Diurnal Blood Pressure Rhythm in Hypertensives With Parental History of Stroke

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To investigate whether the lack of nocturnal decline of blood pressure (nondipper) is a primary cause of stroke or a secondary abnormality due to stroke, we examined the relation between the blood pressure variation and parental history of stroke in 110 hypertensive patients. In nondippers (n = 54), the frequency of positive parental history of stroke was significantly higher than in dippers (n = 56) (53.7% v 33.9%, χ² = 4.37, P = .0366). We observed a significant increase in the incidence of positive parental history of stroke in nondippers, suggesting that some genetic factors may regulate blood pressure profiles before stroke develops.

KEY WORDS: Ambulatory blood pressure, stroke, dipper, genetic risk.

Large epidemiological studies in essential hypertension have demonstrated that systolic and diastolic blood pressure determined in the consultation room (casual blood pressure) are important prognostic determinations of fatal and nonfatal cardiovascular and cerebrovascular events. Nevertheless, many cases have been documented with conflicting results between casual blood pressure and the degree of target organ damage. Recently, it has been shown that target organ damage in essential hypertension is more closely associated with ambulatory blood pressure (ABP) than with casual blood pressure.

Consistent variations in blood pressure occur as a result of circadian rhythm, with the highest pressure seen in the morning and the lowest during sleep. Hypertensive subjects are classified as “dippers” and “nondippers” according to circadian blood pressure rhythm. Many previous studies with ABP monitoring have shown that patients with a truncated drop in nocturnal blood pressure (nondippers) have greater left ventricular mass and higher frequency of stroke than patients with a physiological drop in blood pressure at night (dippers). However, whether the lack of nocturnal decline of blood pressure is genetically determined and a primary cause of target organ damage including stroke or is a secondary abnormality due to target organ damage is not well understood.

To clarify this point, we examined the relation between the blood pressure variation and positive parental history of stroke (PHS) in hypertensive patients without clinically overt hypertensive target organ damage.

MATERIALS AND METHODS

Subjects We investigated 110 untreated hypertensive patients without cerebrovascular disease, ischemic heart disease...
disease, or diabetes mellitus (51 men, 59 women). Mean age was 59.4 ± 10.7 years. Diagnosis of hypertension was based on casual systolic blood pressure exceeding 140 mm Hg and/or diastolic blood pressure exceeding 90 mm Hg. ABP monitoring was also performed, and patients whose 24-h ABP did not exceed 140 mm Hg in systolic and/or 90 mm Hg in diastolic were excluded.

Using a sphygmomanometer on at least three separate occasions in the physician’s office, we measured casual blood pressures with subjects in the sitting position after a 10-min rest period. The ABP of each subject was monitored noninvasively from the right or left arm to record the blood pressure with a TM-2421 ABP monitoring system (A&D Co., Tokyo, Japan). Recording was started at 9 AM, programmed every 30 min, and finished at 10 AM on the following day (daytime: from 8 AM to 10 PM; nighttime: from 10 PM to 8 AM). The two 30-min recordings obtained during the initial 60-min period were excluded from analysis. The subjects were divided into two groups by the presence (dippers, n = 56) or absence (nondippers, n = 54) of a significant nocturnal blood pressure drop, defined as mean nighttime systolic blood pressure 10 mm Hg or less than mean daytime systolic blood pressure.

A standard 12-lead electrocardiogram was recorded at rest in all patients and analyzed with a digital system. Left ventricular hypertrophy was defined according to the criteria of Sokolow and Lyon. Subjects with evidence of bundle branch block or Wolff-Parkinson-White syndrome were excluded from analysis.

Family history of stroke was carefully investigated by medical history. A PHS was regarded as positive if one or both parents had an apparent history of cerebrovascular accident before 60 years of age.

### Statistical Analysis
Values are expressed as means ± SD. For categoric variables, $\chi^2$ test was used. The differences in variables of risk factors between groups were assessed by Student’s $t$ test. A $P < .05$ was considered statistically significant.

### RESULTS

#### Age, body mass index, frequency of smoking, and occurrence of left ventricular hypertrophy

The non-dipper group showed a high frequency of female subjects than the dipper group. Casual blood pressure was significantly higher in nondippers than in dippers. In ABP monitoring, 24-h mean systolic blood pressure and nighttime systolic and diastolic blood pressure were significantly higher in nondippers than in dippers.

The relationship between diurnal blood pressure pattern and PHS was also investigated. Positive PHS was significantly more frequent in nondippers than dippers (53.7% v 33.9%, $\chi^2 = 4.37, P = .0366$) (Table 1).

### DISCUSSION

We observed a significant increase in the incidence of positive PHS in nondippers relative to dippers. None of our subjects had suffered from target organ damage including stroke. Thus, we speculate that the lack of nocturnal decline of blood pressure is not a secondary abnormality due to target organ damage, but is the result of certain as yet unidentified genetic factors that regulate blood pressure profiles before hypertensive organ damage develops.

Among patients with essential hypertension, nondippers are thought to tend toward further cardiovascular complications such as left ventricular hypertrophy and stroke. However, whether nocturnal hypertension is a primary cause or a secondary abnormality of target organ damage is controversial. Previously, Vardecchia et al reported that cardiovascular mortality rate was higher in nondippers than in dippers among women but not among men. Recently, Kario et al reported a case with a change in diurnal blood pressure rhythm due to a small lacunar infarct. They speculated that nondipper hypertension is a sec-
secondary abnormality caused by minor cerebrovascular damage. On the other hand, Timio et al\textsuperscript{14} reported that nondippers had a faster rate of creatinine clearance decline and higher increase in urinary protein excretion than dippers in a 3-year longitudinal study. Verdecchia et al\textsuperscript{6} reported that echocardiographic left ventricular mass was greater in nondippers than in dippers both before and after adjustment for 24-h blood pressure, whereas the difference between the two groups disappeared after adjustment for nighttime blood pressure. They concluded that high nocturnal blood pressure and persistence of vascular strain were additional critical factors of end organ damage.

**Study Limitations** We defined PHS according to patients' family history. An important consideration in this study is the accuracy of the self-reported family history questionnaire, and it is not clear whether the parents had cerebral infarction, embolism, or hemorrhage, although detailed medical records were obtained from patients and families.

In conclusion, we demonstrated that the frequency of PHS is significantly higher in nondippers than in dippers. These findings suggest that the nondipper pattern of blood pressure is not a secondary change due to stroke, but may be an important primary genetic risk factor for stroke in patients with hypertension. However, the precise relationship between the diurnal rhythm of blood pressure and stroke in hypertensive individuals remains to be determined in larger prospective studies.

**REFERENCES**


