Limited Reproducibility of Circadian Variation in Blood Pressure Dippers and Nondippers

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The relation between blood pressure (BP) variation and hypertensive organ damage is controversial. The reproducibility of the circadian variation pattern acceptable as the standard for discriminating between “dippers” and “nondippers” has not yet been evaluated. We evaluated the reproducibility of “dipper” and “nondipper” patterns in essential hypertensives by monitoring BP for 48 h.

Noninvasive ambulatory BP and heart rate (HR) monitoring for 48 h every 30 min were performed in 253 untreated patients with mild-to-moderate essential hypertension. Mean daytime (awake) and nighttime (sleeping) systolic BP, diastolic BP, and HR values were analyzed by reviewing the patients’ diaries. Patients were divided into two groups by presence (dippers) and absence (nondippers) of a reduction of both systolic and diastolic BP during the night of > 10% of the daytime pressure. A subject who was a dipper on day 1 remained a dipper on day 2 in 41% (n = 103, DD group) and changed to nondipper in 16% (n = 41, DN group). A subject who was a nondipper on day 1 remained a nondipper on day 2 in 30% (n = 75, NN group) and changed to a dipper in 13% (n = 34, ND group).

Our findings indicate that there is a high risk of false-positive or false-negative results when 24-h recordings are used to identify dipper and nondipper profiles. Am J Hypertens 1998; 11:403–409 © 1998 American Journal of Hypertension, Ltd.

KEY WORDS: Ambulatory blood pressure, nocturnal reduction rate, dipper, nondipper, hypertension.

Circadian variation in blood pressure has been evaluated in terms of the average, mean, 24-h, daytime, and nighttime blood pressures, as determined by ambulatory blood pressure monitoring (ABPM).1,2 Individuals who do not exhibit a nocturnal decline in blood pressure (nondipper) are believed to have an increased risk of cardiovascular complications compared with individuals who experience a nocturnal decline (dippers). Data on the day-to-day variations in blood pressure and heart rate in dippers and nondippers are inconclusive.3,4

A longer observation period increases the accuracy of ABPM evaluation of the circadian blood pressure profile. However, in the clinical setting practical considerations and patient noncompliance may limit the duration of the observation period. Thus, a compromise is needed between the optimal theoretical duration of ABPM and considerations of practicality and convenience.4,5 Although most studies in hypertensive
patients have performed ABPM for 24 h, Tamura et al.\textsuperscript{5} reported that a 48-h monitoring period was superior to a 24-h monitoring period.

We assessed the day-to-day variations in blood pressure and heart rate in untreated patients with essential hypertension who we classified as dippers or nondippers using 48-h ABPM.

**SUBJECTS AND METHODS**

We studied 253 patients with untreated essential hypertension (134 men, 119 women, 22 to 80 years old) in an open, nonstratified, nonrandomized manner. These patients had never been treated before this study. Casual blood pressure readings were obtained by the cuff method according to the American Heart Association recommendations.\textsuperscript{6} Hypertension was defined according to the World Health Organization/International Society of Hypertension (WHO/ISH) criteria\textsuperscript{7} as follows: systolic blood pressure \(\geq 140\) mm Hg and diastolic pressure \(\geq 90\) mm Hg on at least two occasions in the month preceding the study.\textsuperscript{5,9} Individuals with cardiovascular disorders other than essential hypertension were excluded.

Blood pressure and heart rate were monitored with a noninvasive ABPM system (ABPM-630, Nippon Colin Electronics Co., Ltd, Komaki, Japan) every 30 min for 48 h by the oscillometric method. When the device was attached to the patient, the pressure difference between the device and a mercury manometer was \(< 5\) mm Hg. Subjects were shown how to change the gas cartridges. Patients were asked to go to bed at about 23:00 and to stay in bed until 07:00 and to eat meals between 07:00 and 08:00, 12:00 and 13:00, and 18:00 and 19:00 to lessen the variations in everyday conditions. Apart from these conditions, the patients were free to pursue their normal daily activities. Patients were asked to keep a detailed diary, paying special attention to the times at which they awoke and went to bed, so that we could separate awakening daytime and resting nighttime periods.\textsuperscript{10–15} The data were analyzed with a computer (PC-9801, NEC, Tokyo, Japan) using homemade software.\textsuperscript{16} Some patients had less than five invalid recordings per 24 h of blood pressure. There were no significant differences in the frequency of invalid recording between daytime and nighttime, nor between the first day and the second day. We calculated the mean 48-h, daytime, and nighttime blood pressures and heart rates. The nocturnal decline in blood pressure was calculated according to the method of Verdecchia et al.\textsuperscript{17} Subjects were classified as dippers if they exhibited a \(> 10\%\) nocturnal decline in blood pressure. We divided the subjects into four groups based on their dipper/nondipper profiles for each 24 h: dipper on both day 1 and day 2 (DD group); dipper on day 1 and nondipper on day 2 (DN group); nondipper on day 1 and dipper on day 2 (ND group); and nondipper on both day 1 and day 2 (NN group). Values are expressed as the mean \pm standard deviation. The significance of pairwise differences was assessed using Student’s paired \(t\) test. The differences among the four groups were tested using ANOVA. If significant \((P < .05)\), an F ratio was obtained; Fisher’s protected least significant difference test was used to locate significant differences. \textsuperscript{5,9} A \(P < .05\) was considered statistically significant.

**RESULTS**

There were no significant differences in patient characteristics, except for age, among subgroups classified according to circadian profile (Table 1).

### Day-to-Day Variability of Dipper and Nondipper Profiles

A dipper pattern was observed in 144 (57\%) of 253 patients on day 1 and a nondipper pattern in 100 patients (43\%). Of the 144 patients who showed a dipper pattern on day 1, 108 (72\%)
again showed a dipper pattern on day 2 (DD group), while 41 (28%) showed a nondipper pattern on day 2 (DN group) (Figure 1). Of the 109 patients who showed a nondipper pattern on day 1, 75 (69%) again showed a nondipper pattern on day 2 (NN group), while 34 (31%) showed a dipper pattern (ND group) (Figure 2).

**Systolic Blood Pressure**  The mean 24-h SBP on days 1 and 2 and the mean 48-h SBP were significantly higher in the NN group than in the DD group (Table 2). The mean 48-h daytime SBP did not differ significantly between these groups or between day 1 and day 2. The mean nighttime SBP was significantly higher in the ND and NN groups compared with the DD group on day 1. The day 2 nighttime SBP and the 48-h SBP were significantly lower in the DD group than in the other groups, and higher in the NN group than in the DN and ND groups.

**Mean Diastolic Blood Pressure**  The mean 24-h DBP on day 1 and day 2 and the mean 48-h DBP were significantly higher in the NN group than in the DD group. There were no differences among these groups in the mean daytime DBP. The mean daytime DBP was lower on day 2 compared with day 1 in the DD group. The mean nighttime DBP was significantly lower in the DD group than in the other groups. The mean nighttime DBP was higher on day 2 in the DN group and lower on day 2 in the ND group compared with day 1 values.

**Mean Heart Rate**  The mean 24-h heart rate in the DD group was higher compared with the ND and NN groups on day 1 and as compared with the DN and NN groups on day 2. On day 1, the mean daytime heart rate was higher in the DD group than in the ND and NN groups. On day 2, the daytime heart rate was higher in the DD group than in the DN and NN groups. In the DN group, the mean heart rate on day 2 was lower than that on day 1. The mean 48-h heart rate was lower in the NN group than in the DN and NN groups than in the DD group. The mean nighttime heart rate showed no significant differences between groups or between days.

**Nocturnal Reduction**  As shown in Figure 3, there was significant concordance of the nocturnal reduction of systolic or diastolic BP on day 1 with that on day 2 (r = 0.52 and r = 0.53, respectively).

The nocturnal decline in SBP was significantly greater (P < .01) in the DD group than those in the DN, ND, and NN groups on day 1. On day 2, there were significant (P < .01) differences in the nocturnal decline among each pair of groups (Table 3).

The nocturnal decline in SBP differed between days 1 and 2 in the DN and ND groups. The nocturnal decline in 48-h SBP was greater in the DD group than those in the other groups and the smallest in the NN group. The pattern of the decline in DBP was similar to the pattern of the decline in SBP.

The nocturnal decline in heart rate was smaller in the NN group than in the DD, DN, and ND groups for day 1, day 2, and the 48-h mean, except for day 1 in the ND group. There was no difference between day 1 and day 2 in the ND group.

**DISCUSSION**

Hypertensive subjects exhibit a greater day-to-day variability in blood pressure than normal subjects. Although most studies assessing the circadian blood...
pressure and heart rate profiles have used 24-h monitoring, Tamura et al\textsuperscript{5} suggested that 48-h ABPM is superior to 24-h ABPM for analyzing circadian variations in blood pressure.

Another unresolved issue related to ABPM is the definition of the zero hour. Although the consensus is that daytime and nighttime pressures should be determined based on the biologic zero hour, the determination of the biologic zero hour is controversial. We have proposed use of the midpoint of the sleeping hours as the biologic zero hour for ABPM.\textsuperscript{18} However, in the present study the zero hour was based on the patients’ diaries. We previously found that data obtained from patients’ diaries are consistent with that obtained using an actigraph.\textsuperscript{19,20}

Data on the day-to-day variability of blood pressure in subjects with dipper and nondipper profiles are limited.\textsuperscript{3} Studies have shown that a blunted or absent

![FIGURE 2](image_url) Results of reproducibility analysis of dipper and nondipper status on day 1 and day 2. Numbers of patients and percentages are shown.

![FIGURE 3](image_url) The relationship of nocturnal reduction rate of systolic and diastolic blood pressure and heart rate on day 1 with that on day 2. Significant concordance was seen for nocturnal reduction of blood pressure and heart rate. Nocturnal reduction of blood pressure in most of the subjects was on the order of 10% or so.
The nocturnal decline in blood pressure is associated with a greater left ventricular mass.\textsuperscript{17,21,22}

In the present study, the SBP was higher in subjects who showed a nondipper pattern on both days compared with subjects who showed a dipper pattern on both days. This finding may have been due in part to the fact that NN subjects were older than DD subjects. The nighttime SBP was higher in the DN, ND, and NN groups than in the DD group. The DBP was higher in both groups than in the DD group. The DBP was higher in the NN group than in the DD group, which may also be related to the older age of the NN subjects.

The pathophysiologic mechanism of the nondipper pattern has not been clarified. However, some studies\textsuperscript{3,24} suggest that the nondipper pattern may be related to increased activity at night. The activity level is correlated with changes in heart rate as determined by ABPM.\textsuperscript{25} Therefore, we analyzed the correlation between heart rate and blood pressure. There was no difference among groups in the 24-h heart rate, but the daytime heart rate was decreased in the NN group compared with the DD group. There was no difference among groups in the nighttime heart rate. However, the mean daytime heart rate on a dipper pattern day namely the both days of DD, day 1 of DN, and day 2 of ND, was greater than that on a nondipper pattern day. These findings suggest that daytime activity might be one of the determinants of the dipper/nondipper pattern.

There was no difference in the nocturnal decline in SBP and DBP among the DN, ND, and NN groups. Although the nighttime heart rate was similar in the NN and DD groups, the daytime heart rate was lower in the NN group. Thus, the nocturnal decline in heart rate was smaller in the NN group than in the DD groups.

### TABLE 2. 48-H AMBULATORY MONITORING FINDINGS

|                | DD (n = 103) | DN (n = 41) | ND (n = 34) | NN (n = 75) |
|----------------|-------------|-------------|-------------|-------------|
| **SBP (mm Hg)**|             |             |             |             |
| Day 1          | 139 ± 12    | 141 ± 11    | 145 ± 17\* | 146 ± 14**  |
| Day 2          | 139 ± 12‡   | 141 ± 12‡   | 145 ± 15*  | 147 ± 15**  |
| 48 h           | 139 ± 12‡   | 141 ± 12‡   | 145 ± 15*  | 146 ± 14**  |
| Daytime day 1  | 148 ± 12    | 148 ± 11    | 147 ± 17   | 149 ± 15    |
| Daytime day 2  | 147 ± 13    | 143 ± 13#   | 151 ± 16## | 149 ± 16    |
| Daytime 48 h   | 148 ± 12‡   | 146 ± 12    | 150 ± 15   | 148 ± 14    |
| Nighttime day 1| 121 ± 12    | 126 ± 12**††| 138 ± 17**§§| 141 ± 14**  |
| Nighttime day 2| 121 ± 12‡   | 133 ± 12**††| 128 ± 15**††| 141 ± 15**  |
| Nighttime 48 h | 121 ± 12‡   | 129 ± 12**††| 134 ± 15**††| 142 ± 14**  |

| **DBP (mm Hg)**|             |             |             |             |
| Day 1          | 83 ± 8      | 84 ± 8      | 85 ± 10     | 86 ± 9*     |
| Day 2          | 82 ± 9      | 84 ± 8      | 84 ± 10     | 86 ± 9**    |
| 48 h           | 83 ± 8      | 84 ± 8      | 85 ± 9      | 86 ± 8**    |
| Daytime day 1  | 88 ± 8      | 89 ± 8      | 87 ± 11     | 88 ± 9      |
| Daytime day 2  | 88 ± 9      | 86 ± 9#     | 89 ± 10     | 88 ± 9      |
| Daytime 48 h   | 88 ± 9      | 87 ± 8      | 89 ± 10     | 88 ± 9      |
| Nighttime day 1| 71 ± 8      | 74 ± 8**††  | 81 ± 10**§§ | 82 ± 9**    |
| Nighttime day 2| 70 ± 8      | 78 ± 7**††##| 74 ± 10**††##| 83 ± 9*     |
| Nighttime 48 h | 71 ± 8      | 75 ± 7**††  | 78 ± 9**††##| 83 ± 8**    |

| **HR (beats/min)**|             |             |             |             |
| Day 1          | 74 ± 8      | 72 ± 7      | 71 ± 8*     | 71 ± 7**    |
| Day 2          | 74 ± 8      | 71 ± 7*     | 72 ± 7     | 70 ± 8**    |
| 48 h           | 74 ± 7      | 72 ± 8      | 72 ± 7     | 72 ± 11    |
| Daytime day 1  | 80 ± 8      | 77 ± 8      | 76 ± 8*    | 75 ± 8**    |
| Daytime day 2  | 80 ± 8      | 75 ± 8**††##| 78 ± 7     | 74 ± 8**    |
| Daytime 48 h   | 80 ± 8      | 77 ± 8*     | 78 ± 7     | 75 ± 8**    |
| Nighttime day 1| 63 ± 8      | 61 ± 8      | 61 ± 8     | 62 ± 8      |
| Nighttime day 2| 63 ± 7      | 61 ± 7      | 62 ± 8     | 63 ± 8      |
| Nighttime 48 h | 63 ± 7      | 61 ± 7      | 61 ± 7     | 63 ± 8      |

\textsuperscript{Mm} ± SD:
\* P < .05, ** P < .01, compared with dipper/dipper.
\+ P < .05, †† P < .01, compared with nondipper/nondipper, § P < .05, §§ P < .01, compared with dipper/nondipper.
\# P < .05, ### P < .01, compared with day 1.

DD, dipper/dipper; DN, dipper/nondipper; ND, nondipper/dipper; NN, nondipper/nondipper; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.
The reason why there are four groups under the assessment of blood pressure over 48 h is still speculative based on our own data. The prevalence of “dippers” and “nondippers” as assessed on both of the consecutive days was 41% and 30%, respectively; the remaining 29% showed change from “dipper” to “nondipper” or from “nondipper” to “dipper.” BP circadian variation had limited reproducibility, and there were many subjects whose nocturnal reduction of systolic and diastolic BP was about 10%, contributing to the difference in assessment of the BP variation pattern for the two periods (Figure 3). Our results suggested that some subjects are invariably either “dipper” or “nondippers,” whereas other subjects show fluctuation between the two. Activity may be an important contributor to variations in the circadian blood pressure profile.19,23–26 However, differences in the level of activity appeared to have less influence in the DD and NN groups than in the ND and DN groups. The nondipper pattern is frequently associated with secondary hypertension. These observations suggest that the subjects in the NN group had a primary dysfunction of blood pressure regulation. Day-to-day variations in blood pressure profiles were observed in approximately 80% of the subjects in the present study. Thus, the DN and ND groups may have represented false-positive or false-negative results based on 24-h monitoring. Further study is needed to clarify the mechanisms of these variations in circadian profiles.

SUMMARY

The present results showed that 48-h ABPM was superior to 24-h ABPM for assessing the circadian blood pressure and heart rate profiles. Our findings indicate that there is a high risk of false-positive or false-negative results when 24-h recordings are used to identify dipper and nondipper profiles.

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TABLE 3. NOCTURNAL DECLINE

|        | DD (n = 103) | DN (n = 41) | ND (n = 34) | NN (n = 75) |
|--------|--------------|-------------|-------------|-------------|
| SBP day 1 | 18 ± 5       | 15 ± 5‡†    | 6 ± 6§      | 5 ± 5*      |
| SBP day 2 | 18 ± 5       | 7 ± 3*‡‡‡   | 15 ± 4*‡‡§# | 5 ± 5*      |
| SBP 48h  | 18 ± 4       | 12 ± 3*‡‡   | 10 ± 4*‡‡   | 5 ± 4*      |
| DBP day 1 | 20 ± 5       | 17 ± 5*‡‡   | 6 ± 7§      | 6 ± 5*      |
| DBP day 2 | 20 ± 5       | 9 ± 4*‡‡‡   | 17 ± 5*‡‡§# | 6 ± 7*      |
| DBP 48h  | 20 ± 4       | 13 ± 3*‡‡   | 12 ± 4*‡‡   | 6 ± 4*      |
| HR day 1 | 21 ± 8       | 21 ± 7‡‡‡   | 20 ± 7      | 17 ± 7*     |
| HR day 2 | 21 ± 7       | 19 ± 6‡     | 20 ± 9‡‡    | 15 ± 7*     |
| HR 48h   | 21 ± 7       | 20 ± 6‡‡‡   | 21 ± 9‡‡    | 16 ± 7*     |

(%) mean ± SD.
* P < .01, compared with dipper/dipper.
† P < .05, ‡ P < .01, compared with nondipper/nondipper.
§ P < .01, compared with dipper/nondipper.
# P < .01, compared with day 1.

DD, dipper/dipper; DN, dipper/nondipper; ND, nondipper/dipper; NN, nondipper/nondipper; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.
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