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Ambulatory Blood Pressure Monitoring in Hypertension: Relation with Ambulatory Arterial Stiffness Index and Metabolic Syndrome

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Abstract

The metabolic syndrome (MS) considerably increases the cardiovascular events in hypertensive patients. This study was designed to characterize the results of 24 hour ambulatory blood pressure monitoring (ABPM) in hypertensive patients and to identify the specific patterns of ABPM results including dipping pattern and ambulatory arterial stiffness index (AASI) in the manifestation of MS with hypertension. One hundred four primary hypertension patients who underwent ABPM were enrolled. Fifty patients were the presence of MS according to National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults-Adult Treatment Panel (NCEP-ATP) III criteria and fifty four patients were the absence of MS. AASI was defined as one minus regression slope of diastolic over systolic blood pressure readings from ABPM. Average blood pressure dipping rate was also obtained from ABPM and described in numeric value by calculating reduction rate (%) in day-night average blood pressure. In the presence of MS compared with the absence of MS, patients were older (49.2 ± 7.7 vs. 44.6 ± 11.2, p=0.016), showed higher AASI (0.400 ± 0.196 vs. 0.329 ± 0.146, p=0.038) and lower average blood pressure dipping rate (9.2 ± 6.6 % vs. 11.7 ± 5.8 %, p=0.043). AASI was negatively correlated with numeric values of dipping rate in day-night average blood pressure (r= -0.3; p=0.015). On logistic regression analysis, age (p=0.015) and AASI (p=0.036) were independently associated with MS in hypertensive patients. We conclude that MS in hypertension may contribute to the low dipping rate and has a robust relationship with vascular stiffness such as AASI.

Key Words : Arterial stiffness, Hypertension, Metabolic syndrome, Non-dipping pattern

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Introduction

In hypertensive patients, 24-hour ambulatory blood pressure monitoring (ABPM) provides useful information such as mean 24-hour blood pressure, pulse pressure, non dipping pattern and ambulatory arterial stiffness index (AASI) to predict cardiovascular mortality [1,2]. Particularly, diminished day-night blood pressure difference from 24-hour ABPM has become an important issue for their close relationship with cardio-vascular target organ damage and cardiovascular mortality [3-5]. AASI can also be a marker for cardiovascular complications and cardiovascular mortality, despite of the ongoing debates about their relations with other conventional methods for arterial stiffness [6-8]. Among hypertensive patients, it has been well proven that metabolic syndrome (MS) including central obesity, abnormal lipid profile, abnormal fasting glucose level, high blood pressure (BP) is strongly related with cardiovascular mortality regardless of its diversity of definitions [9-13].

However, the relationship between non-dipping pattern or AASI and MS has rarely been focused together in the hypertensive patients[14-16]. Therefore, this study was designed to characterize the results of 24-hour ABPM in hypertensive patients and to identify the specific patterns of ABPM results including dipping pattern and AASI in the manifestation of MS and hypertension.

Materials and Methods

Study population

Between August 2011 and February 2012, we recruited the patients who were referred to our cardiology outpatient department for evaluation and treatment of hypertension. Patients were enrolled according to the following criteria: 1) age > 18 years; 2) hypertension defined as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg in a sitting position in at least three measurements or previously diagnosed as hypertension with antihypertensive medication; 3) normal or preserved left ventricular ejection fraction ≥ 55%; 4) normal sinus rhythm. Patients were excluded in following conditions: secondary hypertension, diabetes mellitus, a history of coronary artery disease or heart failure, renal impairment (creatinine > 1.5 mg/dL), previous cerebrovascular disease, peripheral arterial disease, more than mild valvular heart disease, or pulmonary disease. Therefore, a total of 104 patients who underwent 24-hour ABPM met the inclusion criteria during the period of enrollment. The study was approved by our institutional ethical committee (IRB No. 2013-10-047).

Definition of metabolic syndrome

MS is defined according to the National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults-Adult Treatment Panel (NCEP-ATP) III criteria [17]. If any of three categories among following five categories are met, the diagnosis of MS was made; 1) BP ≥ 130/85 mmHg; 2) triglyceride ≥ 150 mg/dL; 3) high density lipoprotein-cholesterol < 40 mg/dL in men or < 50 mg/dL in women; 4) fasting blood glucose > 110 mg/dL; 5) central obesity which was defined by the adjusted criteria from Korean studies (waist circumference ≥ 90 cm for men and ≥ 85 cm for women) [18,19].

Ambulatory blood pressure monitoring

Twenty four-hour ABPM was recorded using a validated oscillometric device, Mobil-O-Graph NG (I.E.M. GmbH, Stolberg, Germany) [20]. Non-dominated arm was selected for the recording unless there was more than 10 mmHg of systolic BP difference between the two arms. Day-time BP was obtained for 30 minute interval from 08:00 AM until 10:00 PM and night-time BP was obtained for 1 hour interval from 10:00 PM until 08:00 AM. For the measurement of arterial stiffness, AASI was calculated as 1 minus the regression slope of diastolic BP against systolic BP, which were obtained from individual 24-hour BP measurements [21].

Dipping rate is described in numerical value, determined by calculating the percentage difference between day to night average BP. Systolic dipping rate is defined as 100 × (average day systolic BP - average night systolic BP) / average day systolic BP, whereas diastolic dipping rate is defined as 100 × (average day diastolic BP-average night diastolic BP) / average day diastolic BP. Average dipping rate is taken as the mean of systolic and diastolic dipping rate (systolic dipping rate + diastolic dipping rate) / 2.

Statistical analysis

The data analyses were performed with the Statistical Package for Social Science software (SPSS for Windows 12.0, SPSS Inc., Chicago, IL). Continuous variables are presented as mean ± standard deviation, whereas categorical variables are expressed as counts and percent frequencies and these were compared using the Chi-square test. A multivariate logistic regression analysis was used to explore the associate variables of MS. P-values were two-sided, and a p-value < 0.05 was considered statistically significant.

Results

Baseline characteristics are listed on (Table 1). Fifty patients were diagnosed with MS and fifty four patients were without MS. The patients with MS were likely to be older and showed higher body mass index compare to those without MS. In addition, they had higher values of fasting glucose and triglycerides. Regarding 24-hour ABPM data, the patients with MS showed lower daytime and 24-hour average diastolic BP. They also had lower diastolic dipping rate as well as average dipping rate. AASI was significantly higher for those with MS ($p = 0.038$) (Table 2). The logistic regression analysis was performed to determine associated parameters with MS. Age, average dipping rate, and AASI had strong relationship with MS (Table 3). Furthermore, AASI as well as age were independently associated with MS in the hypertensive patients, apart from average dipping rate. The patients with MS showed much more favorable correlation between AASI and average dipping rate ($r = -0.3$; $p = 0.015$) compared to the patients without MS (Fig. 1).

Discussion

In the current study, the hypertensive patients with MS had lower dipping rate and higher AASI in 24-hour ABPM. Furthermore, the correlation between lower dipping rate and higher AASI were more prominent when MS is present.

AASI has been considered as a novel surrogate for arterial stiffness which has the advantage to be easily measured by the ABPM [21]. The theoretical base is that for a given increase in diastolic BP, systolic BP is expected to increase to a limited extent in a compliant artery due to appropriate accommodation, but this increase will be greater in

Table 1. Clinical characteristics of the patients population with presence (+) or absence (-) of the metabolic syndrome (MS)

	MS + (n=50)	MS – (n=54)	p value
Age, years	49.2 ± 7.7	44.6 ± 11.2	0.016
Male, n (%)	43 (86)	47 (87)	0.877
Height, cm	169.3 ± 6.7	170.0 ± 6.8	0.597
Weight, kg	76.4 ± 9.4	72.5 ± 8.6	0.034
BMI, kg/m^2	26.6 ± 2.4	25.0 ± 2.1	0.001
Smoking, n (%)	16 (32.7)	15 (29.4)	0.726
HTN medication n, (%)	37 (74)	35 (64.8)	0.311
Beta blockers, n (%)	7 (14.3)	5 (9.4)	0.447
Calcium blockers, n (%)	21 (42.9)	19 (35.8)	0.469
ACEI/ARBs, n (%)	25 (50.0)	22 (40.7)	0.343
Diuretics, n (%)	9 (18.4)	9 (17.0)	0.854
Statin medication, n (%)	12 (24.5)	6 (11.3)	0.081
Blood urea nitrogen, mg/dL	14.8 ± 3.9	14.4 ± 3.0	0.674
Creatinine, mg/dL	1.14 ± 0.18	1.09 ± 0.14	0.187
Fasting glucose, mg/dL	112.1 ± 16.1	96.5 ± 10.8	< 0.001
Total cholesterol, mg/dL	211.2 ± 48.3	199.9 ± 33.9	0.175
LDL-cholesterol, mg/dL	118.5 ± 42.8	122.9 ± 31.3	0.577
HDL-cholesterol,mg/dL	50.1 ± 14.1	54.2 ± 10.6	0.104
Triglyceride, mg/dL	210.7 ± 134.7	122.7 ± 56.9	< 0.001

BMI: body mass index, ACEI: angiotensin converting enzyme inhibitors, ARBs: angiotensin receptor blockers, LDL: low-density lipoprotein, HDL: high-density lipoprotein.

a stiff artery [21]. Therefore, the slope derived from individual plotting of 24 hour BP values on the graph of diastole on systole will be less steep in non-compliant artery. AASI derived from 1 minus the regression slope of diastolic BP against systolic BP will be greater in stiffer artery and vice versa. However, there are still debates on reliability of the AASI as a surrogate for systemic arterial stiffness [16,22,23]. Nevertheless according to large population studies, AASI can provide an useful information as a prognostic marker indicating target organ damage [6], fatal stroke [24], and cardiovascular mortality [8].

The prevalence of MS increases with age in both men and women and the association of MS with non dipper hypertension were demonstrated in previous studies [14,15,25]. The independent association between MS and AASI was also revealed by Leocini *et al.* [15]. They hypothesized that the attribution of MS on arterial stiffness could

Table 2. Comparison of 24 hour ambulatory blood pressure monitoring with presence (+) or absence (-) of the metabolic syndrome (MS)

	MS + (n=50)	MS – (n=54)	p value
24-hour average sBP, mmHg	13.61 ± 14.1	135.11 ± 14.7	0.116
24-hour average dBP, mmHg	88.3 ± 9.5	92.4 ± 10.0	0.038
24-hour average PP, mmHg	38.6 ± 5.3	38.8 ± 7.7	0.886
24-hour MAP, mmHg	109.5 ± 11.1	113.7 ± 11.6	0.058
24-hour Average HR, mmHg	69.4 ± 9.0	68.3 ± 9.5	0.624
Dipping rate systolic	8.1 ± 6.3	10.1 ± 5.1	0.085
Dipping rate diastolic	10.2 ± 7.4	13.3 ± 7.1	0.034
Dipping rate average	9.2 ± 6.6	11.7 ± 5.8	0.043
AASI	0.400 ± 0.196	0.329 ± 0.146	0.038

sBP: systolic blood pressure, dBP: diastolic blood pressure, PP: pulse pressure, MAP: mean arterial pressure, HR: heart rate, AASI: ambulatory arterial stiffness index.

Table 3. Multivariate regression analysis demonstrating association between metabolic syndrome and potential predictors in entire hypertension patients

Variables	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	1.054	1.007 ~ 1.103	0.023	1.062	1.012 ~ 1.114	0.015
AASI*	1.285	1.011 ~ 1.634	0.041	1.340	1.020 ~ 1.761	0.036
Dipper average	0.935	0.876 ~ 0.999	0.047	0.931	0.863 ~ 1.004	0.064
Average MAP	0.966	0.932 ~ 1.002	0.063	0.959	0.920 ~ 0.999	0.045

* Per 0.1 increase, AASI: ambulatory arterial stiffness index, MAP: mean arterial pressure.

be due to its own components from definition such as obesity, hypertension, glucose intolerance and hyperlipidemia. Furthermore, it might be affected by unmeasured variables such as pro-inflammatory state, endothelial dysfunction, hyperactivity of the sympathetic nervous system and the renin-angiotensin system that are often concomitant with MS [15]. These are all in the same line with our study results which MS in the hypertensive patients could be featured well with increased age, low dipping rate, and higher AASI.

In the present study, we have demonstrated that the correlation between AASI and average dipping rate was higher in the patients with MS than those without MS. Non-dipping pattern from the 24-hour ABPM data has been considered as an indicator for target organ damage or a predictor for cardiovascular events, considering its association with alteration in the autonomic nervous activity and inflammation status [26,27]. Long duration of

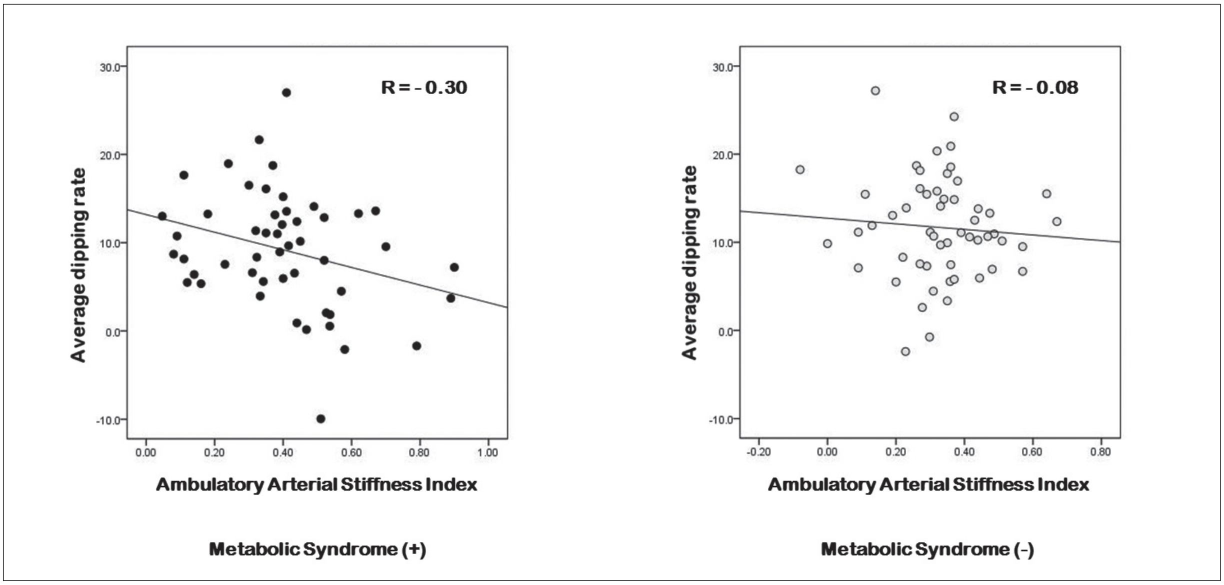

Fig. 1. Correlation between average dipping rate and ambulatory arterial stiffness index varies with presence or absence of metabolic syndrome.

these alterations would indeed impair the vascular response resulting in altered BP and increased arterial stiffness. Actually, Schillaci *et al.* [16] proposed close relationship between high ambulatory stiffness index and reduced nocturnal BP decline. As a mathematical consequence, in non-dipping subjects, the coefficient of regression B of diastolic over systolic BP over the 24-hours tends to decrease, and its reciprocal (AASI, or 1-B) tends to increase [16]. Along with these results, we also found the inverse relationship between AASI and day-night BP dipping rate, and the correlation increased with the presence of MS. The explanation for this result is that the patients with MS will possess the typical characteristics such as pro-inflammatory state, endothelial dysfunction, hyperactivity of the sympathetic nervous system and the renin-angiotensin system with the insulin resistance, and these characteristics can affect decreased day-night BP difference as well as arterial stiffness (or mathematically derived AASI), increasing the relation of the two variables.

Study limitations

There were several limitations in this study. First, the present study is a single center study and the study populations were relatively small. Therefore, further study with larger populations would be needed. Second, 24-hr ABPM was done by the clinician's discretion and there may be selection bias. Third, although there have been several diagnostic criteria for the MS, we only applied NCEP-ATP III criteria because it was the most popular in current era and the articles we referred were using the NCEP-ATP III criteria. Fourth, we measured BP twice per hour at day-time and once per hour at night-time. Low frequency of BP data acquisition compare to other studies that measured three times per hour at day-time and twice per hour at night-time can result in relatively lower predictive power [8,21]. Last, we did not compare AASI with other stiffness measures such as pulse wave velocity.

Conclusion

In the present study, we show that MS in hypertension may contribute to the phenomenon of low dipping rate and has a robust relationship with vascular stiffness such as AASI. We focused on the AASI and day-night BP dipping rate as determinants for MS. Therefore, these results would be useful to provide information to improve the understanding of characteristics of MS.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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