Original Article

Masked Nocturnal Hypertension and Target Organ Damage in Hypertensives with Well-Controlled Self-Measured Home Blood Pressure

Satoshi HOSHIDE[1)], Joji ISHIKAWA[1)], Kazuo EGUCHI[1)], Toshiyuki OJIMA[2)], Kazuyuki SHIMADA[1)], and Kazuomi KARIO[1)]

It has been reported that masked hypertension, a state in which patients show normal clinic blood pressure (BP) but elevated out-of-clinic BP by self-measured home BP, is a predictor of cardiovascular morbidity much like sustained hypertension. In addition, nocturnal BP is closely associated with cardiovascular disease. This might mean that ambulatory and self-measured home BP monitoring each provide independent information. We performed ambulatory BP monitoring, self-measured home BP monitoring, echocardiography and carotid ultrasonography in 165 community-dwelling subjects. We subclassified the patients according to the ambulatory and self-measured home BP levels as follows: in the masked nocturnal hypertension group, the self-measured home BP level was <135/85 mmHg and the ambulatory nocturnal BP level was ≥120/75 mmHg; in the normotensive group, the self-measured home BP level was <135/85 mmHg and the ambulatory nocturnal BP level was <120/75 mmHg. The intima-media thickness (IMT) and relative wall thickness (RWT) were greater in the masked nocturnal hypertension group than in the normotensive group (IMT: 0.76±0.20 *vs.* 0.64±0.14 mm, $p<0.05$; RWT: 0.50±0.14 *vs.* 0.41±0.10, $p<0.05$). Even in hypertensives with well-controlled self-measured home BP, elevated ambulatory nocturnal BP might promote target organ damage. We must rule out masked hypertension using self-measured home BP monitoring, and we might also need to rule out nocturnal masked hypertension using ambulatory BP monitoring. (*Hypertens Res* 2007; 30: 143–149)

***Key Words*: nocturnal hypertension, self-measured home blood pressure, ambulatory blood pressure**

Introduction

In the condition known as "masked hypertension," the ambulatory blood pressure (BP) level estimated by ambulatory BP monitoring is elevated although the clinic BP level in normal (*1*). The frequency of this condition has been estimated to be around 20% (*1*, *2*). Masked hypertension has also been called isolated ambulatory hypertension (IAH), and recently it was reported that both IAH and sustained hypertension predicted cardiovascular morbidity (*3*, *4*). Masked hypertension can be evaluated using self-measured home BP monitoring. It has also been reported that masked hypertension detected by self-measured home BP monitoring predicted cardiovascular events (*5*).

The nocturnal BP level is one of the most important of the parameters evaluated by ambulatory BP monitoring. It has been proposed that nondippers, who exhibit a diminished nocturnal BP fall, constitute a subgroup whose abnormal diurnal BP variation is associated with increased rates of target organ damage and poorer prognosis for cardiovascular events compared with dippers, who exhibit a normal nocturnal BP fall (*6*, *7*). Some authors have reported that ambulatory nocturnal BP was closely associated with cardiovascular dis-

From the [1)]Division of Cardiovascular Medicine and [2)]Department of Public Health, Jichi Medical University School of Medicine, Shimotsuke, Japan.
Address for Reprints: Satoshi Hoshide, M.D., Division of Cardiovascular Medicine, Jichi Medical University School of Medicine, 3311–1, Yakushiji, Shimotsuke 329–0498, Japan. E-mail: hoshide@jichi.ac.jp
Received July 3, 2006; Accepted in revised form September 26, 2006.

ease (*8–10*). Even if the self-measured home BP level is normal, elevated ambulatory nocturnal BP might promote target organ damage.

Methods

Subjects

This cross-sectional study was conducted in 1998, in the Miyori district in the rural community of Kinugawa, Tochigi Prefecture, Japan. A total of 181 adults (33% of the 541 residents aged 20 years or older) gave informed consent and participated in this study. Sixteen subjects were excluded because ambulatory and self-measured home BP monitoring could not be performed. We excluded subjects with renal failure (serum creatinine level ≥176 μmol/l) or hepatic damage (aspartate aminotransferase or alanine aminotransferase >40 IU/l), or with a past history of coronary artery disease, stroke, congestive heart failure, or atrial fibrillation. There was no subject with a past history of a diagnosis of secondary hypertension.

Diabetes mellitus was defined by a fasting glucose level ≥7.0 mmol/l, a random nonfasting glucose level ≥11.1 mmol/l, hemoglobin A1c ≥6.2%, or the use of an oral hypoglycemic agent (no patients used insulin). Hyperlipidemia was defined by a total cholesterol level ≥6.2 mmol/l or the use of a lipid-lowering agent. Body mass index (BMI) was calculated as weight (kg)/height $(m)^2$.

Clinic BP, 24-h Ambulatory BP Monitoring and Self-Measured Home BP Monitoring

Clinic BP was measured using a cuff oscillometric device (UA-631; A&D, Tokyo, Japan). Two consecutive readings were taken at clinic visits by physicians at 1-min intervals after 5 min of rest in a sitting position. Noninvasive ambulatory BP monitoring was carried out on a weekday with an automatic device (TM-2425; A & D Company Inc., Tokyo, Japan) that recorded BP and heart rate every 30 min for 24 h. The accuracy of these devices was demonstrated previously (*11*). The ambulatory BP data used in the present study were obtained by the oscillometric method. Ambulatory nocturnal BP was defined as the average of the BPs from the time when the subjects went to bed until the time they got out of bed, and awake BP as the average of BPs recorded during the rest of the day. We defined nocturnal hypertension as an ambulatory nocturnal BP level ≥120/75 mmHg (*12*). All patients were instructed to measure BP using a cuff oscillometric device (UA-631; A & D Company Inc.) at the same upper arm position. The self-measured BP was the average of all readings collected during 3 days. After 5 min of rest in the sitting position, patients performed 2 consecutive self-measurements of BP twice daily, in the morning between 5 and 10 AM and in the evening between 5 and 10 PM. We defined hypertension as an average self-measured home BP level ≥135/85 mmHg (*12*). We subclassified the patients according to the ambulatory and self-measured home BP levels as follows: Group A, the self-measured home BP level was ≥135/85 mmHg and the ambulatory nocturnal BP level was <120/75 mmHg; Group B, the self-measured home BP level was ≥135/85 mmHg and the ambulatory nocturnal BP level was ≥120/75 mmHg; Group C (normotensive group), the self-measured home BP level was <135/85 mmHg and the ambulatory nocturnal BP level was <120/75 mmHg; Group D (masked nocturnal hypertension group), the self-measured home BP level was <135/85 mmHg and the ambulatory nocturnal BP level was ≥120/75 mmHg (Fig. 1).

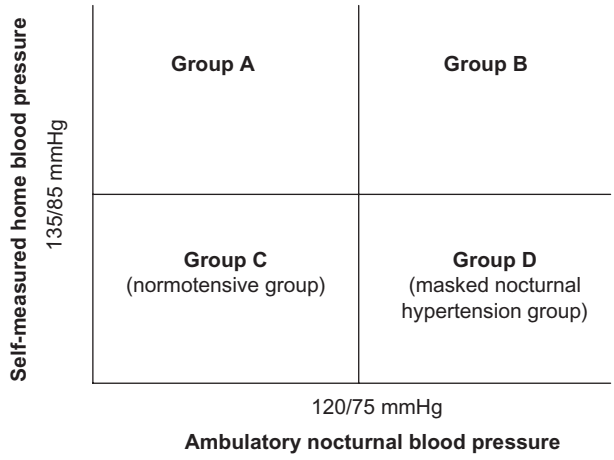

Fig.1. *Masked nocturnal hypertension defined by self-measured home blood pressure (BP) and ambulatory BP.*

Echocardiographic Examination

M-mode echocardiography was performed with two-dimensional monitoring. The left ventricular (LV) chamber recording was obtained at the tip of the mitral valve. The interventricular septal thickness (IVST) and posterior wall thickness (PWT) were measured at end diastole. LV internal dimensions were made at end diastole (LVIDd) and end systole (LVIDs), in accordance with the recommendations of the American Society of Echocardiography.

LV mass (LVM) was calculated using the regression equation recommended by the American Society of Echocardiography (ASE) (*13*):

$$\mathrm{LVM} = 0.8\ \{1.04\ (\mathrm{IVST} + \mathrm{LVIDd} + \mathrm{PWT})^3 - (\mathrm{LVIDd})^3\} + 0.6.$$

The LVM index (LVMI) was calculated using standard formulae. The relative wall thickness (RWT) was calculated as 2 × PWT/LVID (*13*).

Table 1. Characteristics of Subjects

	Group A	Group B	Group C	Group D
Self-measured home BP (mmHg)	≥135/85	≥135/85	<135/85	<135/85
Ambulatory nocturnal BP (mmHg)	<120/75	≥120/75	<120/75	≥120/75
n	32	39	77	17
Age (years)	63±11	63±9.8	59±10	63±8.6
Male (%)	62	55	42	23*
BMI (kg/m^2)	24±3.5	25±2.7	24±3.1	25±4.2
Smoking (%)	21	26	13	24
Hyperlipidemia (%)	47	55	34	47
Diabetes mellitus (%)	6	11	1	6
HT treatment (%)	35	45	9*,††	41‡
Clinic SBP (mmHg)	145±16	157±20*	123±12**,††	142±11†,‡‡
Clinic DBP (mmHg)	88±12	95±12*	78±7.4**,††	85±7.2†,‡
Clinic PR (bpm)	71±9.4	69±12	68±10	74±9.7
24-h SBP (mmHg)	123±10	142±12**	114±8.9**,††	136±11**,‡‡
24-h DBP (mmHg)	75±6.5	84±8.0**	70±6.1*,††	80±8.8‡‡
24-h PR (bpm)	67±7.1	68±6.2	67±7.9	73±9.8*,‡
Awake SBP (mmHg)	128±12	146±13**	119±11*,††	137±11†,‡
Awake DBP (mmHg)	79±8.0	87±8.5**	73±6.7††	81±8.7†,‡
Awake PR (bpm)	71±8.3	72±6.6	70±7.8	75±10
Nocturnal SBP (mmHg)	110±6.7	133±16**	102±7.7*,††	134±14**,‡‡
Nocturnal DBP (mmHg)	67±4.7	78±8.4**	63±6.2††	78±9.9**,‡‡
Nocturnal PR (bpm)	60±6.4	62±7.7	60±6.3	69±10**,†,‡
Home SBP (mmHg)	142±19	149±24	114±11**,††	119±8.6**,††
Home DBP (mmHg)	84±9.7	89±14	73±7.7**,††	79±12**,††
Home PR (mmHg)	71±7.8	70±9.4	70±8.3	76±6.7‡

BMI, body mass index; HT, hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure; PR, pulse rate. Values are reported as mean±SD or percentages. Overall *p* values for 4-group comparison of means (ANOVA) or percentages (χ^2 test). *$p<0.05$, **$p<0.01$ *vs*. Group A, †$p<0.05$, ††$p<0.01$ *vs*. Group B, ‡$p<0.05$, ‡‡$p<0.01$ *vs*. Group C.

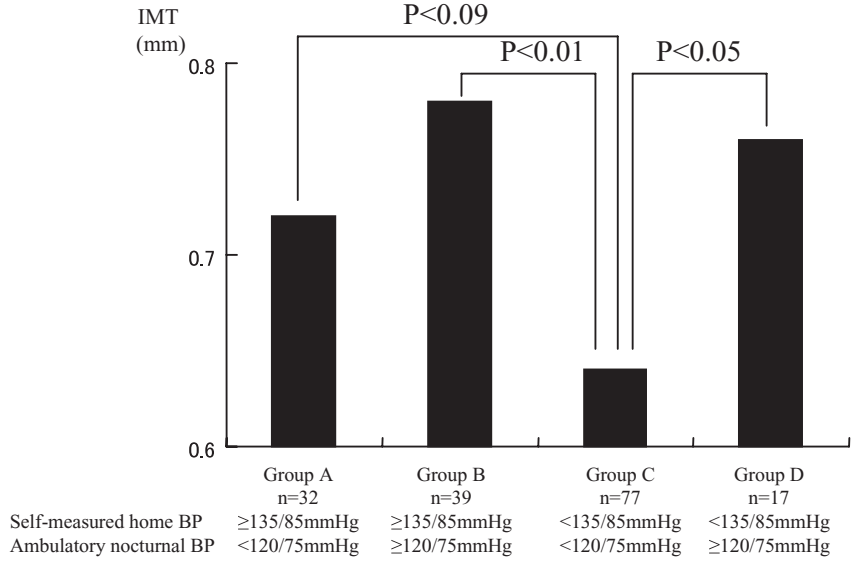

Fig. 2. *Intima-media thickness (IMT) of each group. BP, blood pressure.*

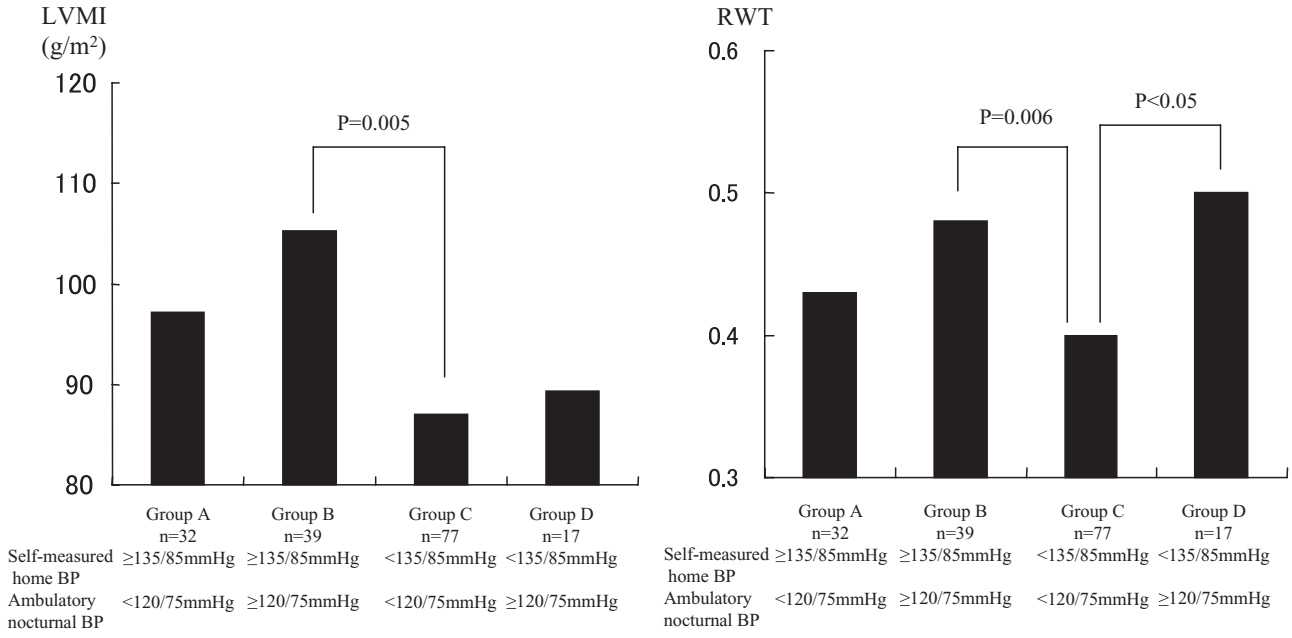

Fig. 3. *Left ventricular mass index (LVMI) and relative wall thickness (RWT) of each group. BP, blood pressure.*

Carotid Ultrasonography

Imaging of the right and left extracranial carotid arteries was performed using a 7.5 MHz transducer with the subject supine and the neck hyperextended. Measurement of the intima-media thickness (IMT) of the far wall at the end of diastole was performed in B-mode. A minimum of 3 measurements of the right and left common carotid far wall were taken 10 mm proximal to the bifurcation to derive the mean carotid IMT.

Statistical Analysis

All statistical analyses were carried out with SPSS/Windows, version 11.0J (SPSS Inc., Chicago, USA). One-way analysis of variance (ANOVA) was performed to detect differences among groups, and Tukey's honestly significant differences (HSD) test was used for multiple pairwise comparisons of means among groups. The χ^2-test was used to evaluate differences in prevalence rates. A value of $p<0.05$ was considered significant.

Results

Table 1 shows the characteristics of each group. There were no significant differences in age, BMI, smoking, hyperlipidemia, or diabetes mellitus among the four groups. The prevalence of males was lower in Group D than in Group A. The prevalence of hypertensive treatment was lower in Group C than in any other group. Clinic systolic blood pressure (SBP) and diastolic blood pressure (DBP), 24-h SBP and DBP, awake SBP, and nocturnal SBP were lower in Group C than in any other group.

IMT was higher in Group B than in Group C, and was higher in Group D than in Group C, and tended to be higher in Group A than in Group C (Fig. 2).

Figure 3 shows the LVMI and RWT values in each group. LVMI was higher in Group B than in Group C. RWT was higher in Groups B and D than in Group C. Multiple regression analysis showed that nocturnal SBP was independently associated with IMT ($\beta=0.10$, $p<0.05$) and RWT ($\beta=0.28$, $p<0.001$) adjusted by age, male gender, BMI and self-measured home SBP in all subjects. In the subjects with elevated home BP level ≥135/85 mmHg; Groups A and B), nocturnal SBP was independently associated with RWT ($\beta=0.30$, $p<0.05$), but was not associated with IMT. However, in the subjects with normal home BP level (<135/85 mmHg; Groups C and D), nocturnal SBP was independently associated with IMT ($\beta=0.27$, $p<0.01$) and RWT ($\beta=0.25$, $p<0.05$) (Table 2).

Discussion

In this study, the masked nocturnal hypertension group with an elevated nocturnal BP and normal home BP levels had significantly higher IMT and RWT than the group with a normal nocturnal and home BP level. Masked nocturnal hypertension detected in normotensives by home BP measurement might promote the progression of cardiovascular disease. Recently, there have been some reports about the benefits of self-measurement of home BP for antihypertensive treatment and the association with hypertensive target organ damages (*5*, *14–16*). However, as shown by this study, there are also nocturnal

Table 2. Multiple Regression Analysis for Target Organ Damages in Each Groups

	IMT		LVMI		RWT	
	β	p	β	p	β	p
All subjects						
Age	0.36	<0.001	0.29	<0.001	0.24	<0.005
Male	0.13	n.s.	0.15	<0.05	0.11	n.s.
BMI	0.17	<0.05	0.10	n.s.	0.13	n.s.
Nocturnal SBP	0.10	<0.05	0.04	n.s.	0.28	<0.001
Home SBP	0.03	n.s.	0.50	<0.005	−0.10	n.s.
Groups A and B (self-measured home BP ≥135/85 mmHg)						
Age	0.50	<0.001	0.11	n.s.	0.15	n.s.
Male	0.19	n.s.	0.04	n.s.	0.15	n.s.
BMI	0.10	n.s.	0.00	n.s.	0.09	n.s.
Nocturnal SBP	0.12	n.s.	0.08	n.s.	0.30	<0.05
Home SBP	−0.02	n.s.	0.31	<0.05	−0.02	n.s.
Groups C and D (self measued home BP <135/85 mmHg)						
Age	0.27	<0.01	0.40	<0.001	0.32	<0.005
Male	0.09	n.s.	0.22	<0.05	0.08	n.s.
BMI	0.27	0.01	0.16	n.s.	0.17	n.s.
Nocturnal SBP	0.27	<0.01	−0.00	n.s.	0.25	<0.05
Home SBP	−0.12	n.s.	0.11	n.s.	−0.10	n.s.

IMT, intima-media thickness; LVMI, left ventricular mass index; RWT, relative wall thickness; BMI, body mass index; SBP, systolic blood pressure; n.s., not significant.

hypertensives with normal home BP levels. Thus, there is a possibility that it would not be possible to make a diagnosis of masked nocturnal hypertension in these patients with only self-measured home BP measurement.

Masked hypertension is defined as normal clinic BP and elevated out-of-clinic BP assessed using either self-measured BP or ambulatory BP monitoring (*1*, *2*). In a previous study in an urban population in Japan, 10% to 32% of treated hypertensives were classified as hypertensive by home BP measurement, even if they were classified as normotensive by clinic BP (*2*). The SHEAF study showed that cardiovascular risk in subjects with masked hypertension is identical to that in subjects with uncontrolled hypertension (*5*). One report showed that self-measured home BP monitoring might be a more promising option than ambulatory BP monitoring, because it causes less discomfort and disturbance of life and sleep (*14*). However, ambulatory and self-measured home BP do not provide the same information. In the PAMELA study, only two-thirds of the patients identified as having isolated clinic hypertension (≥140/90 mmHg) based on 24-h BP normality (<125/79 mmHg) estimated by ambulatory BP monitoring had isolated clinic hypertension based on home BP normality (<132/83 mmHg) (*17*). Furthermore, in only approximately half of the patients with elevated 24-h BP and normal clinic BP, home BP was not concomitantly elevated (*17*). In this study, there was also not a significant difference in home BP level between Group C (normotensive group) and Group D (masked nocturnal hypertension group); however, the 24-h and awake BP of Group D were significantly higher than those of Group C. Our results showed that the hypertensive group with elevated ambulatory BP level did not necessarily have an elevated home BP level.

This study showed that masked nocturnal hypertension (*i.e.*, elevated nocturnal BP and normal home BP level) was associated with increased cardiac structure change and carotid atherosclerosis. Many studies have demonstrated that IMT or carotid plaque are markers of atherosclerosis (*18–21*). Ambulatory nocturnal BP level was also independently associated with IMT and RWT. In hypertensive patients, some studies have shown that nocturnal BP is associated with changes of the cardiac structure and IMT (*22*, *23*). In addition, several studies have found that an abnormal diurnal BP variation characterized by diminished nocturnal BP dipping is associated with clinical and subclinical target organ damage (*5*, *24*, *25*). Moreover, BP variability evaluated by ambulatory BP monitoring was also found to be an independent risk factor for cardiovascular events in Japanese elderly hypertensive patients (*26*). However, we cannot make a diagnosis of nocturnal BP dipping using only home BP monitoring. In this study, RWT was greater in the masked nocturnal hypertension group than in the normotensive group. However, there was no significant difference in LVMI between these groups. One report showed that LV concentric remodeling (characterized by normal LVM and increased RWT) was associated with parallel structural changes in large conductance arteries, such as the carotid arteries (*27*). LV concentric remodeling is

an early and frequent adaptation in arterial hypertension (*28*). Therefore, there might be a discrepancy between the progression of LVMI and RWT in hypertensive target organ damage.

White-coat hypertension, defined by persistently high clinic BP levels and normal out-of-clinic BP levels, is common in clinical practice (*29*). However, it is still controversial whether white-coat hypertension is a benign condition (*30–32*). In this study, some patients in Group D ($n=5$) were white-coat hypertensive patients. A fraction of the patients with white-coat hypertension defined by clinic and home BP level might have elevated nocturnal BP level and a prognosis of future hypertensive target organ damage.

The mechanism of ambulatory nocturnal hypertension might involve an effect of antihypertensive agents. It is possible that a more complete effect of BP reduction is exerted while awake, but an incomplete effect is exerted during sleep. In this study, the patient group with an elevated nocturnal but a normal home BP had a significantly higher frequency of antihypertensive agent use than the group with both normal nocturnal and normal home BP. Nocturnal BP might increase as a result of the progression of target organ damage. It has been reported that dippers with target organ damage sometimes show a diminished nocturnal BP fall, becoming non-dippers, while patients who have experienced cerebral infarction show a normal nocturnal BP fall in order to maintain cerebral blood flow (*33*). Therefore, in this study, we excluded subjects with a past history of cardiovascular disease.

It is important to estimate BP levels by measuring not only clinic BP but also out-of-clinic BP. We must first rule out masked hypertension using self-measured home BP monitoring, and then might need to rule out nocturnal masked hypertension using ambulatory BP monitoring. Hermida *et al*. reported a reduction in the prevalence of non-dipping from 81.9% to 56.9% when patients with resistant hypertension who had been receiving all their drugs on awaking began to take one of their drugs at bedtime (*34*). Hypertensive treatment of high-risk patients who require strict antihypertensive therapy might require ambulatory BP monitoring as well as self-measured home BP monitoring.

References

1. Pickering TG, Davidson K, Gerin W, Schwartz JE: Masked hypertension. *Hypertension* 2002; **40**: 795–796.
2. Kawabe H, Saito I, Saruta T: Status of home blood pressure measured in morning and evening: evaluation in normotensives and hypertensives in Japanese urban population. *Hypertens Res* 2005; **28**: 491–498.
3. Bjorklund K, Lind L, Zethelius B, Andren B, Lithell H: Isolated ambulatory hypertension predicts cardiovascular morbidity in elderly men. *Circulation* 2003; **107**: 1297–1302.
4. Palatini P, Winnicki M, Santonastaso M, *et al*: Prevalence and clinical significance of isolated ambulatory hypertension in young subjects screened for stage 1 hypertension. *Hypertension* 2004; **44**: 170–174.
5. 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.
6. Verdecchia P, Porcellati C, Schillaci G, *et al*: Ambulatory blood pressure. An independent predictor of prognosis in essential hypertension. *Hypertension* 1994; **24**: 793–801 [published erratum appears in *Hypertension* 1995; **25**: 462].
7. Ohkubo T, Imai Y, Tsuji I, *et al*: Relation between nocturnal decline in blood pressure and mortality. The Ohasama Study. *Am J Hypertens* 1997; **10**: 1201–1207.
8. 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.
9. Sega R, Facchetti R, Bombelli M, *et al*: Prognostic value of ambulatory and home blood pressures compared with office blood pressure in the general population: Follow-Up Results from the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) Study. *Circulation* 2005; **111**: 1777–1783.
10. Nakano S, Ito T, Furuya K, *et al*: Ambulatory blood pressure level rather than dipper/nondipper status predicts vascular events in type 2 diabetic subjects. *Hypertens Res* 2004; **27**: 647–656.
11. Tochikubo O, Ikeda A, Miyajima E, Ishii M: Effects of insufficient sleep on blood pressure monitored by a new multibiomedical recorder. *Hypertension* 1996; **27**: 1318–1324.
12. 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**: 2560–2571.
13. Lang RM, Bierig M, Devereux RB, *et al*: Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005; **18**: 1440–1463.
14. Little P, Barnett J, Barnsley L, Marjoram J, Fitzgerald-Barron A, Mant D: Comparison of agreement between different measures of blood pressure in primary care and daytime ambulatory blood pressure. *BMJ* 2002; **325**: 254.
15. Tachibana R, Tabara Y, Kondo I, Miki T, Kohara K: Home blood pressure is a better predictor of carotid atherosclerosis than office blood pressure in community-dwelling subjects. *Hypertens Res* 2004; **27**: 633–639.
16. Nishinaga M, Takata J, Okumiya K, Matsubayashi K, Ozawa T, Doi Y: High morning home blood pressure is associated with a loss of functional independence in the community-dwelling elderly aged 75 years or older. *Hypertens Res* 2005; **28**: 657–663.
17. Sega R, Trocino G, Lanzarotti A, *et al*: Alterations of cardiac structure in patients with isolated office, ambulatory, or home hypertension: data from the general population (Pressione Arteriose Monitorate E Loro Associazioni [PAMELA] Study). *Circulation* 2001; **104**: 1385–1392.
18. Sumino H, Ichikawa S, Kasama S, *et al*: Effect of transder-

mal hormone replacement therapy on carotid artery wall thickness and levels of vascular inflammatory markers in postmenopausal women. *Hypertens Res* 2005; **28**: 579–584.
19. Munakata M, Sakuraba J, Tayama J, *et al*: Higher brachial-ankle pulse wave velocity is associated with more advanced carotid atherosclerosis in end-stage renal disease. *Hypertens Res* 2005; **28**: 9–14.
20. Masugata H, Senda S, Yoshikawa K, *et al*: Relationships between echocardiographic findings, pulse wave velocity, and carotid atherosclerosis in type 2 diabetic patients. *Hypertens Res* 2005; **28**: 965–971.
21. Ishizaka N, Ishizaka Y, Toda E, Hashimoto H, Nagai R, Yamakado M: Hypertension is the most common component of metabolic syndrome and the greatest contributor to carotid arteriosclerosis in apparently healthy Japanese individuals. *Hypertens Res* 2005; **28**: 27–34.
22. Salvetti M, Muiesan ML, Rizzoni D, *et al*: Night time blood pressure and cardiovascular structure in a middle-aged general population in northern Italy: the Vobarno Study. *J Hum Hypertens* 2001; **15**: 879–885.
23. Verdecchia P, Schillaci G, Guerrieri M, *et al*: Circadian blood pressure changes and left ventricular hypertrophy in essential hypertension. *Circulation* 1990; **81**: 528–536.
24. Shimada K, Kawamoto A, Matsubayashi K, Nishinaga M, Kimura S, Ozawa T: Diurnal blood pressure variations and silent cerebrovascular damage in elderly patients with hypertension. *J Hypertens* 1992; **10**: 875–878.
25. Kario K, Pickering TG, Matsuo T, Hoshide S, Schwartz JE, Shimada K: Stroke prognosis and abnormal nocturnal blood pressure falls in older hypertensives. *Hypertension* 2001; **38**: 852–857.
26. Eto M, Toba K, Akishita M, *et al*: Impact of blood pressure variability on cardiovascular events in elderly patients with hypertension. *Hypertens Res* 2005; **28**: 1–7.
27. Cuspidi C, Lonati L, Sampieri L, *et al*: Left ventricular concentric remodelling and carotid structural changes in essential hypertension. *J Hypertens* 1996; **14**: 1441–1446.
28. Verdecchia P, Schillaci G, Borgioni C, *et al*: Adverse prognostic significance of concentric remodeling of the left ventricle in hypertensive patients with normal left ventricular mass. *J Am Coll Cardiol* 1995; **25**: 871–878.
29. Pickering TG, James GD, Boddie C, Harshfield GA, Blank S, Laragh JH: How common is white coat hypertension? *JAMA* 1988; **259**: 225–228.
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. White WB, Schulman P, McCabe EJ, Dey HM: Average daily blood pressure, not office blood pressure, determines cardiac function in patients with hypertension. *JAMA* 1989; **261**: 873–877.
32. Nakashima T, Yamano S, Sasaki R, *et al*: White-coat hypertension contributes to the presence of carotid arteriosclerosis. *Hypertens Res* 2004; **27**: 739–745.
33. Yamamoto Y, Akiguchi I, Oiwa K, Satoi H, Kimura J: Diminished nocturnal blood pressure decline and lesion site in cerebrovascular disease. *Stroke* 1995; **26**: 829–833.
34. Hermida RC, Ayala DE, Calvo C, *et al*: Effects of time of day of treatment on ambulatory blood pressure pattern of patients with resistant hypertension. *Hypertension* 2005; **46**: 1053–1059.