded at the discretion of the attending physician.

The home BP was measured by patients who agreed to monitor themselves. Participating subjects generally used an electronic automated sphygmomanometer based on the cuff-oscillometric principle (HEM-740A; Omron Healthcare Co., Ltd., Kyoto, Japan) but were allowed to use other devices already being used if the patient insisted. Patients were asked to measure their BP while at rest in the sitting position once every morning just after waking and urinating. The home BP was measured once at each scheduled time of measurement. If

Table 1. Characteristics of Patients with/without Home Blood Pressure Monitoring

	Home BP monitored (<i>n</i> =4,596)	No home BP monitored (<i>n</i> =21,916)
Baseline		
Male (%)	43.2	44.0
Age (years)*	60.8±11.7	62.5±12.1
BMI (kg/m ²)*	24.2±3.5	24.0±3.5
Clinic SBP (mmHg)*	167.1±16.6	165.6±17.2
Clinic DBP (mmHg)*	95.9±11.1	94.5±11.6
Home SBP (mmHg)*	160.3±18.0	N/A
Home DBP (mmHg)*	93.2±12.0	N/A
During treatment		
Clinic SBP (mmHg)*	140.9±10.2	141.8±11.9
Clinic DBP (mmHg)*	81.7±7.7	82.1±8.5
Home SBP (mmHg)*	139.3±11.5	N/A
Home DBP (mmHg)*	81.9±8.7	N/A
Clinic BP controlled <140/90 mmHg (%)	48.4	45.3
Follow-up (years)*	3.5±1.3	2.9±1.5

*Mean±SD. BP, blood pressure; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; N/A, not applicable.

the patient measured the BP twice or more, the first value was reported. All home BP data obtained prior to starting losartan therapy were used for the calculation of the mean baseline home BP value. Morning home BP values were measured each month, usually on the day of a hospital visit and reported to attending physician by the patient.

Clinic and home BP data thus obtained during treatment were used for the analysis of the relationship between BP and cardiovascular events. For sub-analyses that assessed the risk of masked HT or white-coat HT, both clinic and home BP data upon receiving 6 months of treatment was used.

Evaluation of Endpoints

The endpoints of this study were cardiovascular events, including fatal or non-fatal stroke (new or recurrent cerebral hemorrhage, cerebral infarction, transient ischemic attack(s), or subarachnoid hemorrhage detected on the basis of typical symptoms and computed tomography/magnetic resonance imaging findings), fatal or non-fatal MI (new or recurrent and detected on the basis of typical symptoms, and elevation of cardiac enzymes), and sudden cardiac death (defined as a death within 1 h of the onset of chest pain, including shortness of breath/syncope and death not considered to have any causes apart from coronary artery disease, occurring within 24 h after the onset of acute symptoms). Death within 4 weeks after an MI was defined as death due to MI. The independent event assessment and classification committee reviewed each endpoint event on the basis of the information documented in the case report form by the study investigators.

Statistical Analysis

Variables were compared by the *t*-test and the χ^2 test. Results were expressed as the mean±SD, and differences were considered statistically significant at *p*<0.05.

Statistical analysis of the overall results was based on survival analysis. Subgroups were classified by their BP values during treatment. Relationships between the endpoints and the BP, as well as prognostic factors, were assessed with the Cox proportional hazards model, with adjustment for sex; age; a past history of diabetes mellitus, cerebrovascular disease, or cardiovascular disease; and smoking and alcohol consumption. Statistical analysis was conducted with the SAS software package (version 8.02; SAS Institute Inc., Cary, USA).

Results

Patient Characteristics

Of the 26,512 patients of the J-HEALTH cohort, a total of 4,596 patients performed home BP monitoring during the study period. Their characteristics are listed in Table 1. The mean follow-up period was 3.5±1.3 years and 2.9±1.5 years for the patients who did and did not perform home BP monitoring, respectively. The mean age of the subjects with and without home BP monitoring was 60.8±11.7 and 62.5±12.1 years, respectively, and the mean clinic BP of each group was 167.1/95.9 and 165.6/94.5 mmHg, respectively.

Clinic BP showed a significantly greater decrease in the home BP monitoring group than in the group without home BP monitoring. The mean home BP was significantly reduced from 160.3/93.2 mmHg at baseline to 139.3/81.9 mmHg dur-

Table 2. Incidence of Stroke and Myocardial Infarction

Events	Home BP (<i>n</i> =4,596)		No home BP (<i>n</i> =21,916)	
	No. of events	Incidence	No. of events	Incidence
Stroke	46	2.88	261	4.16
Cerebral infarction	27		178	
Transient ischemic attack	2		17	
Cerebral hemorrhage	13		42	
Subarachnoid hemorrhage	3		17	
Unclassified stroke	1		7	
MI	14	0.87	66	1.05
Total	60	3.75	327	5.21

Incidence rate: per 1,000 patient-years. BP, blood pressure; MI, myocardial infarction including sudden cardiac death.

Table 3. Relationship between SBP on Treatment and Stroke and MI in Patients Monitored Both Clinic and Home BP

SBP (mmHg)	<i>n</i>	Stroke and MI				Stroke				MI			
		Events	Incidence*	Relative risk [‡] (95% CI)	<i>p</i>	Events	Incidence*	Relative risk [‡] (95% CI)	<i>p</i>	Events	Incidence*	Relative risk [‡] (95% CI)	<i>p</i>
Clinic													
<130	521	3	1.62	1	†	2	1.08	1	†	1	0.54	1	†
130–139	1,791	17	2.61	1.7 (0.50–5.83)	0.397	13	2.00	1.9 (0.43–8.48)	0.396	4	0.61	1.3 (0.14–11.88)	0.816
140–149	1,516	16	3.00	1.9 (0.56–6.62)	0.300	11	2.06	1.9 (0.42–8.65)	0.399	5	0.94	2.1 (0.24–18.77)	0.495
150–159	585	16	8.80	5.5 (1.58–18.81)	0.007	13	7.15	6.5 (1.46–28.92)	0.014	3	1.65	3.2 (0.33–32.06)	0.316
≥160	183	8	17.56	10.3 (2.73–39.23)	<0.001	7	15.36	13.4 (2.77–64.75)	0.001	1	2.19	4.2 (0.26–69.33)	0.312
Home													
<130	885	4	1.29	1	†	2	0.65	1	†	2	0.65	1	†
130–139	1,658	19	3.18	2.3 (0.76–6.62)	0.142	13	2.18	3.2 (0.72–14.17)	0.127	6	1.00	1.3 (0.26–6.48)	0.761
140–149	1,377	20	4.14	2.8 (0.96–8.34)	0.059	17	3.52	5.1 (1.17–22.11)	0.031	3	0.62	0.8 (0.12–4.65)	0.761
150–159	483	9	5.81	3.6 (1.11–11.88)	0.033	8	5.16	7.1 (1.49–33.56)	0.014	1	0.65	0.6 (0.05–6.77)	0.679
≥160	193	8	15.03	8.8 (2.63–29.69)	<0.001	6	11.28	14.7 (2.92–73.48)	0.001	2	3.76	3.2 (0.44–24.14)	0.251

SBP, systolic blood pressure; MI, myocardial infarction including sudden cardiac death. †Reference category; CI, confidence interval. *per 1,000 patient-years. ‡Adjusted for sex; age; a past history of diabetes mellitus, cerebrovascular disease, or cardiovascular disease; and smoking and alcohol consumption.

ing the treatment period.

Incidence of Cardiovascular Events

Cardiovascular events were reported in 60 and 327 patients from the home BP monitoring group and the non-home BP monitoring group, respectively, and the crude incidence of cardiovascular events during the study was 3.75 and 5.21 per 1,000 patient-years, respectively (Table 2). The incidence in each group was not significantly different after adjustment for

sex; age; past history of diabetes mellitus, cerebrovascular disease, or cardiovascular disease; and smoking and alcohol consumption, using the Cox proportional hazards model.

Clinic/Home Blood Pressure and Events

The relationship between the clinic/home BP during treatment and the relative risk of cardiovascular events (stroke and MI combined) in patients who monitored both BPs is shown in Table 3. The relative risk of all cardiovascular events and

Fig. 1. Distribution of well-controlled HT, white-coat HT, masked HT and poorly controlled HT, categorized by clinic SBP and home SBP at baseline and 6 months of treatment. HT, hypertension; SBP, systolic blood pressure.

Table 4. Patients' Characteristics in Patients with Well-Controlled Hypertension, White-Coat Hypertension, Masked Hypertension, and Poorly Controlled Hypertension

	Well-controlled HT [†] (n=689)	White-coat HT [†] (n=364)	Masked HT [†] (n=566)	Poorly controlled HT [†] (n=1,277)	Total (n=2,896)
Baseline					
Male (%)	38.0	35.4	45.9	44.6	42.2
Age (years)*	58.9±11.9	59.8±11.0	61.3±11.4	62.0±11.8	60.8±11.7
Clinic SBP (mmHg)*	160.9±14.8	168.5±15.9	165.6±15.1	170.2±16.9	166.9±16.4
Clinic DBP (mmHg)*	95.0±10.3	95.4±11.1	95.7±10.5	96.1±11.6	95.7±11.0
Home SBP (mmHg)*	153.8±17.5	155.9±18.7	160.8±16.4	164.5±17.0	160.1±17.8
Home DBP (mmHg)*	92.4±11.8	90.7±12.2	93.9±11.9	93.9±11.8	93.1±11.9
During treatment					
Clinic SBP (mmHg)*	133.2±7.1	142.7±8.3	136.8±6.4	145.5±9.0	140.5±9.6
Clinic DBP (mmHg)*	79.3±6.9	82.1±7.4	80.2±6.6	82.9±7.6	81.4±7.4
CBP controlled <140/90 mmHg (%)	81.4	39.6	71.2	25.5	49.5
Home SBP (mmHg)*	129.8±7.0	130.8±6.8	141.1±7.7	144.8±9.3	138.7±10.6
Home DBP (mmHg)*	78.6±7.3	78.0±7.4	82.7±7.6	83.3±8.2	81.4±8.1
HBP controlled <135/85 mmHg (%)	66.8	65.4	14.5	8.1	30.5
Follow-up (years)*	3.6±1.2	3.5±1.3	3.6±1.2	3.6±1.3	3.6±1.2

*Mean±SD. [†]Classified with clinic and home SBPs at 6 months. HT, hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure; CBP, clinic blood pressure; HBP, home blood pressure.

that of stroke increased along with increases in both clinic and home BP. The relative risk of all cardiovascular events was significantly higher for a BP ≥ 150 mmHg, compared with that for a BP < 130 mmHg, for both clinical and home BP measurements. In addition, the relative risk of stroke was significantly higher for a clinic BP ≥ 150 mmHg or a home BP ≥ 140 mmHg, compared with that for a BP < 130 mmHg. However, a clear relationship between the risk of MI and BP

was not detected, probably because the event occurred in only a small number of patients.

Prevalence of White-Coat Hypertension and Masked Hypertension

Clinical guidelines recommend that the clinic BP be maintained at $< 140/90$ mmHg and the home BP at $< 135/85$

Fig. 2. Relative risk of well-controlled HT, white-coat HT, masked HT and poorly controlled HT for cardiovascular events. Incidence is per 1,000 patient-years. HT, hypertension; CI, confidence interval. Adjusted for sex; age; a past history of diabetes mellitus, cerebrovascular disease, and cardiovascular disease; and smoking, and alcohol consumption. [#]Categorized with clinic and home systolic blood pressures after 6 months of treatment. [†]Reference category.

mmHg (18, 19). Table 1 shows that the difference between the baseline values for clinic and home BP was 6.8/2.7 mmHg, suggesting that a home BP <135/85 mmHg is a reasonable target. Therefore, we categorized our patients into the following four groups, based on the clinic and home systolic BP values: well-controlled HT (clinic BP <140 mmHg and home BP <135 mmHg), masked HT (clinic BP <140 mmHg and home BP ≥135 mmHg), white-coat HT (clinic BP ≥140 mmHg and home BP <135 mmHg), and poorly controlled HT (clinic BP ≥140 mmHg and home BP ≥135 mmHg). The distribution of these categories varied during the study period (data not shown), so we assessed the BP at 6 months after the initiation of treatment because the control BP stabilized by 6 months in our previous study (11). A total of 2,896 patients with BP measurements available at 6 months were included in the analysis of these four subgroups. Figure 1 depicts the distribution of these categories at baseline (left) and after 6 months of treatment (right). At baseline, 5.9% of our hypertensive patients had white-coat HT. After 6 months, 12.6% of the patients had white-coat HT and 19.5% had masked HT. Table 4 details the characteristics of each subgroup at baseline and during treatment. Patients with poorly controlled HT

or masked HT were older, and a higher percentage were men. The baseline BP values were significantly higher in the subgroup with poorly controlled HT than in patients with well-controlled HT.

Risk of Cardiovascular Events in Patients with White-Coat Hypertension and Masked Hypertension

White-coat HT and masked HT were defined on the basis of BP values measured after 6 months for the 2,896 patients with BP data available at the time. Patients who developed cardiovascular events during the first 3 months were excluded from this sub-analysis, as these patients did not have available BP data at the 6-month mark.

The relative risk (95% confidence interval [CI]) of cardiovascular events in the white-coat HT, masked HT, and poorly controlled HT subgroups compared with that for the well-controlled HT subgroup was 0.77 (0.15–3.96), 2.00 (0.67–5.98), and 2.05 (0.77–5.45), respectively (Fig. 2). Possibly because the number of events was low, we did not detect a significant increase in the relative risk of cardiovascular

events in any of the three hypertensive subgroups compared with the reference subgroup (well-controlled HT). The incidence of cardiovascular events among the well-controlled HT, white-coat HT, masked HT, and poorly controlled HT subgroups was 2.04, 1.56, 4.41, and 4.55 per 1,000 patient-years, respectively. Although the relative risk did not differ significantly among the four subgroups, a higher incidence was noted in the masked HT and poorly controlled HT subgroups.

Discussion

This study demonstrates the importance of measuring home BP among hypertensive Japanese patients receiving treatment.

Assessment of the clinical profile of the home BP group ($n=4,596$) revealed a significantly higher baseline BP than that of the other patients, although they were significantly younger (Table 1). This suggests that younger patients with more severe HT may be more interested in monitoring their own health. In fact, the follow-up period was longer and the rate of achievement of the target BP ($<140/90$ mmHg) was higher in the home BP group as compared with the other patients. Since measuring the home BP was not mandatory in the J-HEALTH study, it was performed according to physician or patient preference. This may have led to the bias of home BP measurement being performed by physicians who managed HT more actively or by patients who were younger or who wished to receive the best treatment. Interestingly, the overall incidence of cardiovascular events was lower in the home BP measurement group than in the group without home BP measurement (3.75 and 5.21 per 1,000 patient-years, respectively), but there was no significant difference in the risk of cardiovascular events between the two groups. Although these results indicate that home BP measurement may not decrease the incidence of cardiovascular events, it is important to consider the potential biases in the analysis of its influence. As shown in Table 1, there was a greater reduction of BP during treatment in the home BP group, suggesting that home BP measurement may be a useful tool for improving patient motivation and compliance.

Next, we analyzed the relationship between clinic/home BP during treatment and cardiovascular events. As shown in Table 3, an increase in the home BP resulted in a higher incidence of cardiovascular events among the Japanese hypertensive patients who were being managed in daily clinical practice; the same consequence was observed for increases in the clinic BP. A similar relationship between clinic or home BP and stroke was observed, but the starting BP level associated with a significantly higher risk was lower in home BP than in clinic BP. In the Ohasama study, self-measured home BP was a better predictor of total mortality than clinic BP, and there was a strong correlation between home systolic BP and mortality (20), but in the present study we could not demonstrate that home BP was a better predictor than clinic BP.

White-coat HT and masked HT are important problems in the management of HT, whether ABP monitoring or home BP measurement is performed. The Self-Measurement of Blood Pressure at Home in the Elderly; Assessment and Follow-up (SHEAF) investigators proposed a home BP of 135/85 mmHg as the threshold for normotension (21), so a home BP of 135/85 mmHg should probably be considered to be the upper limit of normal (18, 19, 22). Therefore, we defined a home systolic BP <135 mmHg as normal in this study. Our data indicated that the prevalence of white-coat HT and masked HT after initiation of antihypertensive therapy was 12.6% and 19.5%, respectively. The prevalence of white-coat HT has been reported to range from 15% to $>50\%$ (7, 8, 23, 24), and it varies widely depending on the study population. With regard to masked HT, the prevalence was 9.4% among treated hypertensives in the SHEAF study (25) and 9.9% among the general population in the Pressioni Alteriose Monitorate e Loro Associazioni (PAMELA) study (26). The prevalence of masked HT was 19.5% in the J-HEALTH cohort, which was considerably higher than that in the other studies. Figure 1 displays changes in the prevalence of white-coat HT and masked HT between baseline measurements and measurements after 6 months of treatment. These findings suggest that differences in the prevalence of masked HT may depend on the time at which patients are categorized after the start of treatment.

Table 4 summarizes the characteristics of the well-controlled HT, white-coat HT, masked HT, and poorly controlled HT subgroups of the J-HEALTH cohort. The masked HT subgroup was older and had a higher percentage of men; these findings were similar to those of other studies (21, 25, 26). The BP was significantly different between white-coat HT or masked HT and well-controlled HT, suggesting that a higher baseline BP is a risk factor for a high prevalence of white-coat HT or masked HT during treatment.

In the majority of trials using home BP measurement or ABP monitoring, white-coat HT has been compared with poorly controlled HT, and a worse prognosis has usually been found for the latter group (24, 25, 27–32). On the other hand, a recent study suggested that masked HT is associated with the same risk of cardiovascular events as poorly controlled HT (25). Ohkubo *et al.* used ABP monitoring to demonstrate that the risk of cardiovascular events was significantly higher for Japanese subjects with masked HT or poorly controlled HT than for Japanese subjects with a normal BP (33). We found that the overall cardiovascular risk associated with masked HT was similar to that for poorly controlled HT, as reported by other authors, but we did not detect a significant difference compared with the well-controlled HT subgroup.

Because the presence of masked HT seemed to indicate poor BP control, the use of home BP measurement to identify masked HT may contribute to improving the management of HT. The dispersion of clinic and home systolic BP values after 6 months of treatment was wide in the present study population (Fig. 1), with hundreds of patients exceeding the

target BP at home while being below the target clinic BP, or *vice versa*. We found that both masked HT and poorly controlled HT were risk factors for cardiovascular events. In these two subgroups, home BP exceeded the target level irrespective of the clinic BP, suggesting that the measurement of home BP may be important to identify patients with a higher cardiovascular risk. Although the clinic BP should remain the standard when assessing the efficacy of treatment for HT, the usefulness of home BP monitoring has also been supported by the results of the Treatment of Hypertension Based on Home or Office Blood Pressure (THOP) trial (13).

The present study was not a randomized controlled trial but a prospective observational study supported by general practitioners in daily clinical practice. Although a large-scale observational study could provide valuable information about current management in general practice that is not available from conventional controlled trials, it has some limitations. First, this was not an intervention trial, and a target BP was not set in the study protocol, so the intensity of antihypertensive treatment probably varied among the participating patients. Second, home BP measurement was not mandatory and was performed only on the basis of physician or patient preference. This may have led to bias if home BP measurement was promoted by physicians who managed HT more actively or was adopted more often by patients who were younger or who desired the best treatment.

In conclusion, the prevalence of white-coat HT and masked HT was 12.6% and 19.5%, respectively, for hypertensive Japanese patients receiving treatment in the general practice setting. Cardiovascular risk was found to increase as the home or clinic BP became higher. Patients with masked HT can be detected by home BP measurement, and given that this group had a higher relative risk of cardiovascular disease than patients with well-controlled HT, the measurement of the home BP may be important for the management of such patients. However, there were no significant differences among our subgroups, so further investigation is required to fully characterize the cardiovascular risk associated with masked HT in hypertensive Japanese patients under treatment.

Acknowledgements

We are grateful to the Monitoring, Event Assessment and Safety Assessment Committee members for evaluating the data. Gratitude is also expressed to the Sumisho Computer Systems Corporation for analyzing the data.

Appendix

J-HEALTH Study Committees

Monitoring Committee: Takenori Yamaguchi (Chair), Tanenao Eto, Toshiharu Furukawa, Katsumi Yoshida.

Event Assessment Committee: Hiroaki Naritomi (Chair), Yoichiro Hashimoto, Uichi Ikeda, Mitsuaki Isobe, Toshio

Kushiro, Ken Nagata, Kazuyuki Shimada, Takemori Yamawaki. *Safety Assessment Committee:* Kendo Kiyosawa (Chair), Hiroshi Hirose, Sadayoshi Ito, Akinori Kasahara, Hiroshi Kawabe, Genjiro Kimura, Hirofumi Makino, Mitsuhiro Moriyama, Ikuo Saito, Hiromichi Suzuki, Eiji Tanaka.

Medical Expert Advisory and Publication Committee: Hiroaki Naritomi (Chair), Toshiro Fujita, Sadayoshi Ito, Toshio Ogihara, Kazuyuki Shimada, Kazuaki Shimamoto, Heizo Tanaka, Nobuo Yoshiike.

The Administrative Office: The Post-Marketing Surveillance Department of Banyu Pharmaceutical Co., Ltd. (Tokyo, Japan).

References

1. Amery A, Birkenhager W, Brixko P, *et al*: Mortality and morbidity results from the European Working Party on High Blood Pressure in the Elderly trial. *Lancet* 1985; **1**: 1349–1354.
2. Bulpitt CJ, Palmer AJ, Fletcher AE, *et al*: Optimal blood pressure control in treated hypertensive patients. Report from the Department of Health Hypertension Care Computing Project (DHCCP). *Circulation* 1994; **90**: 225–233.
3. Dahlöf B, Lindholm LH, Hansson L, Schersten B, Ekblom T, Wester PO: Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension). *Lancet* 1991; **338**: 1281–1285.
4. Clement DL, De Buyzere ML, De Bacquer DA, *et al*: Prognostic value of ambulatory blood-pressure recordings in patients with treated hypertension. *N Engl J Med* 2003; **348**: 2407–2415.
5. Dolan E, Stanton A, Thijs L, *et al*: Superiority of ambulatory over clinic blood pressure measurement in predicting mortality: the Dublin outcome study. *Hypertension* 2005; **46**: 156–161.
6. Staessen JA, Thijs L, Fagard R, *et al*: Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension. *JAMA* 1999; **282**: 539–546.
7. Verdecchia P, Porcellati C, Schillaci G, *et al*: Ambulatory blood pressure. An independent predictor of prognosis in essential hypertension. *Hypertension* 1994; **24**: 793–801.
8. Pickering TG, James GD, Boddie C, Harshfield GA, Blank S, Laragh JH: How common is white coat hypertension? *JAMA* 1988; **259**: 225–228.
9. Celis H, Den Hond E, Staessen JA: Self-measurement of blood pressure at home in the management of hypertension. *Clin Med Res* 2005; **3**: 19–26.
10. Pickering TG, Davidson K, Gerin W, Schwartz JE: Masked hypertension. *Hypertension* 2002; **40**: 795–796.
11. Naritomi H, Fujita T, Ito S, *et al*: Efficacy and safety of long-term losartan therapy demonstrated by a cohort study in Japanese patients with hypertension: the Japan Hypertension Evaluation with Angiotensin II Antagonist Losartan Therapy (J-HEALTH) Study. *Hypertens Res* 2008; **31**: 295–304.
12. Thijs L, Staessen JA, Celis H, *et al*: Reference values for self-recorded blood pressure: a meta-analysis of summary data. *Arch Intern Med* 1998; **158**: 481–488.
13. Staessen JA, Den Hond E, Celis H, *et al*: Antihypertensive treatment based on blood pressure measurement at home or

- in the physician's office: a randomized controlled trial. *JAMA* 2004; **291**: 955–964.
14. Staessen JA, Wang J, Bianchi G, Birkenhager WH: Essential hypertension. *Lancet* 2003; **361**: 1629–1641.
 15. Den Hond E, Celis H, Fagard R, et al: Self-measured versus ambulatory blood pressure in the diagnosis of hypertension. *J Hypertens* 2003; **21**: 717–722.
 16. Guidelines Committee: 2003 European Society of Hypertension–European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens* 2003; **21**: 1011–1053.
 17. Shimamoto K, Fujita T, Ito S, et al: Impact of blood pressure control on cardiovascular events in 26,512 Japanese hypertensive patients: the Japan Hypertension Evaluation with Angiotensin II Antagonist Losartan Therapy (J-HEALTH) Study, a prospective nationwide observational study. *Hypertens Res* 2008; **31**: 469–478.
 18. Naritomi H, Fujita T, Ito S, et al: Design and baseline characteristics of a cohort study in Japanese patients with hypertension: Japan Hypertension Evaluation with Angiotensin II Antagonist Losartan Therapy (J-HEALTH). *Hypertens Res* 2007; **30**: 807–814.
 19. O'Brien E, Asmar R, Beilin L, et al: European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens* 2003; **21**: 821–848.
 20. Tsuji I, Imai Y, Nagai K, et al: Proposal of reference values for home blood pressure measurement: prognostic criteria based on a prospective observation of the general population in Ohasama, Japan. *Am J Hypertens* 1997; **10**: 409–418.
 21. Bobrie G, Genes N, Vaur L, et al: Is “isolated home” hypertension as opposed to “isolated office” hypertension a sign of greater cardiovascular risk? *Arch Intern Med* 2001; **161**: 2205–2211.
 22. Chobanian AV, Bakris GL, Black HR, et al: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003; **289**: 2560–2572.
 23. Khatrar RS, Senior R, Lahiri A: Cardiovascular outcome in white-coat versus sustained mild hypertension: a 10-year follow-up study. *Circulation* 1998; **98**: 1892–1897.
 24. Martinez MA, Garcia-Puig J, Martin JC, et al: Frequency and determinants of white coat hypertension in mild to moderate hypertension: a primary care-based study. *Am J Hypertens* 1999; **12**: 251–259.
 25. Bobrie G, Chatellier G, Genes N, et al: Cardiovascular prognosis of “masked hypertension” detected by blood pressure self-measurement in elderly treated hypertensive patients. *JAMA* 2004; **291**: 1342–1349.
 26. Mancia G, Facchetti R, Bombelli M, Grassi G, Sega R: Long-term risk of mortality associated with selective and combined elevation in office, home, and ambulatory blood pressure. *Hypertension* 2006; **47**: 846–853.
 27. Cavallini MC, Roman MJ, Pickering TG, Schwartz JE, Pini R, Devereux RB: Is white coat hypertension associated with arterial disease or left ventricular hypertrophy? *Hypertension* 1995; **26**: 413–419.
 28. Glen SK, Elliott HL, Curzio JL, Lees KR, Reid JL: White-coat hypertension as a cause of cardiovascular dysfunction. *Lancet* 1996; **348**: 654–657.
 29. Karter Y, Curgunlu A, Altinisik S, et al: Target organ damage and changes in arterial compliance in white coat hypertension. Is white coat innocent? *Blood Press* 2003; **12**: 307–313.
 30. Palatini P, Mormino P, Santonastaso M, et al: Target-organ damage in stage I hypertensive subjects with white coat and sustained hypertension: results from the HARVEST study. *Hypertension* 1998; **31**: 57–63.
 31. Pierdomenico SD, Lapenna D, Guglielmi MD, et al: Target organ status and serum lipids in patients with white coat hypertension. *Hypertension* 1995; **26**: 801–807.
 32. Segre CA, Ueno RK, Warde KR, et al: White-coat hypertension and normotension in the league of hypertension of the hospital das clinicas, FMUSP: prevalence, clinical and demographic characteristics. *Arq Bras Cardiol* 2003; **80**: 117–126.
 33. Ohkubo T, Kikuya M, Metoki H, et al: Prognosis of “masked” hypertension and “white-coat” hypertension detected by 24-h ambulatory blood pressure monitoring: 10-year follow-up from the Ohasama study. *J Am Coll Cardiol* 2005; **46**: 508–515.