Original Article

Use of Plasma B-Type Natriuretic Peptide Level to Identify Asymptomatic Hypertensive Patients with Abnormal Diurnal Blood Pressure Variation Profiles: Nondippers, Extreme Dippers, and Risers

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We examined the relationship between plasma B-type natriuretic peptide (BNP) level and diurnal variability pattern of blood pressure (BP). Twenty-four-hour ambulatory BP monitoring was performed in 98 patients with asymptomatic essential hypertension, and the patients were classified into four groups according to their circadian BP variation profiles: dippers (n=29), nondippers (n=36), extreme dippers (n=19), and risers (n=14). Plasma BNP was measured by enzyme immunoassay. Based on the distribution pattern of BNP values, the values were analyzed after logarithmic transformation. Significant differences in plasma BNP levels among the types of circadian BP variations were demonstrated by analysis of variance (p<0.0005). Nondippers and risers showed significantly higher plasma BNP levels (mean [range: −1 SD and +1 SD]: 16.1 [6.3, 41.6] pg/mL and 29.2 [15.9, 53.4] pg/mL, respectively) than dippers (8.4 [3.7, 19.1] pg/mL). The area under the receiver operating characteristics curve for distinguishing patients with abnormal circadian BP variation from those with normal variation was 0.72, indicating that plasma BNP levels were useful for distinguishing between these patients. Specificity of 69% and sensitivity of 72% were obtained with a cut-off value of 10.5 pg/mL (log plasma BNP, 1.02) for distinguishing the abnormal diurnal BP profile group from the normal group. In conclusion, hypertensive patients with abnormal diurnal BP variation patterns (nondippers, extreme dippers, and risers) showed higher plasma BNP levels than those with normal circadian BP variation (dippers). Plasma BNP level is clinically useful for the identification of hypertensive patients who have abnormal circadian BP variability, which increases the risk of cardiovascular events. (*Hypertens Res* 2007; 30: 651–658)

***Key Words*: clinical study, essential hypertension, ambulatory blood pressure monitoring, peptide, immunoassay**

Introduction

Ambulatory blood pressure monitoring (ABPM) has been used to evaluate the relationship between the diurnal variation of blood pressure (BP) and various cardiovascular risks. Circadian variation of BP determined by 24-h ABPM can be classified into four types of patterns: dippers, who show normal circadian variations of BP, *i.e.*, appropriate nocturnal BP fall patterns; nondippers, who have diminished nocturnal BP

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Table 1. Patients' Characteristics and Echocardiographic Findings

	All patients	Dippers	Nondippers	Extreme dippers	Risers (inversed dippers)	*p**	Patients with abnormal diurnal BP profile (nondipprers+extreme dippers+risers)	*p***
Number of patients	98	29	36	19	14		69	
Age (years)	57.2±11.1	54.3±11.3	57.5±11.2	56.0±10.2	64.1±9.6	n.s.	58.4±10.9	n.s.
Men:Women	58:40	17:12	22:14	9:10	10:4	n.s.	41:28	n.s.
Weight (kg)	65.3±11.1	65.1±11.5	66.6±10.5	64.4±10.2	63.6±13.5	n.s.	65.4±11.0	n.s.
Height (cm)	162.1±8.7	163.9±9.9	162.8±8.2	158.9±8.5	161.2±7.0	n.s.	161.4±8.2	n.s.
BMI (%)	24.8±3.5	24.0±2.4	25.2±3.8	25.5±3.8	24.4±4.2	n.s.	25.1±3.9	n.s.
Obesity (−:+)	56:42	18:11	20:16	10:9	8:6	n.s.	38:31	n.s.
DM (−:+)	72:26	24:5	27:9	14:5	7:7	n.s.	48:21	n.s.
HbA1c (%)	5.537±0.813	5.288±0.440	5.474±0.975	5.721±0.766	5.931±0.863	n.s.	5.635±0.903	n.s.
HL (−:+)	75:23	19:10	31:5	15:4	10:4	n.s.	56:13	n.s.
Cerebral infarction (−:+)	84:14	27:2	31:5	17:2	9:5	n.s.	57:12	n.s.
Creatinine (mg/dL)	0.779±0.179	0.791±0.173	0.786±0.194	0.741±0.129	0.788±0.218	n.s.	0.774±0.182	n.s.
Urinary protein (−: ± [10–20 mg/dL]: + [≒30 mg/dL])	66:21:11	19:8:2	25:7:4	11:3:5	11:3:0	n.s.	47:13:9	n.s.
Drug administration (*n*)								
α-Blocker	4	1	1	0	2	n.s.	3	n.s.
β-Blocker	10	3	3	1	3	n.s.	7	n.s.
ACEI	0	0	0	0	0	—	0	n.s.
ARB	29	6	12	7	4	n.s.	23	n.s.
CCB	23	5	10	2	6	n.s.	18	n.s.
Echocardiography								
LVDd (cm)	4.73±0.46	4.62±0.51	4.88±0.44	4.68±0.35	4.63±0.46	n.s.	4.77±0.43	n.s.
LVDs (cm)	2.80±0.52	2.67±0.68	2.94±0.46	2.79±0.40	2.70±0.36	n.s.	2.85±0.43	n.s.

BMI, body mass index; DM, diabetes mellitus; HL, hyperlipidemia; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; *n*, number of patients; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic volume. *Probability of differences among 4 group patients determined by ANOVA. **Probability value between patients with normal diurnal BP profile (dippers) and with abnormal diurnal BP profiles (nondippers+extreme dippers+risers). n.s., not significant.

falls; extreme dippers, who show marked nocturnal BP falls; and risers (inverted dippers), who exhibit reversible nocturnal BP "riser" patterns (*1*). Many studies (*2–6*) have found that nondippers are more likely than dippers to have impaired organs such as brain, heart, and kidney, and to show poorer prognoses for cardiovascular events. Furthermore, extreme dippers, who have a subtype of abnormal diurnal BP variation (*7*), show higher frequencies of both silent and clinical cerebrovascular disease than dippers in elderly patients with sustained hypertension (*2*, *7*). Risers have also been reported to show increased cardiac mortality (*8*). These lines of evidence indicate that diurnal variation of BP is associated with a risk of cardiovascular events, and that determination of the circadian BP change pattern is essential for decreasing the risk of cardiovascular events in patients with hypertension.

B-type natriuretic peptide (BNP) is a peptide hormone derived from atrial and ventricular cardiomyocytes (*9–11*). It has been well documented that circulating plasma BNP levels are elevated under conditions characterized by various types of cardiac overload (*11–13*). BNP activation reflects hemodynamic alterations and left ventricular dysfunction. The plasma BNP level thus provides prognostic information and has been reported to be an important clinical tool (*9*, *14–17*). It has also been reported that plasma BNP levels are higher in patients with hypertension associated with changes in ventricular function and structure than in those without such changes (*18*, *19*).

Based on these reported findings, it can be theoretically assumed that ventricular overload would be larger in patients with essential hypertension in association with abnormal circadian BP changes—that is, nondippers, extreme dippers, and risers—than in those with a normal diurnal BP variation pattern, *i.e.*, dippers. We hypothesized that plasma BNP levels would be higher in hypertensive patients with abnormal diurnal BP variation patterns than in those with normal patterns. No reported study, however, has examined plasma BNP lev-

Table 2. Results of Blood Pressure (BP) Measurements in Dippers, Nondippers, Extreme Dippers and Risers

	All patients	Dippers	Nondippers	Extreme dippers	Risers (inversed dippers)	*p**	Patients with abnormal diurnal BP profile (nondipprers+extreme dippers+risers)	*p***
Office blood pressure								
SBP (mmHg)	149.1±21.8	147.1±21.9	150.3±21.0	150.7±25.4	148.3±20.5	n.s.	150.0±21.9	n.s.
DBP (mmHg)	89.7±14.7	90.5±12.7	90.1±16.8	89.1±14.3	88.1±15.2	n.s.	89.4±15.6	n.s.
MBP (mmHg)	109.5±16.2	109.4±14.9	110.1±17.2	109.6±17.2	108.2±16.2	n.s.	109.6±16.8	n.s.
HR (bpm)	71.9±12.7	74.6±15.3	69.9±11.5	74.2±12.5	68.1±8.6	n.s.	70.7±11.3	n.s.
24-h ABPM								
SBP (mmHg)	139.3±15.5	140.9±14.7	141.3±14.4	136.5±18.0	135.0±16.4	n.s.	138.7±15.8	n.s.
DBP (mmHg)	90.5±12.5	93.5±11.9	92.3±12.1	87.6±13.9	83.3±10.2	<0.05	89.2±12.7	n.s.
MBP (mmHg)	106.8±12.7	109.3±11.9	108.6±12.0	103.9±14.5	100.5±11.4	n.s.	105.7±12.9	n.s.
HR (bpm)	76.7±10.5	79.3±10.5	75.2±9.9	81.4±10.0	68.9±7.5	<0.005	75.6±10.3	n.s.
SD of SBP (mmHg)	17.4±4.7	16.7±2.9	15.1±3.8	23.0±4.7	17.5±3.8	<0.0001	17.8±5.3	n.s.
SD of DBP (mmHg)	12.2±3.4	11.2±2.7	12.7±4.3	13.2±2.5	11.7±2.3	n.s.	12.6±3.6	n.s.

SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; HR, heart rate; ABPM, ambulatory blood pressure monitoring. *Probability of differences among 4 group patients determine by ANOVA. **Probability value between patients with normal diurnal BP profile (dippers) and with abnormal diurnal BP profiles (nondippers+extreme dippers+risers); n.s., not significant.

els in hypertensive patients in connection with the 24-h BP variation pattern. We accordingly performed 24-h ABPM in patients with essential hypertension concomitantly with plasma BNP level measurements and analyzed the relationship between plasma BNP level and diurnal BP variation pattern.

Methods

Patients

We performed 24-h ABPM in asymptomatic patients with essential hypertension. Patients with hypertension who had identifiable or "secondary" disorders responsible for the elevated BP were excluded from the present study (*20*, *21*). Patients with pathological conditions other than diurnal BP pattern that caused an increase in plasma BNP level were also excluded from the study. The underlying pathological conditions for the exclusion were ischemic heart disease, cardiomyopathy, and arrhythmia, decreased left ventricular systolic function (left ventricular ejection fraction $<50\%$), increased left ventricular mass (left ventricular mass index >143 g/m^2), disturbed renal function (serum creatinine greater than our institutional normal range: 100 μmol/L), and heart failure (New York Heart Association functional class $\geq$II). Finally, 98 patients with essential hypertension who did not meet the exclusion criteria were analyzed. The patients' characteristics are listed in Table 1.

Twenty-Four-Hour ABPM

We performed 24-h ABPM using an appropriate device (FM-200 or FM-800, Fukuda Denshi Co., Ltd., Tokyo, Japan). The test procedure complied with the rules of the Helsinki Declaration; informed consent was obtained from all subjects, and the study was approved by our institutional ethics committee for human research under the guidelines for clinical studies of the Helsinki Declaration of 1975, as revised in 1997 (*22*). After we checked the performance of the equipment and carefully instructed the patients on how to use the equipment, ABPM was performed. BP and heart rate (HR) were recorded every 30 min for 24 h. Each patient's diary and 24-h ABPM tracing were evaluated immediately after completion of the recording. The averaged values of systolic BP (SBP), mean BP (MBP), diastolic BP (DBP), pulse pressure, and HR from the 48 readings in the 24-h ABPM were used for statistical analyses.

The sleep BP was obtained from the time when the patient went to bed until the time of awakening, and the awake BP was acquired during the remaining portion of the day. The nocturnal SBP fall was calculated as (awake SBP − sleep SBP)/awake SBP. The diurnal variation pattern of BP was classified into four types in accordance with established reports: dippers, who had appropriate nocturnal SBP fall patterns (10–20% SBP decrease compared with awake SBP); nondippers, who had almost no nocturnal SBP falls (0–10% SBP fall compared with awake SBP); extreme dippers, who showed marked nocturnal SBP falls (>20% SBP fall compared with awake SBP); and risers (inverted dippers), who exhibited nocturnal BP "riser" patterns (SBP elevation compared with awake SBP) (*1*, *8*).

Office BP was obtained in the sitting position using an automated oscillometric BP measuring device (HEM-907, Omron Healthcare Co., Ltd., Kyoto, Japan). The average of

Table 3. Correlation of Plasma log BNP Level with Blood Pressure Measurements at Office and by 24-h ABPM

	r	*p*
Office blood pressure		
SBP	—	n.s.
DBP	—	n.s.
HR	−0.22	<0.05
24-h ABPM		
SBP	—	n.s.
DBP	—	n.s.
HR	−0.47	<0.0001
SD of SBP	—	n.s.
SD of DBP	—	n.s.

BNP, B-type natriuretic peptide; ABPM, ambulatory blood pressure monitoring; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; *p*, probability value; n.s., not significant.

two measurements was used to determine office BP.

Blood Sampling

Blood samples were drawn from a peripheral vein into ethylenediaminetetraacetic acid–containing tubes on the day when 24-h ABPM was performed. The BNP concentration was measured using the Determiner BNP Test™ by enzyme immunoassay (Kyowa Medex Co., Ltd., Tokyo, Japan). The precision, analytical sensitivity, and stability characteristics of the system have been described previously (*9*, *23*, *24*).

Statistics

Based on the distribution patterns of BNP values, the values were transformed into a common logarithm (*25*, *26*). Data are expressed as mean±SD. For continuous variables, the *F*-test was used to analyze equal variance of the data between the two groups. Student's *t*-test or the Mann-Whitney *U* test was used to compare data between groups when the variance of the data was equal or not, respectively. We employed one-way analysis of variance with Bonferroni's *t*-test to assess the differences in data among the dippers, extreme dippers, nondippers, and risers. For categorical variables, the χ^2 test with crosstabs was used for comparison. The receiver operating characteristic (ROC) curve was used to estimate the sensitivity and specificity of plasma BNP levels for distinguishing patients with abnormal diurnal BP variation patterns (nondippers, extreme dippers, and risers) from patients with normal diurnal BP variation patterns (dippers). A *p* value of <0.05 was considered significant.

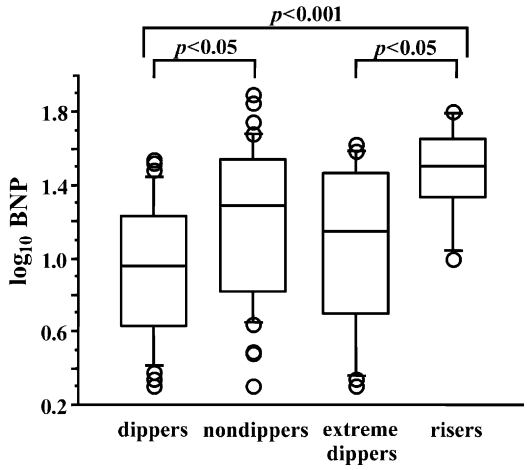

Fig. 1. *Box-plot representation of the common log-transformed plasma BNP level (log BNP) distribution among dippers, extreme dippers, nondippers, and risers. The box represents the middle half of the data, the whiskers extend to the extreme values, and the line inside the box represents the median. p, probability value.*

Results

Characteristics of the Study Participants

There were no significant differences in age, gender, or body mass index among the four BP diurnal profile groups or between patients with normal diurnal BP profiles (dippers) and those with abnormal profiles (nondippers, extreme dippers, and risers) (Table 1). Furthermore, there were no significant differences in the proportion of patients with hyperlipidemia or diabetes mellitus among the four BP diurnal profile groups or between the normal and abnormal diurnal BP profile groups. The present study included only patients with serum creatinine in the normal range. Few patients showed proteinuria, and there were no significant differences in serum creatinine levels or proteinuria among the four groups or between patients with normal and abnormal diurnal BP profiles, though extreme dippers showed a somewhat high percentage with proteinuria. There were also no significant differences in silent cerebral infraction detected by computed tomography (*27*, *28*) among the four groups or between the two groups. The χ^2 test with cross tabulation showed no significant differences in the percentage of use of any drugs among the four daily profile patterns. Similarly, no significant differences were observed in the percentage of the use of any drugs between the patients with normal and those with abnormal diurnal BP profiles.

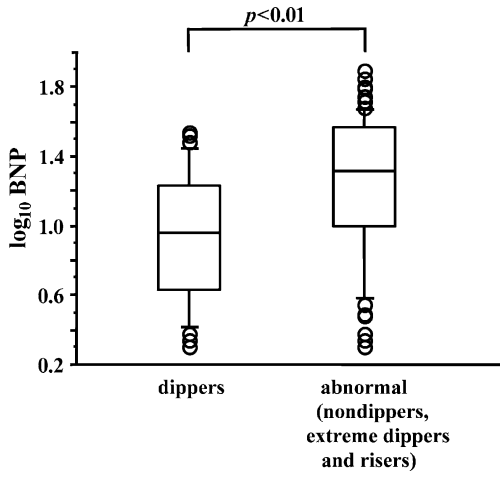

Fig. 2. *Box-plot representation of log-transformed plasma BNP level (log BNP) distribution in patients with normal (dippers) and abnormal (extreme dippers, nondippers, and risers) diurnal BP variation profiles. The box represents the middle half of the data, the whiskers extend to the extreme values, and the line inside the box represents the median. p, probability value.*

Echocardiographic Findings

There were no significant differences in left ventricular end-diastolic or end-systolic dimensions among the four different BP diurnal profile groups or between patients with normal and those with abnormal diurnal BP profiles (Table 1). There were no significant correlations between logarithmic-transformed plasma BNP levels (log BNP) and left ventricular end-diastolic or end-systolic volumes.

Twenty-Four-Hour ABPM

Table 2 shows the results of 24-h ABPM measurements in the four groups. Among the 98 patients studied, 29, 36, 19, and 14 patients were classified as dippers, nondippers, extreme dippers, and risers, respectively. There were no significant differences in average whole 24-h SBP among the four groups, though the diurnal SBP variation patterns did differ among them.

Relationship between Plasma BNP Level and BP Measurements

Table 3 summarizes the relationship between plasma log BNP and BP data obtained from official measurements and 24-h ABPM. There were no significant correlations between plasma log BNP level and office BP indices. Similarly, no significant correlations were obtained between plasma log BNP level and BP values obtained from 24-h ABPM.

Plasma BNP Levels among Dippers Compared to Extreme Dippers, Nondippers, and Risers

Significant differences in plasma BNP levels among the different types of circadian BP variations were demonstrated by analysis of variance ($p<0.0005$) (Fig. 1). Nondippers and risers showed significantly higher plasma BNP levels (mean, [range −1 SD and +1 SD]; 16.1 [6.3, 41.6] pg/mL and 29.2 [15.9, 53.4] pg/mL, respectively) than dippers (8.4 [3.7, 19.1] pg/mL). The plasma BNP levels in extreme dippers were 12.2 (4.3, 34.7 pg/mL). Plasma BNP levels were thus higher in the order of: dippers, nondippers and extreme dippers, and risers. Consequently, patients with abnormal diurnal BP profiles (nondippers, extreme dippers, and risers) showed significantly higher plasma BNP levels (16.8 [6.5, 43.8] pg/mL) than those with normal diurnal BP profiles (8.4 [3.7, 19.1] pg/mL) ($p<0.01$) (Fig. 2).

ROC curve analysis was performed to obtain a cutoff value of plasma BNP levels for distinguishing the dippers from extreme dippers, nondippers, and risers (Fig. 3). The area under the ROC curve of 0.72 (95% confidence interval, 0.62–0.83) indicated that plasma BNP was useful for distinguishing dippers from patients other than dippers. The specificity-sensitivity curve showed 69% specificity and 72% sensitivity with a cut-off value of 10.5 pg/mL (plasma log BNP, 1.02) for distinguishing dippers from patients other than dippers.

Discussion

The present study revealed that hypertensive patients with abnormal diurnal BP variation patterns (risers, nondippers, and extreme dippers) showed significantly higher plasma BNP levels than those with normal circadian BP variations (dippers). ROC curve analysis revealed that plasma BNP level was clinically useful for identifying hypertensive patients with abnormal diurnal BP variations, which increase the risk of cardiovascular events and worsen the prognosis of underlying conditions.

We excluded patients with decreased left ventricular function, increased left ventricular mass, decreased renal function, or association with heart failure. Patients with ischemic heart disease and cardiomyopathy were also excluded. To clarify the relationships between plasma BNP level and circadian BP variability pattern, it is essential to exclude patients with pathological conditions other than diurnal BP profiles with an increase in plasma BNP level. To obtain the circadian variation of BP, we employed 24-h ABPM. ABPM has been well demonstrated to show sufficient reproducibility and to be free of the white-coat phenomenon (*8*, *29*). Twenty-four-hour ABPM was performed with precise instrumentation and careful instructions to patients. The present methods for determining the circadian variation of BP were valid. The precision, analytical sensitivity, and stability characteristics of the present methods for the measurement of plasma BNP levels are well established (*9*, *23*, *24*). The methods for selecting

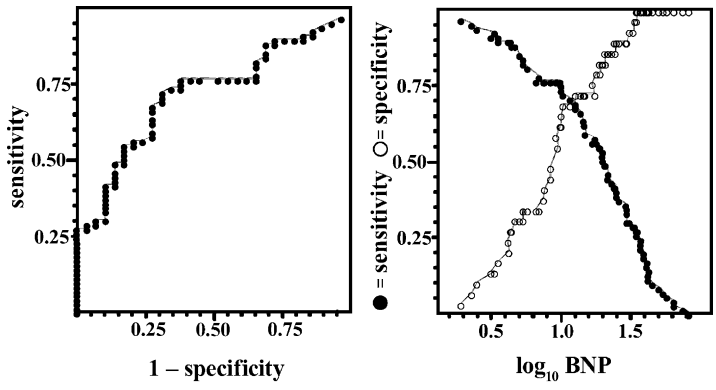

Fig. 3. *Receiver operating characteristic and specificity-sensitivity curves of log-transformed plasma BNP level (log BNP) for distinguishing patients with normal (dippers) from those with abnormal (extreme dippers, nondippers, and risers) diurnal BP variation profiles.*

patients and for measuring ABPM and plasma BNP were valid, and therefore the implications of the results can be discussed.

There were no significant differences in patient characteristics in the present study, and plasma BNP levels could thus be compared among the four groups. Several studies indicated that patients with abnormal diurnal BP variation had increased rates of cerebrovascular events and/or proteinuria (*5*, *7*, *30*). There were, however, no significant differences in silent cerebral infarction or proteinuria among the four diurnal BP variation pattern groups or between the two patient groups (those with normal or abnormal diurnal BP profiles). To make comparisons among the four groups, we excluded patients with elevated serum creatinine levels, ischemic heart disease, arrhythmia (especially atrial fibrillation), heart failure, and left ventricular hypertrophy, all of which have the potential to increase plasma BNP levels. This strict patient selection accounts for the lack of significant differences in the proportion of silent cerebral infarction or proteinuria among the four groups and between the two groups. The uniformity of the patients' characteristics confirmed that plasma BNP could be compared among the four groups and the two groups.

Although the present results revealed that patients with abnormal diurnal BP variation profiles (nondippers, extreme dippers, and risers) had higher plasma BNP levels than those without (dippers), the plasma BNP values of the patients with abnormal BP variation profiles ranged from within the normal range up to 100 pg/mL. Several studies indicated that approximately >100 pg/mL was clearly an abnormally high plasma BNP level (*25*, *31*, *32*). In contrast, plasma BNP levels of approximately <20 pg/mL were clearly shown not to be elevated (*9*, *26*, *33*). Plasma BNP levels between 20 and 100 pg/mL were thus in a gray zone of plasma BNP levels or in a mildly elevated range. Three-quarters of dippers had plasma BNP levels within the normal range. In contrast, approximately half of patients with abnormal diurnal BP variation patterns (nondippers, extreme dippers, and risers) showed plasma BNP levels between 20 and 100 pg/mL, that is, in the gray zone of plasma BNP levels. The present results also indicated that the high normal range of plasma BNP levels may be a helpful marker for the identification of asymptomatic hypertensive patients with abnormal diurnal BP profiles. Although there was some overlap in plasma BNP levels between patients with abnormal BP daily patterns and those without, and the area under the ROC curve was not so high, the present results indicate that plasma BNP levels provide some information useful for identifying patients with abnormal daily BP profiles, which increase the risk for cardiovascular events.

There were no significant differences in left ventricular end-systolic or end-diastolic dimensions between patients with normal diurnal BP variation and those without. In addition, plasma log BNP was not significantly correlated with these indices. Only hypertensive patients with preserved left ventricular function and without an increase of left ventricular mass index were included in the present study. This strict patient selection may account for the lack of a significant difference in log BNP among the four groups and for the dissociation of plasma BNP and these left ventricular indices. Our comparison between plasma BNP levels and echocardiographic indices among patients with the four different types of diurnal BP profiles indicated that plasma BNP level was more sensitive than echocardiographic indices for detecting hypertensive patients with abnormal diurnal BP variations.

The present study did not primarily deal with the mechanisms underlying plasma BNP elevation in patients with abnormal daily BP sequence patterns. It is well known that autonomic nervous function with baroreflex sensitivity plays essential roles in the circadian variation of BP. Impairment of autonomic nervous function and/or baroreflex sensitivity evokes pathological conditions. In fact, changes in the sympathetic nervous system and baroreflex sensitivity have been

demonstrated in patients with abnormal diurnal BP variation patterns (*7*, *34–36*). A disturbed balance of autonomic nervous activity causes an abnormal daily BP profile associated with cardiac overload. In fact, several studies clarified that patients without reduced nocturnal BP reduction (nondippers) showed larger cardiac structural changes and greater left ventricular hypertrophy than dippers (*37–40*). These studies indicated that greater left ventricular overload occurs in patients with abnormal circadian BP variation than in those without. There were no significant differences in left ventricular diastolic dimension or systolic dimension between patients with normal *vs*. abnormal diurnal BP profiles in the present study. Abnormal daily changes of BP produce ventricular overloading, resulting in plasma BNP elevation. One study (*41*) examined the relationship between adiponectin levels and insulin sensitivity in untreated uncomplicated patients with essential hypertension. In that study, although left ventricular mass, relative wall thickness, and both early and late diastolic peak flow velocity ratios were comparable between dippers and nondippers, dippers showed higher insulin resistance as evaluated by HOMA (homeostasis model assessment) index, as well as lower adiponectin levels than dippers. These results indicated that the atherosclerotic process may progress more prominently in nondippers than dippers before cardiac structural changes occur. These are possible mechanisms accounting for the association between plasma BNP levels and abnormal circadian variability of BP observed in the present study. Further discussion of this issue is inappropriate here because of the lack of direct results concerning this issue.

One of the limitations of the present study was that it included a relatively small number of patients due to the strict patient selection. On the other hand, this careful patient selection, based on theoretical considerations and precise methods, may compensate for this limitation. This limitation is thus not a major weakness of the present study.

In conclusion, the present study revealed that plasma BNP level is clinically useful for the identification of hypertensive patients who have abnormal circadian BP variability (nondippers, extreme dippers, and risers), which increases the risk of cardiovascular events.

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