Prognostic Relevance of Blood Pressure Variability

Gianfranco Parati, Mariaconsuelo Valentini

The possible prognostic relevance of different patterns characterizing blood pressure (BP) fluctuations during the day and night was first suggested in the late 1980s, based on observations made possible by 24-hour continuous intraarterial ambulatory BP monitoring in normotensive and hypertensive subjects. Since then, this issue has been repeatedly addressed in studies carried out either in animals and in humans and is still matter of debate.

Evidence is available that in normal subjects 24-hour ambulatory BP recordings are characterized by a fairly smooth BP profile during daytime activities and by a significant BP decline during night sleep. Most, although not all, studies exploring the prognostic relevance of BP variations have shown that alterations in these 24-hour BP variability patterns are associated with hypertensive target organ damage and with a higher rate of cardiovascular events. This is the case for an increased amplitude and frequency of BP variations occurring during the daytime, the night-time, or the entire 24-hour period. It is also the case for alterations in the components of 24-hour BP variability related to the shift between wakefulness and sleep, namely the nocturnal BP decline and the morning BP surge.

A reduced degree of nocturnal BP fall, and even more so the reverse pattern characterized by a BP increase at night, has been found to be associated with cardiac, cerebral, renal, and vascular damage. Several studies have also shown that lack of nocturnal dipping carries a higher risk of stroke, whereas conflicting findings were reported on the prognostic relevance of an excessive BP fall at night. Finally, data are available that a steeper morning BP surge is associated with a higher risk of cardiac and cerebrovascular events, although such an association was not found by other investigators.

The article by Metoki et al published in this issue of Hypertension offers additional information in this field by exploring the risk either of ischemic and hemorrhagic cerebrovascular events, respectively, in association with different behaviors (narrow fixed criteria). Third, the definition of night-time BP dipping pattern when comparing data from 2 consecutive ambulatory BP recordings. The study by Metoki et al thus provides additional support to the concept that, in the management of patients with arterial hypertension, care has to be paid not only to the reduction of mean BP levels by treatment, but also to the normalization of deranged BP variability patterns, such as those between day and night. In particular, the data provided by this and by other similar articles appear to suggest that inhibition of a steep morning BP surge by antihypertensive treatment might reduce the risk of events and, specifically, the risk of cerebrovascular hemorrhage. They also suggest that in nondipper patients or, even more so, in patients with an inversion of the physiological nocturnal BP dipping, improving the nocturnal BP decline through proper titration and scheduling of antihypertensive treatment might improve prognosis by specifically reducing the risk of ischemic stroke.

These perspectives are of great potential interest. Their generalized extrapolation to patients’ management in clinical practice, however, must be considered with some caution. This is because of a number of problems still affecting the assessment of the clinical relevance of BP variability through the day and night (Table). First, there are differences between studies in the methods for the quantification of overall blood pressure variability. This is exemplified by the variable use of standard deviations of mean BP values or of coefficients of variations. It is also exemplified by some studies focusing on the whole 24-hour time, whereas others considered daytime or nighttime subperiods only. Second, different definitions of daytime and nighttime were often used. Some studies based their identification of day and night on information derived from patients’ logbooks; other studies adopted a fixed definition of daytime and nighttime. This was done either by considering all 24 recording hours (wide fixed criteria) or by skipping transitional periods between wakefulness and sleep (ie, by excluding a few hours in the evening and in the early morning during which different subjects were engaged in different behaviors (narrow fixed criteria)). Third, the changes in BP between day and night as well as those between night and day may not be reproducible in all subjects, a variability of at least 40% having been reported in the definition of night-time BP dipping pattern when comparing data from 2 consecutive ambulatory BP recordings. Fourth, as shown also by Metoki et al in their article, the degree of nocturnal BP fall is significantly related to the rate of morning BP rise, and such a correlation between 2 hemodynamic phenomena that are reported to have opposite prognostic value makes their clinical interpretation more...
Problems in Assessing the Clinical Relevance of Blood Pressure Variability

Limited reproducibility of BP variability
Lack of BP variability normal reference values, and their dependence on subjects’ behavior during BP monitoring
Limitations of conventional discontinuous, low frequency, ambulatory BP monitoring in assessing BP variability (oversmoothing, aliasing, overmodeling, failure to assess fast BP changes)
Possible different impact of BP variability on vascular and cardiac targets
Inclusion of different populations of subjects in different studies (differences in age, gender, race, BP levels, presence or absence of antihypertensive treatment)

Need of evidence from intervention trials that reduction of overall BP variability, improvement of nocturnal BP decline and/or buffering of a steep morning BP surge by treatment, might lead to reduction of CV morbidity and mortality

difficult. Fifth, available studies on BP variability often considered different populations of subjects. As an example, in the Ohasama Study12 on the prognostic value of circadian BP changes, subjects were recruited from a general population, had an average age of 61 years, and 30% of them were treated. In the study by Kario et al on a similar issue,11 recruited subjects were hypertensive, of older age (≈72 years), and their antihypertensive treatment was withdrawn at the time of the study. These differences may have contributed at least in part to the discrepant results obtained. An additional source of methodological problems in assessing BP variability is likely to have been represented by use of ambulatory BP monitoring techniques based on use of discontinuous, low frequency, automated BP measurements and by the inclusion of relatively small groups of subjects (Table).

Finally, what is still missing in this field to fully support the clinical applicability of the available observations on the prognostic value of circadian BP variations is a convincing demonstration that pharmacological correction of abnormal BP variability patterns is associated with an improved prognosis. The stimulating perspectives opened by Metoki et al15 on the possibility to achieve cerebrovascular and cardiovascular protection by correcting abnormal BP variability patterns thus further emphasize the need of intervention trials aimed at addressing this issue in a sufficiently large sample of subjects with different age and BP levels.

References
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