Original Article

The Association between Morning Hypertension and Metabolic Syndrome in Hypertensive Patients

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Morning hypertension (MHT) and metabolic syndrome (MS) have been reported as important risk factors for stroke and cardiovascular events. We investigated the prevalence of MHT and MS among hypertensive patients in our outpatient clinic from June to August, 2005. We studied 181 hypertensive patients (91 men and 90 women) in our outpatient clinic using home-use electronic sphygmomanometers. Seventy-nine of these 181 patients (43.6%) demonstrated MHT, defined as systolic blood pressure (SBP) ≥135 mmHg in the morning. Only 48.1% of the patients demonstrated normal SBP both at the clinic and in the morning at home, whereas 72.9% of the patients demonstrated normal diastolic blood pressure (DBP) under the same conditions. Sixty-one patients (33.7%) had MS, and 34 patients had both MHT and MS. Twenty-seven of the 102 patients (26.5%) without MHT had MS. The frequency of MS was significantly higher among those with MHT than those without MHT (p=0.019). Multiple logistic regression analysis including smoking, alcohol consumption, sex, and age as confounding factors showed significant association between MHT and MS (odds ratio: 1.99; 95% confidence interval: 1.04–3.80; p=0.039). In conclusion, although 1 year has passed since the JSH 2004 guidelines, 43.6% of our patients still showed MHT, and there was a significantly higher prevalence of MS among those with MHT. Our results suggest the need for a more vigorous intervention for controlling BP. (*Hypertens Res* 2006; 29: 783–788)

***Key Words*: morning hypertension, metabolic syndrome, JSH 2004**

Introduction

Several prospective studies have indicated that morning hypertension (MHT) and morning blood pressure (BP) surge are important risk factors for stroke and cardiovascular events. Cardiovascular events occur most frequently in the morning hours (*1*, *2*). Kario *et al*. reported that, in older hypertensive subjects, a higher morning BP is associated with the risk of stroke (*3*). Ohkubo *et al*. reported that home BP is an independent predictor of hemorrhagic and ischemic stroke in the general population (*4*), and also reported that home BP measurement had a stronger predictive power for mortality than screening BP measurement in the general population (*5*). The level and variability of hypertension as assessed by ambulatory BP and home BP are independent predictors of cardiovascular mortality (*6*). Kamoi *et al*. reported that repeated home BP measurements in the morning for a long period had a stronger predictive power for mortality in patients with hypertension than occasional casual/clinic BP measurements (*7*).

Previously, we reported that 66.9% of patients being treated

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Table 1. Characteristics of the Study Population

	Men	Women	*p*-value
N (181)	91	90	
Age (years)	64.8±10.4	66.0±10.3	0.4692
BMI (kg/m^2)	24.2±3.3	23.9±3.9	0.5142
Waist (cm)	87.2±8.6	83.6±11.5	0.0179
Outpatient clinic			
SBP (mmHg)	132.3±14.4	132.5±14.1	0.9234
DBP (mmHg)	70.5±10.2	71.2±9.9	0.6645
Morning			
SBP (mmHg)	134.5±13.0	131.4±14.4	0.1320
DBP (mmHg)	80.4±10.1	77.6±11.2	0.0857
Evening			
SBP (mmHg)	125.4±14.3	121.8±13.8	0.0974
DBP (mmHg)	73.4±11.4	72.2±9.7	0.4529
M-E			
SBP (mmHg)	9.4±13.6	9.9±13.8	0.8069
DBP (mmHg)	7.2±9.5	5.6±10.0	0.2822
MHT (P/N)	45/46 (49.5%)	34/56 (37.8%)	0.1134
Alcohol (P/N)	44/47	2/88	<0.0001
Smoking (P/N)	51/40	5/85	<0.0001
MS (P/N)	40/51 (44.0%)	21/69 (23.3%)	0.0033

Values are the means±SD. *N*: number of subjects. BMI, body mass index; Waist, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; Morning, home blood pressure in the morning before breakfast; Evening, home blood pressure before going to bed; M-E, differences of evening to morning blood pressure; MHT, frequency of morning hypertension; Alcohol, alcohol drinking habit; P/N, positive/negative; Smoking, smoking habit; MS, frequency of metabolic syndrome.

Table 2. Characteristics of Patients Divided into with MS and without MS

	Patients with MS	Patients without MS	*p*-value
N (181)	61	120	
Age (years)	66.0±9.2	65.1±10.9	0.5531
BMI (kg/m^2)	26.4±3.2	22.9±3.2	<0.0001
Waist (cm)	94.2±7.0	80.9±8.6	<0.0001
Outpatient clinic			
SBP (mmHg)	134.5±14.1	131.4±14.2	0.1578
DBP (mmHg)	71.4±7.9	70.6±11.0	0.5880
Morning			
SBP (mmHg)	136.1±14.0	131.3±13.4	0.0254
DBP (mmHg)	80.1±9.6	78.4±11.2	0.3206
Evening			
SBP (mmHg)	128.7±15.3	121.2±12.9	<0.0001
DBP (mmHg)	74.9±10.5	71.8±10.6	0.0744
M-E			
SBP (mmHg)	8.3±13.4	10.3±13.7	0.3796
DBP (mmHg)	5.6±7.9	6.8±10.5	0.4591
MHT (P/N)	34/27 (55.7%)	45/75 (37.5%)	0.0194

Values are the means±SD. *N*: number of subjects. MS, metabolic syndrome; BMI, body mass index; Waist, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; Morning, home blood pressure in the morning before breakfast; Evening, home blood pressure before going to bed; M-E, differences of evening to morning blood pressure; MHT, patients with morning hypertension (frequency of morning hypertension); P/N, positive/negative.

for essential hypertension demonstrated MHT (*8*). Recently, in 2004, the Japanese Society of Hypertension (JSH) reported that MHT is an important risk factor for stroke and cardiovascular events (*9*).

People with metabolic syndrome (MS) are at a higher risk for developing type 2 diabetes (*10*) and cardiovascular disease (*11*). The Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (NCEP-ATP III) proposed a new definition of MS (*12*). Lakka *et al*. reported that cardiovascular disease and all-cause mortality in men with MS were higher than in those without MS (*13*).

In 2005, a committee composed of 8 Japanese domestic societies proposed a new diagnostic criteria for MS in Japanese (*14*, *15*). However, there have been no reports about the association between MS, as defined by the new Japanese criteria, and MHT. Therefore, in this study, we investigated the frequency of MS and MHT in hypertensive patients, and evaluated their association.

Methods

Study Population

The study subjects had already been receiving medical treatment for hypertension in our outpatient clinic in the months of June to August 2005. Among the 415 hypertensive subjects (201 men, 214 women) in our outpatient clinic during these 2 months, 181 subjects (43.6%) gave informed consent for this study, and took home the home-use electronic sphygmomanometers. This study was approved by the Institutional Review Board of Kohka Public Hospital (No. 16-9, 2004).

Measurement of Waist Circumference

The waist was measured with a tape measure at the level of the umbilicus with subjects wearing an undergarment and standing at end-exhale. Waist measurements were taken by the same staff member; each measurement was performed in triplicate and the average value was used.

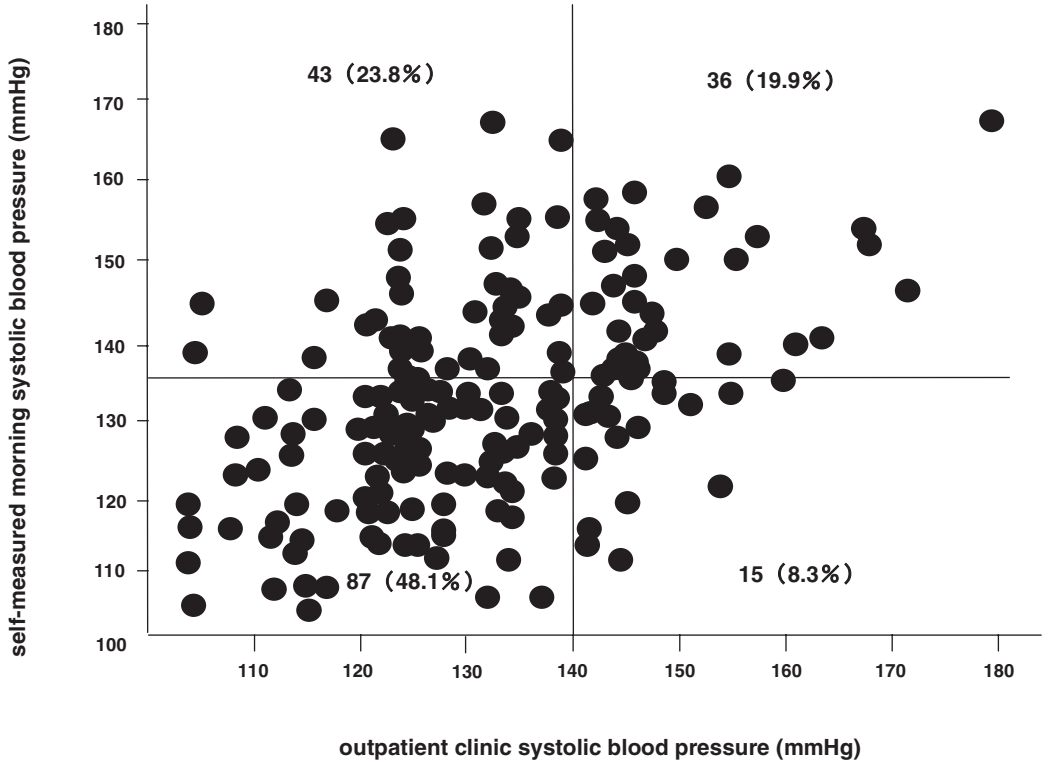

Fig. 1. *Relationship between morning systolic blood pressure and outpatient clinic systolic blood pressure.*

Blood Pressure and Biochemical Examinations

Systolic BP (SBP) and diastolic BP (DBP) were measured twice using a standard sphygmomanometer on the right arm while the subject was seated after having rested for at least 5 min. Korotkov's first and fifth sounds were used for measuring the SBP and DBP, respectively, and the BP was measured by a well-trained nurse. The mean of the 2 measurements in each subject was used for data analysis. Home BP measurements were taken using home-use electronic sphygmomanometers before going to bed and in the morning before breakfast. We used the evening BP of the day before clinic, and the morning BP of the clinic day. The body mass index (BMI) was calculated as the weight (kg) divided by the square of the height (m). Fasting blood was drawn and serum blood sugar (BS), serum total triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C) levels were determined in our hospital.

The Criteria for MS

We used the Japanese criteria for MS in 2005 (*14*, *15*). Briefly, men with a waist circumference ≥85 cm and women with a waist circumference ≥90 cm were considered abdominally obese. All participants in this study were already being treated for hypertension. Therefore, MS was considered a condition in which people have abdominal obesity and at least 1 of the following abnormalities: hypertriglyceridemia (TG ≥150 mg/dl) and/or low HDL-C (HDL-C <40 mg/dl) or already treated hyperlipidemia; or impaired fasting glucose (fasting blood glucose level ≥110 mg/dl) or already treated diabetes mellitus.

Statistical Analysis

Data are expressed as the mean±SD. All statistical analyses were performed using the SAS statistical package. Two-way ANOVA and the χ^2 test were used to assess differences among subjects. To examine the independent contribution of MS to the risk of MHT while adjusting for the effects of other clinical characteristics, logistic analysis was used with the following variables as covariates: sex, age, smoking, and alcohol.

Results

Table 1 summarizes the characteristics of the subjects according to sex. The mean waist circumference was significantly larger in men than in women ($p=0.018$). Alcohol drinking and smoking were much more prevalent in men ($p<0.0001$, respectively). The frequency of MS was 44.0% among the men and 23.3% among the women. The frequency of MS in men was much higher than in women ($p=0.003$).

Table 2 summarizes the characteristics of subjects divided

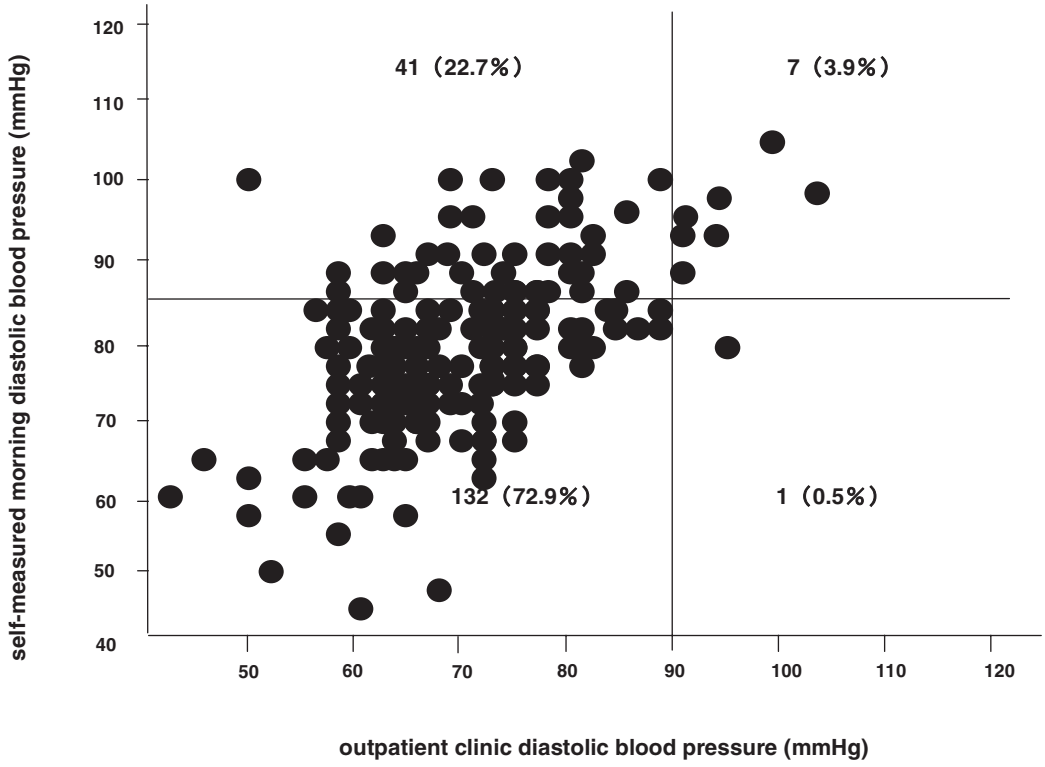

Fig. 2. *Relationship between morning diastolic blood pressure and outpatient clinic diastolic blood pressure.*

into a group with MS and a group without MS. Age did not differ significantly between the two groups; however, BMI and waist circumferences were much higher in the group with MS than in the group without MS ($p<0.0001$, respectively). Both morning and evening SBP at home were much higher in the group with MS than in the group without MS ($p=0.0254$, $p<0.0001$, respectively). Thirty-four of 61 patients (55.7%) with MS demonstrated MHT, while 45 of 120 patients (37.5%) without MS demonstrated MHT. The frequency of MHT among those with MS was much higher than among those without MS ($p=0.019$). For MHT, defined as DBP $\geq$85 mmHg, the frequency of MS was not significantly higher among those with MHT than those without MHT ($p=0.950$) (data not shown).

Multiple logistic regression analysis including smoking, alcohol consumption, sex, and age as confounding factors showed that the association between MHT and MS was significant (odds ratio: 1.99; 95% confidence interval: 1.04–3.80; $p=0.039$).

Figure 1 shows the relationship between the self-measured morning SBPs and the outpatient clinic SBPs. Seventy-nine patients (43.6%) demonstrated MHT, and only 48.1% of the patients demonstrated normal SBP both at the clinic and in the morning at home. The number of patients whose clinic and home morning SBPs were both high was 36 (19.9%).

Figure 2 shows the relationship between the self-measured morning DBPs and the outpatient clinic DBPs. Forty-eight patients (26.5%) had MHT, and 72.9% of the patients had normal DBP both at the clinic and in the morning at home. The number of patients whose clinic and home morning DBPs were both high was 7 (3.9%).

Discussion

In this study, our data indicated that only 48.1% of the patients had normal SBP both at the clinic and in the morning at home, and 43.6% of the patients had MHT. In the Ohasama study, diastolic home hypertension was associated with no significant increase in risk (*16*), so in this study, we analyzed MHT according to systolic home BP. The Japan Home *versus* Office Blood Pressure Measurement Evaluation (J-HOME) study was conducted to assess BP control as evaluated by home BP measurement (*17*). It reported that BP levels were not adequately controlled among approximately 60% of patients, according to the reference values described in the national guidelines (office BP: <140/90 mmHg; home BP: <135/85 mmHg). Before the JSH 2004 guidelines, the recommended target BP levels for middle-aged patients in the JSH 2000 guidelines were higher than those after the JSH 2004 guidelines, and therefore, by the current criteria, office and home BP values were not adequately controlled in approximately 50% of the middle-aged patients whose BP control had been evaluated as good by JSH 2000. In this study, the participants' ages were comparatively high, so the goal of BP

control was slightly optimistic; however, in the JSH 2004 guidelines, more positive intervention for BP was proposed. Our findings suggest that an important reason why home and office BP values were not adequately controlled was that physicians tolerated relatively higher BP levels under treatment, even among middle-aged patients.

MS is characterized as abdominal obesity with the clustering of moderate glucose, lipid metabolism and hypertension issues. In our study population, MS patients had a higher prevalence of MHT. Unfortunately, the mechanism of MS in MHT has not been clarified. Although the mechanism of MS in MHT has not been clarified, several possible mechanisms have been proposed. First, Sironi *et al*. reported that visceral adiposity is quantitatively related to both the rate of BP and the severity of insulin resistance (*18*). Essential hypertension has been reported to be associated with insulin resistance. Visceral obesity has been reported to have a significant effect on glucose metabolism; moreover, Alvarez *et al*. reported that muscle sympathetic nerve activity was elevated in obese humans (*19*). MHT is therefore understood in the context of sympathetic nerve activities (*20*). Thus, it is thought that subjects with MS had MHT through sympathetic nerve activities.

With respect to a second possible mechanism, Nakazato *et al*. reported that sympathetic baroreflex sensitivity was significantly lower during sleep than while subjects were awake in the evening and it remained low after the subjects woke up in the morning (*21*). Sympathetic nerve traffic was found to be significantly greater in subjects with MS than in without MS (*22*), so subjects with MS might have had MHT through baroreflex sensitivity.

With respect to a third possible mechanism, Panza *et al*. reported a circadian rhythm of basal vascular tone, due either partly or entirely to increased α-sympathetic vasoconstrictor activity during the morning; this variation may contribute to higher BP (*23*). Wofford *et al*. suggested that overweight was indirectly correlated with vascular α-tone *via* a relationship with arterial plasma norepinephrine concentration, a marker of sympathetic drive (*24*). It seems likely that one or more of these three mechanisms are responsible for the connection between MS and MHT.

In our hypertensive patients, the prevalence of MS was 44.0% in men and 23.3% in women. In another Japanese analysis, the Tanno and Sobetsu study reported that the prevalence of MS in a rural Japanese sample was 25.3% in men (*25*), and in Okinawa, the prevalence of MS was 30.2% in men and 10.3% in women (*26*); compared with these results, our study data were much higher. Naturally, this may be because our study subjects were all being treated for hypertension and thus both the prevalence of MS and the average age were much higher than in other previous cohorts. For example, in the Tanno and Sobetsu study, the prevalence of MS was higher in treated patients than in untreated patients (men: 23% in untreated *vs*. 32% in treated patients; women: 7% in untreated *vs*. 11% in treated patients) (*25*). This is possibly because the criteria for MS in their study were based on the criteria of NCEP-ATP III, whereas we used the new MS criteria for Japanese (*14*, *15*). In addition, since Ford *et al*. reported that the prevalence of MS is associated with age (*27*), our cohort, which included relatively older subjects than the study of Tanno and Sobetsu, would be expected to show a higher prevalence of MS.

There are some limitations in our study. First, because home BP records were simply written down by the subjects themselves, and were written only once, there may have been inaccurate data. Second, not all patients in our outpatient clinic were enrolled in this study. We studied 181 subjects (43.7%) who used the equipment for home-use BP measurements and came back to the hospital; their compliance was very good. However, we could not study the remaining patients, whose compliance may not have been as good as the studied patients. Third, Imai *et al*. reported that seasonal variation in BP should be considered (*28*); however, in this study, the seasonal variation of BP was not taken into consideration.

In conclusion, 43.6% of treated hypertensive patients showed MHT, and there was a significantly higher prevalence of MHT among patients with MS. Our results suggest the need for a more vigorous intervention for controlling BP.

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