# **Original** Article

# Difference between Home and Office Blood Pressures among Treated Hypertensive Patients from the Japan Home *versus* Office Blood Pressure Measurement Evaluation (J-HOME) Study

Tsuyoshi HORIKAWA<sup>1</sup>), Taku OBARA<sup>1),2</sup>), Takayoshi OHKUBO<sup>2),3</sup>), Kei ASAYAMA<sup>2</sup>), Hirohito METOKI<sup>4</sup>), Ryusuke INOUE<sup>2</sup>), Masahiro KIKUYA<sup>1</sup>), Junichiro HASHIMOTO<sup>2),3</sup>), Kazuhito TOTSUNE<sup>1),2</sup>), and Yutaka IMAI<sup>1),2</sup>), the J-HOME Study Group\*

This study sought to clarify the factors associated with the magnitude of the difference between home and office blood pressures in treated hypertensive patients. Study subjects consisted of 3,308 essential hypertensive patients (mean age, 66 years; males, 44%) receiving antihypertensive treatment in primary care settings in Japan. Patients were classified into 3 groups (the home effect group, small difference group, and office effect group) according to tertiles of the magnitude of the office-home systolic blood pressure difference. Compared to the other two groups, the home effect group patients were significantly and independently older, were more often habitual drinkers, had a greater family history of cerebrovascular disease or personal history of ischemic heart disease, and were prescribed a greater number of antihypertensive drugs, non-amlodipine calcium channel blockers, and  $\alpha$ -blockers as antihypertensive drugs. Compared to the other two groups, the office effect group patients were significantly and independently younger, included more females, less frequently had a family history of cerebrovascular disease or personal history of ischemic heart disease, and were less often prescribed  $\alpha$ -blockers as antihypertensive drugs. The characteristics of home effect group patients and the factors negatively affecting the blood pressure difference were the same. Among treated hypertensive patients, compared to patients in the other groups, office effect group patients had a lower-risk profile, whereas home effect group patients had a higher-risk profile. These predictive factors might be useful clinically to help identify patients who may have a large difference between home and office blood pressures. (Hypertens Res 2008; 31: 1115-1123)

Key Words: white-coat effect, home blood pressure, office blood pressure, antihypertensive treatment

From the <sup>1</sup>Department of Clinical Pharmacology and Therapeutics and <sup>3</sup>Department of Planning for Drug Development and Clinical Evaluation, Tohoku University Graduate School of Pharmaceutical Sciences, Sendai, Japan; <sup>2</sup>Tohoku University 21st Century COE Program "Comprehensive Research and Education Center for Planning of Drug Development and Clinical Evaluation," Sendai, Japan; and <sup>4</sup>Department of Medical Genetics, Tohoku University Graduate School of Medicine, Sendai, Japan.

<sup>\*</sup>See Appendix.

This work was supported by Grants-in-Aid for Scientific Research (15790293, 1654041, and 1854042) from the Ministry of Education, Culture, Sports, Science and Technology, by Health Science Research Grants on Health Services (13072101, H12-Medical Care-002) from the Ministry of Health, Labour and Welfare, by Junkanki-Byou-Itaku-Kenkyuhi (H19-Kou-8) from the National Cardiovascular Center, and by Nouvelle Place Inc., Japan.

Address for Reprints: Takayoshi Ohkubo, M.D., Ph.D., Department of Planning for Drug Development and Clinical Evaluation, Tohoku University Graduate School of Pharmaceutical Sciences, Tohoku University Hospital, 1–1 Seiryo-cho, Aoba-ku, Sendai 980–8574, Japan. E-mail: tohkubo@mail.tains.tohoku.ac.jp

Received July 23, 2007; Accepted in revised form January 28, 2008.

### Introduction

It has been reported that the magnitude of the difference between the office blood pressure (BP) and the home BP (the so-called "white-coat effect"(1)) in untreated hypertensive patients is greater than in treated hypertensive patients (2). This finding suggests that the difference between the office BP and the home BP might be affected by antihypertensive medication. Although a gender difference in the prevalence of a negative difference between the office BP and the home BP (the so-called "reverse white-coat effect" (3)) has not been observed, such a negative difference has been negatively correlated with age and office BP levels (4). Therefore, it may be difficult for physicians to identify patients with a negative BP difference. The identification of patients with a positive BP difference and those with a negative BP difference may have important implications for the management of hypertensive patients. Although the factors mediating white-coat hypertension and so-called "masked hypertension" (defined as a normal office BP and hypertensive home or ambulatory BP levels (5) have already been studied extensively (6, 7), little information is available about the factors that affect the difference between the office BP and the home BP among treated hypertensive patients. The objective of the present study was to clarify the factors that affect the difference between the office systolic BP (SBP) and the home SBP (the office-home SBP difference). This study was based on data from the Japan Home versus Office BP Measurement Evaluation (J-HOME) study, conducted to measure BP control as evaluated by home BP and office BP measurements among essential hypertensive patients receiving antihypertensive treatment in primary care settings in Japan (8, 9).

#### Methods

### Patients

The details of patient selection have been previously described (8, 9). Briefly, 7,354 physicians randomly selected from all over Japan were invited to take part in this project. Of the 1,477 who agreed to participate, 751 collected data for the study. By the end of August 2003, 3,586 patients who gave their informed consent to participate in the study were enrolled. Each participating physician was asked to enroll 5 patients. Most physicians (79.3%) enrolled 5 or fewer patients. Sixty-six patients were excluded because they were not taking antihypertensive medications. An additional 120 were excluded due to insufficient data about BP values or patient characteristics. Furthermore, subjects whose office BP was measured by an aneroid sphygmomanometer were excluded, since aneroid devices are not recommended unless they are calibrated every 6 months (10), and calibration of aneroid devices every 6 months could not be assured. Thus, the study population consisted of 3,308 essential hypertensive



**Fig. 1.** The relationship A: between office SBP and the magnitude of the office-home SBP difference and B: between the home SBP and the magnitude of the office-home SBP difference. SBP, systolic blood pressure.

outpatients treated with antihypertensive medications. The Institutional Review Board of Tohoku University School of Medicine approved the study protocol.

# **Home BP Measurements**

Patients were asked to measure their BP once every morning in the sitting position, within 1 h of waking, after more than 2 min of rest, but before drug ingestion and breakfast, as specified by the Japanese guidelines for home BP measurement (11). They were asked to record the results over a 2-week period. The patients used electronic arm-cuff devices that operate on the basis of the cuff-oscillometric method. All such devices available in Japan have been validated and approved by the Ministry of Health, Labour and Welfare, Japan (12).

The manufacturers of these devices were Omron Healthcare Co., Ltd. (Kyoto, Japan), A&D Co., Ltd. (Tokyo, Japan), Terumo Co., Ltd. (Tokyo, Japan), and Matsushita Electric Works, Ltd. (Osaka, Japan). The actual model of each device was not provided by the physicians involved in the study. All devices for the self-measurement of BP used in the present study were certified as having been adjusted to the Association for the Advancement of Medical Instrumentation (AAMI) standard (12, 13). The mean of all measurements over the 2-week period was calculated for each patient and

	Total	Home effect group	Small difference	Office effect group
	(n=3,308)	(n=1,099)	group ( <i>n</i> =2,210)	( <i>n</i> =1,099)
Age, years	$66.2 \pm 10.5$	67.7±10.3**	$65.9 \pm 10.4$	65.0±10.8**
BMI, kg/m <sup>2</sup>	$23.8 \pm 3.3$	$23.8 \pm 3.1$	$23.9 \pm 3.3$	$23.7 \pm 3.5$
Men, %	44.4	49.2**	46.3	37.6**
Home SBP, mmHg	$139.5 \pm 13.8$	148.5±13.4**	$138.1 \pm 11.0$	132.1±11.7**
Home DBP, mmHg	81.6±9.6	85.3±9.7**	$81.4 \pm 8.7$	78.1±8.9**
Home HR, beats/min	$67.2 \pm 9.1$	$67.3 \pm 9.4$	$67.5 \pm 9.0$	$66.9 \pm 9.0$
Office SBP, mmHg	$142.7 \pm 14.5$	134.9±11.6**	$140.6 \pm 11.2$	152.6±14.4**
Office DBP, mmHg	80.7±9.4	77.5±8.7**	$80.4 \pm 8.7$	84.0±9.8**
Office-home SBP difference, mmHg	$3.2 \pm 16.1$	$-13.5 \pm 9.2 **$	$5.6 \pm 3.4$	20.5±10.1**
Office-home DBP difference, mmHg	$-0.9 \pm 9.6$	$-1.8\pm8.2^{**}$	$-1.0\pm6.9$	5.9±8.3**
Office BP mesurement				
By a nurse, %	18.7	18.9	16.9	20.3
By an electronic device, %	22.3	19.8*	22.1	25.2*
Habitual smoker, %	14.1	14.6	15.6	12.2*
Habitual drinker, %	34.5	38.7**	35.5	29.4**
Family history of HT, %	56.3	56.3	56.5	56.1
Family history of CVD, %	27.8	31.2**	28.3	23.8**
Stroke, %	9.2	11.0*	7.5	9.0
History of IHD, %	8.3	11.5**	7.4	6.0**
Diabetes mellitus, %	13.7	14.0	12.3	14.7
Hypercholesterolemia, %	40.4	39.7	40.8	40.7
High uric acid, %	11.6	13.7*	12.1	8.8**
Antihypertensive medication				
CCBs (all), %	69.6	73.0*	68.7	67.2*
DHP (amlodipine), %	37.8	35.8	39.9	37.8
DHP (non-amlodipine), %	29.4	34.2**	26.5	27.7
ARBs, %	43.7	44.5	43.0	43.5
ACEIs, %	16.8	16.6	16.2	17.5
α-Blockers, %	13.4	17.6**	12.6	10.0**
β-Blockers, %	11.8	11.7	11.8	11.8
Diuretics, %	9.2	8.9	9.4	9.3
Number of drugs, <i>n</i>	$1.72 \pm 0.9$	1.82±0.90**	$1.68 \pm 0.84$	1.66±0.80**
Duration of treatment, months	29.5±42.9	31.8±45.2*	$28.3 \pm 40.4$	$28.4 \pm 42.8$

Table 1.	Comparison	of the Patients	According to	the Magnitude	e of Office-	-Home SBP Difference
	000000000000000000000000000000000000000	or the rate	TRACT GALLE TO	the handline and		

Data are mean±SD or percentage of patients. \*p < 0.05 vs. the other two groups. \*\*p < 0.02 vs. the other two groups. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; HT, hypertension; CVD, cerebrovascular disease; IHD, ischemic heart disease; CCBs, calcium channel blockers; DHP, dihydropyridine; ARBs, angiotensin II receptor blockers; ACEIs, angiotensin-converting enzyme inhibitors. Due to multiple analyses performed, the level of significance has been adjusted according to Bonferoni; p < 0.002 is considered significance.

used for the analysis. The patients' treatment regimen was kept constant during the 2 weeks of home BP measurements.

#### **Office BP Measurements**

Office BP was measured twice consecutively in the sitting position after a rest of at least 2 min at each regularly scheduled visit by a physician (81.0%) or a nurse (19.0%). The physicians and nurses used either the auscultatory method with a mercury device (77.7%) or the cuff-oscillometric method with an electronic arm-cuff device (22.3%) that had

been validated and approved by the Ministry of Health, Labour and Welfare, Japan. All automatic devices used in the present study were certified as having been adjusted to the AAMI standard (13). The office BP value for each patient that was used for the analysis was defined as the average of 4 measurements taken at 2 office visits during the time period that home measurements were being done.

#### **Data Collection and Statistical Analysis**

Patients' information was collected using a questionnaire

Variables	Odds ratio	95% CI	p value
a: Home effect			
Age (10 years)	1.23	1.14-1.32	< 0.0001
Sex (men=1)	1.17	0.98-1.40	0.09
Habitual drinking	1.26	1.05-1.52	0.02
Family history of CVD	1.28	1.09-1.50	0.003
History of IHD	1.58	1.23-2.04	0.0004
Non-amlodipine*	1.35	1.15-1.58	0.0002
α-Blockers*	1.56	1.27-1.91	< 0.0001
Number of antihypertensive drugs $\geq 2^*$	1.27	1.10-1.47	0.002
b: Office effect			
Age (10 years)	0.86	0.80-0.93	< 0.0001
Sex (men=1)	0.76	0.63-0.91	0.003
Habitual drinking	0.83	0.68-1.00	0.051
Family history of CVD	0.74	0.63-0.88	0.0005
History of IHD	0.70	0.52-0.94	0.02
High uric acid	0.79	0.62-1.02	0.07
α-Blockers**	0.68	0.54-0.85	0.001

Table 2. Multiple Logistic Regression Analysis for Home Effect or Office Effect

CI, confidence interval; CVD, cerebrovascular disease; IHD, ischemic heart disease. \*Adjusted for age, habitual drinking, a family history of CVD, and a history of CVD. \*\*Adjusted for age, sex, a family history of CVD, and a history of IHD.

administered by the attending physicians. Therefore, the identification of complications was based on the attending physicians' judgment. Dihydropyridine calcium channel blockers (CCBs) were classified into two groups: "non-amlodipine" and "amlodipine." Amlodipine was used most frequently in the J-HOME study; it is the most long-acting of the antihypertensive drugs. Therefore, we discriminated between amlodipine and dihydropyridine CCBs other than amlodipine. Thus the term "non-amlodipine" in the present study indicates any dihydropyridine CCB other than amlodipine.

The office-home SBP difference was calculated for each individual. Patients were classified into 3 groups according to whether the office-home SBP difference was in the lowest tertile (group 1; office-home SBP difference  $\leq -3.1$  mmHg), the intermediate tertile (group 2; -3.1 < office-home SBP difference < 8.9 mmHg), or the highest tertile (group 3; office-home SBP difference  $\geq 8.9$  mmHg) based on the French Self-Measurement of Blood Pressure at Home in the Elderly: Assessment and Follow-up (SHEAF) study (14). Group 1 (home effect group) included patients whose home BP was higher than their office BP. Group 2 included patients who had a small office-home SBP difference. In these patients, office BP and home BP were relatively close. This group was referred to as the small difference group. Group 3 (office effect group) included patients whose office BP was higher than their home BP.

Based on the patients' characteristics and their use of antihypertensive medications, univariate analysis was performed to determine which factors influenced the home effect, the office effect, and the magnitude of the office-home SBP difference. In this analysis, the home and office SBP values were not included as factors, since these terms were not fully independent of the BP difference (Fig. 1). The Bonferroni correction was applied for multiple comparisons. Multiple logistic regression analysis was performed to obtain the best-fit model showing the most important independent variables that significantly related to the difference between home effect patients and the others, or between office effect patients and the others. Multivariate regression analysis was performed to obtain the best-fit model to identify the most important independent variables that were significantly related to the office-home SBP difference on univariate analysis. Variables were compared using Pearson's regression analysis, Student's *t*-test, and the  $\chi^2$ -test as appropriate.

Data are shown as mean $\pm$ SD. A *p* value less than 0.05 was accepted as indicative of statistical significance. All statistical analyses were conducted using the SAS package (Version 9.1; SAS Institute Inc., Cary, USA).

#### Results

#### Patients

The mean age of patients was 66.2 years, and 44.4% were male. Overall, the mean home SBP/diastolic BP (DBP) was  $139.5\pm13.8/81.6\pm9.6$  mmHg, the mean office SBP/DBP was  $142.7\pm14.5/80.7\pm9.4$  mmHg, and the mean office-home SBP/DBP difference was  $3.2\pm16.1/-0.9\pm9.6$  mmHg. Whether office BP was measured by a physician or a nurse did not significantly affect the office-home SBP difference. Furthermore, whether the office BP was measured using the auscultatory method with a mercury device or the cuff-oscil-

lometric method with an electronic arm-cuff device also did not significantly affect the office-home SBP difference (Table 1).

# Patient Characteristics by the Magnitude of the Office–Home SBP Difference

Compared to the other two groups, home effect group patients were significantly and independently older, were more often habitual drinkers, more often had a family history of cerebrovascular disease (CVD) and a history of ischemic heart disease (IHD), and were prescribed a greater number of antihypertensive drugs, non-amlodipine CCBs, and  $\alpha$ -blockers as antihypertensive drugs (Table 2). Compared to the other two groups, office effect group patients were significantly and independently younger, included more females, less frequently had a family history of CVD and a history of IHD, and were less often prescribed  $\alpha$ -blockers as antihypertensive drugs (Table 2).

## Factors Affecting the Difference between Office and Home SBP: Multivariate Regression Analysis

The multivariate analysis included the variables that were significantly associated with the office-home SBP difference on the univariate analysis (Tables 3-5). It was found that older age, habitual drinking, a family history of CVD, and a history of IHD were negatively associated with the magnitude of the office-home SBP difference (Table 5). Morning home SBP was also significantly higher in patients with habitual drinking, a family history of CVD, and history of IHD than in those without, respectively (with habitual drinking vs. without,  $140.7 \pm 13.7$  vs.  $138.9 \pm 13.8$  mmHg; with a family history of CVD vs. without, 140.9±14.4 vs. 139.0±13.6 mmHg; with history of IHD vs. without, 142.7±15.6 vs. 139.3±13.6 mmHg; all p < 0.001). The use of amlodipine was positively associated with the magnitude of the office-home SBP difference. The use of non-amlodipine CCBs and  $\alpha$ -blockers was negatively associated with the magnitude of the office-home SBP difference (Table 5). The results did not change when subjects whose office BP was measured by a nurse were excluded from the analysis.

#### Discussion

# Characteristics of Home Effect Patients and the Factors That Negatively Affected the Office-Home SBP Difference

In the present study, the characteristics of home effect patients and the factors that negatively affected the BP difference were the same. On multivariate regression analysis, habitual drinking, a family history of CVD, and a history of IHD were negatively related to the magnitude of the officehome SBP difference. Treatment with a greater number of  
 Table 3. Correlation between the Office-Home SBP Difference and Continuous Variables

			-
	Pearson's		
	correlation	p value	
	coefficients		
Age	-0.114	< 0.0001	
BMI	-0.017	0.33	
Home HR	0.002	0.93	
Number of antihypertensive	-0.091	< 0.0001	
drugs			
Duration of antihypertensive	-0.039	0.03	
treatment			

SBP, systolic blood pressure; BMI, body mass index; HR, heart rate.

antihypertensive drugs, non-amlodipine CCBs, and  $\alpha$ -blockers was negatively related to the magnitude of the officehome SBP difference. This suggests that these factors were independent predictive factors that increase the magnitude of the home effect.

In previous studies, Ishikawa *et al.* reported that alcohol intake was related to morning hypertension (15) and Kawano *et al.* reported that restriction of alcohol intake lowered morning BP (16). In the present study, habitual drinking was also negatively related to the BP difference. Thus it is likely that such effects of alcohol intake on morning home BP could contribute to the negative relation between habitual drinking and the magnitude of the office–home SBP difference.

A family history of CVD and a history of IHD were also associated with the magnitude of the office-home SBP difference. This finding was related to the fact that patients with a family history of CVD and a history of IHD had an elevated morning BP in the present study. This trend was also supported by the results of the categorical analysis of patients based on the magnitude of their office-home SBP difference.

A previous study reported that the insufficient duration of action of non-amlodipine CCBs induced morning hypertension in treated hypertensive patients (17); in the present study, the prescription of non-amlodipine CCBs was negatively related to the magnitude of the office-home SBP difference.

Pickering *et al.* reported that  $\alpha$ -blockers taken in the evening would have their greatest effect in the morning when the sympathetic nervous system was extensively activated (18). Thus one might expect that  $\alpha$ -blockers taken in the evening would effectively suppress morning BP elevation. Indeed, of patients given  $\alpha$ -blockers, 39.1% took their  $\alpha$ -blockers after dinner and 27.3% took their  $\alpha$ -blockers before going to bed in the present study. Therefore, in the present study, it is likely that  $\alpha$ -blockers would be frequently prescribed to patients with a large home effect to adequately control their high morning home BP levels.

Home effect group patients had a higher-risk profile (habitual drinking, a family history of CVD, and a history of IHD)

	1	Mean value	p value			Mean value	p value
Age	<65 years	5.1	-0.0001	Office BP mesurement			
	≥65 years	2.0	< 0.0001	By a nurse	(-)	3.1	0.20
Sex	Men	1.7	<0.0001		(+)	3.8	0.39
	Women	4.4	< 0.0001	By an electronic device	(-)	2.9	0.00
BMI	$<\!25 \text{ kg/m}^2$	3.7	0.004		(+)	4.4	0.06
	$\geq$ 25 kg/m <sup>2</sup>	2.0	0.004	Antihypertensive medication	n		
Habitual smoking	(-)	3.4	0.04	CCBs (all)	(-)	4.5	0.002
	(+)	1.8	0.04		(+)	2.6	0.002
Habitual drinking	(-)	4.1	< 0.0001	DHP (amlodipine)	(-)	2.7	0.02
	(+)	1.4	< 0.0001		(+)	4.0	0.02
Family history of HT	(-)	3.5	0.28	DHP (non-amlodipine)	(-)	4.1	< 0.0001
	(+)	2.9	0.28		(+)	0.9	< 0.0001
Family history of CVD	(-)	4.0	< 0.0001	ARBs	(-)	3.4	0.25
	(+)	1.1	< 0.0001		(+)	2.9	0.35
History of stroke	(-)	3.3	0.06	ACEIs	(-)	3.1	0.72
	(+)	1.5	0.00		(+)	3.4	0.75
History of IHD	(-)	3.7	< 0.0001	α-Blockers	(-)	3.9	< 0.0001
	(+)	-2.4	< 0.0001		(+)	-1.3	< 0.0001
Diabetes mellitus	(-)	3.1	0.72	β-Blockers	(-)	3.1	0.76
	(+)	3.5	0.72		(+)	3.4	0.70
Hypercholesterolemia	(-)	3.0	0.25	Diuretics	(-)	3.2	0.80
	(+)	3.5	0.35		(+)	3.3	0.89
High uric acid	(-)	3.5	0.0003	Number of drugs	<2 drugs	4.3	< 0.0001
	(+)	0.3	0.0003		$\geq 2 \text{ drugs}$	2.1	<0.0001
				Duration of treatment	<6 months	3.8	0.10
					$\geq 6$ months	s 2.8	0.10

Table 4. Comparison of the Mean Value of the Office-Home SBP Difference (mmHg) by Each Category

Mean value, mean of the office-home SBP difference; SBP, systolic blood pressure; BMI, body mass index; HT, hypertension; CVD, cerebrovascular disease; IHD, ischemic heart disease; CCBs, calcium channel blockers; DHP, dihydropyridine; ARBs, angiotensin II receptor blockers; ACEIs, angiotensin-converting enzyme inhibitors.

#### Table 5. Multivariate Regression Analysis of Office-Home SBP Difference

	Coefficient	SEM	p value
Age ≥65 years	-2.87	0.58	< 0.0001
Sex (men=1)	-1.23	0.69	0.07
BMI $\geq 25 \text{ kg/m}^2$	-1.80	0.59	0.002
Habitual smoking	-0.14	0.87	0.87
Habitual drinking	-1.94	0.72	0.008
Family history of CVD	-2.64	0.62	< 0.0001
History of IHD	-5.01	1.01	< 0.0001
High uric acid	-1.59	0.89	0.07
Amlodipine*	1.38	0.57	0.02
Non-amlodipine*	-2.86	0.61	< 0.0001
α-Blockers*	-4.49	0.81	< 0.0001
Number of antihypertensive drugs $\geq 2^*$	-1.43	0.56	0.01

SBP, systolic blood pressure; BMI, body mass index; CVD, cerebrovascular disease; IHD, ischemic heart disease. \*Adjusted for age, BMI, habitual drinking, a family history of CVD, and a history of IHD.

than the other patients. In the SHEAF study, Bobrie et al. studied 3 groups of patients that were almost equivalent to the 3 groups employed in the present study (14). They found that treated elderly hypertensive patients in the home effect group most often had a history of cardiovascular disease (14). Recently, it has been reported that the reverse white-coat effect, based on office BP and daytime ambulatory BP readings, is a significant predictor for microalbuminuria and an independent risk factor for left ventricular hypertrophy in patients with treated essential hypertension (19, 20). Moreover, in the Ohasama study, the white-coat effect based on the office BP and the home BP readings was not significantly related to cardiovascular mortality, while the reverse whitecoat effect was a strong predictive factor of cardiovascular risk (21). Thus, it is necessary to identify patients with the reverse white-coat effect and to follow them up more carefully than patients in the small difference group or those in the office effect group.

# Characteristics of Office Effect Patients and the Factors That Positively Affected the Magnitude of the Office–Home SBP Difference

In the present study, increasing age decreased the difference between office and home BP. This is consistent with our previous study of the Japanese general population (22) and a study of hypertensive patients (23) that investigated the office-home BP difference. The office effect group included more females than the other two groups. It has already been reported that the magnitude of the BP difference was lower in men than in women (6, 22, 24). Our results are consistent with those of previous studies. However, the reason for this gender difference is unclear. It may be related to the difference in reactivity to the stress of a clinic visit.

The present results show that, among the 3 groups, patients with an office effect had the lowest-risk profile. In some studies (25-27), but not in all (28), no association was found between the magnitude of the white-coat effect and widely used measures of target-organ damage, such as left ventricular mass. However, in other studies, it has been reported that intimal-medial thicknesses and carotid cross-sectional areas were similar in patients with a white-coat effect and sustained hypertension but were significantly higher than in normotensive subjects (29). The plasma C-reactive protein and B-type natriuretic peptide levels did not differ between patients with white coat hypertension and those with sustained hypertension (30). Patients with a white coat effect have been shown to have increased BP reactivity to activity (31). Therefore, a greater BP load during normal daily activities may contribute to target organ damage due to the increased BP reactivity found among patients with the white coat effect (31).

In the Ohasama study, the odds ratio for the progression of white-coat hypertension to home hypertension was significantly higher than that of sustained normotension (normal home BP and normal office BP) (*32*). Moreover, Verdecchia

*et al.* reported that after 6 years of follow-up, the incidence of stroke tended to increase in the white-coat hypertension group, and the corresponding hazard curve crossed that of the ambulatory hypertension group by the 9th year of follow-up (*33*). It is possible that the white-coat effect and white-coat hypertension represent similar phenomena, since they both deal with BP readings that are higher in the medical setting than outside the medical setting. Therefore, patients with a large white-coat effect might require careful long-term follow-up using home BP measurements.

#### **Study Limitations**

There are some limitations to this study. In the present study, office BP was measured twice during each session, while home BP was measured once per session. Home BP was based on an average of about 14 measurements, while office BP was based on an average of 4 measurements. These differences in the methodology of collecting BP values at home and in the office might have affected the results. However, these methods were based on the Japanese Society of Hypertension (JSH) guidelines for self-monitoring of BP at home and JSH 2004. Therefore, these methods could be considered to be the current standard for evaluating office BP and home BP in Japan; thus, the findings are applicable to primary care settings in Japan. In the present study, office BP was assessed by a physician (81.0%) or by a nurse (19.0%). It has been reported that the magnitude of the difference between office BP and out-of office BP was different when office BP was measured by a physician or a nurse (34). However, in the present study, the magnitude of the difference between office and home BPs was not significantly different between measurements taken by physicians and those taken by nurses. Factors affecting the difference between home and office BP were comparable after exclusion of subjects whose office BP was measured by a nurse. Therefore, in the present study, these methodological differences did not substantially affect the results. Since most physicians in the present study were general practitioners, and the patients were supposed to have been receiving primary care by the physicians for a certain period of time, it is possible that most patients were familiar with their physicians. In the present study, the proportion of subjects whose office BP was measured using the auscultatory method with a mercury sphygmomanometer and the cuff-oscillometric method with an electronic arm-cuff device was 77.7% and 22.3%, respectively. However, the magnitude of the difference between office and home BP was not significantly different between the 2 methods. Therefore, in the present study, the methodological differences would not be large enough to substantially affect the overall results. Finally, in the present study, we could not ensure whether the doctors who measured patients' office BP using an oscillometric device had used the same oscillometric device employed by their patients at home or not. Furthermore, since we did not provide oscillometric devices to the study patients, the

patients used their own oscillometric devices that used different algorithms to compute SBP and DBP. The use of such different devices might have introduced an important technical bias in the comparison between home and office BP. However, all devices for BP measurements available in Japan have been validated and approved by the Ministry of Health, Labour and Welfare, Japan (12). Further consideration of this issue is beyond the scope of the J-HOME study, which was a survey done to evaluate, on the basis of home BP measurements, the actual BP control that was achieved with antihypertensive treatment in the primary care setting in Japan. Moreover, since such cases were often identified in primary care settings, our findings reflect the current situation in primary care settings and could be applied to primary care settings in Japan.

## Conclusion

Among treated hypertensive patients, patients with an office effect had a low-risk profile, whereas patients with a home effect had a high-risk profile. Knowing the factors associated with these phenomena might be useful for helping physicians identify patients who may have large differences between home BP and office BP.

# Appendix

The study was designed, conducted, and interpreted by the investigators, independent of the sponsors. This study was conducted by the J-HOME Study Group.

#### Members of the J-HOME Study Group

Principal Investigator: Yutaka Imai.

Advisory Committee: Masatoshi Fujishima (deceased), Takao Saruta.

*Steering Committee*: Toshio Ogihara, Kazuaki Shimamoto, Toshiro Fujita, Kazuyuki Shimada, Toshio Ikeda, Iwao Kuwajima, Satoru Kuriyama, Kazuomi Kario.

*Coordinating and Data Management Center*: Takayoshi Ohkubo, Taku Obara, Tsuyoshi Horikawa, Tetsuo Kato, Koji Tanaka, Taku Shibamiya, Azusa Hara, Takuya Oikawa, Rie Komai, Kayo Murai, Masahiro Kikuya, Kei Asayama, Hirohito Metoki, Kazuhito Totsune, and Junichiro Hashimoto.

All names of participating practitioners have been previously published (9).

#### References

- 1. Mancia G, Bertinieri G, Grassi G, *et al*: Effects of bloodpressure measurement by the doctor on patient's blood pressure and heart rate. *Lancet* 1983; **24**: 695–698.
- Stergiou GS, Efstathiou SP, Argyraki CK, Roussias LG, Mountokalakis TD: White coat effect in treated *versus* untreated hypertensive individuals: a case-control study using ambulatory and home blood pressure monitoring. *Am J Hypertens* 2004; 17: 124–128.

- Wing LM, Brown MA, Beilin LJ, Ryan P, Reid CM: 'Reverse white-coat hypertension' in older hypertensives. J *Hypertens* 2002; 20: 639–644.
- Bombelli M, Sega R, Facchetti R, *et al*: Prevalence and clinical significance of a greater ambulatory *versus* office blood pressure ('reversed white coat' condition) in a general population. *J Hypertens* 2005; 23: 513–520.
- Pickering TG, Davidson K, Gerin W, Schwartz JE: Masked hypertension. *Hypertension* 2002; 106: e196–e197.
- 6. MacDonald MB, Laing GP, Wilson MP, Wilson TW: Prevalence and predictors of white-coat response in patients with treated hypertension. *CMAJ* 1999; **161**: 265–269.
- Niiranen TJ, Jula AM, Kantola IM, Reunanen A: Prevalence and determinants of isolated clinic hypertension in the Finnish population: the Finn-HOME study. *J Hypertens* 2006; 24: 463–470.
- Obara T, Ohkubo T, Funahashi J, *et al*: Isolated uncontrolled hypertension at home and in the office among treated hypertensive patients from the J-HOME study. *J Hypertens* 2005; 23: 1653–1660.
- Ohkubo T, Obara T, Funahashi J, *et al*: Control of blood pressure as measured at home and office, and comparison with physicians' assessment of control among treated hypertensive patients in Japan: first report of the J-HOME study. *Hypertens Res* 2004; 27: 755–763.
- 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.
- Imai Y, Otsuka K, Kawano Y, *et al*: Japanese Society of Hypertension (JSH) guidelines for self-monitoring of blood pressure at home. *Hypertens Res* 2003; 26: 771–782.
- Shirasaki O, Terada H, Niwano K, *et al*: The Japan Home-Health Apparatus Industrial Association: investigation of home-use electronic sphygmomanometers. *Blood Press Monit* 2001; 6: 303–307.
- Association for the Advancement of Medical Instrumentation: American National Standard for Electronic or Automated Sphygmomanometers. Washington DC, AAMI Analysis and Review, 1987.
- 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.
- 15. Ishikawa J, Kario K, Eguchi K, et al: Regular alcohol drinking is a determinant of masked morning hypertension detected by home blood pressure monitoring in medicated hypertensive patients with well-controlled clinic blood pressure: the Jichi Morning Hypertension Research (J-MORE) study. Hypertens Res 2006; 29: 679–686.
- Kawano Y, Abe H, Takishita S, Omae T: Effects of alcohol restriction on 24-hour ambulatory blood pressure in Japanese men with hypertension. *Am J Med* 1998; 105: 307– 311.
- Chonan K, Hashimoto J, Ohkubo T, *et al*: Insufficient duration of action of antihypertensive medications mediates high blood pressure in the morning in hypertensive population: the Ohasama study. *Clin Exp Hypertens* 2002; 24: 261–275.
- 18. Pickering TG, Levenstein M, Walmsley P: Nighttime dos-

ing of doxazosin has peak effect on morning ambulatory blood pressure. Results of the HALT Study. Hypertension and Lipid Trial Study Group. *Am J Hypertens* 1994; **7**: 844–847.

- 19. Tomiyama M, Horio T, Kamide K, *et al*: Reverse whitecoat effect as an independent risk for left ventricular concentric hypertrophy in patients with treated essential hypertension. *J Hum Hypertens* 2007; **21**: 212–219.
- Kato T, Horio T, Tomiyama M, Kamide K, *et al*: Reverse white-coat effect as an independent risk for microalbuminuria in treated hypertensive patients. *Nephrol Dial Transplant* 2007; 22: 911–916.
- Hozawa A, Imai Y, Ohkubo T, *et al*: Prognostic significance of the white coat effect defined as the difference between home and screening blood pressure measurements: the Ohasama study. *J Hypertens* 1999; 17: S23.
- Hozawa A, Ohkubo T, Nagai K, *et al*: Factors affecting the difference between screening and home blood pressure measurements: the Ohasama Study. *J Hypertens* 2001; 19: 13–19.
- Mallion JM, Clerson P, Bobrie G, *et al*: Predictive factors for masked hypertension within a population of controlled hypertensives. *J Hypertens* 2006; 24: 2365–2370.
- Myers MG, Reeves RA: White coat effect in treated hypertensive patients: sex differences. *J Hum Hypertens* 1995; 9: 729–733.
- Verdecchia P, Schillaci G, Borgioni C, *et al*: White coat hypertension and white coat effect. Similarities and differences. *Am J Hypertens* 1995; 8: 790–798.

- Gosse P, Promax H, Durandet P, Clementy J: 'White coat' hypertension. No harm for the heart. *Hypertension* 1993; 22: 766–770.
- 27. Schillaci G, Verdecchia P, Boldrini F, *et al*: The irrelevance of the clinical arterial pressure with respect to outpatient pressure in defining the risk of left ventricular hypertrophy in essential arterial hypertension. *G Ital Cardiol* 1991; **21**: 651–659.
- 28. Penzo M, Guzzardi G, Palatini P: Relationship between blood pressure determination anxiety and hypertensive complications. *Cardiologia* 1995; **40**: 117–122.
- Nakashima T, Yamano S, Sasaki R, *et al*: White-coat hypertension contributes to the presence of carotid arteriosclerosis. *Hypertens Res* 2004; 27: 739–745.
- Conen D, Dieterle T, Utech K, *et al*: C-reactive protein and B-type natriuretic peptides in never-treated white coat hypertensives. *Hypertens Res* 2006; 29: 411–415.
- Leary AC, Donnan PT, MacDonald TM, Murphy MB: The white-coat effect is associated with increased blood pressure reactivity to physical activity. *Blood Press Monit* 2002; 7: 209–213.
- Ugajin T, Hozawa A, Ohkubo T, *et al*: White-coat hypertension as a risk factor for the development of home hypertension. *Arch Intern Med* 2005; 165: 1541–1546.
- Verdecchia P, Reboldi GP, Angeli F, *et al*: Short- and longterm incidence of stroke in white-coat hypertension. *Hypertension* 2005; 45: 203–208.
- Mancia G: Methods for assessing blood pressure values in humans. *Hypertension* 1983; 5: III5–III13.