Nocturnal Blood Pressure Versus Nondipping Pattern
What Do They Mean?
Josep Redon, Empar Lurbe

Thirty years ago methods to assess blood pressure (BP) automatically during regular living conditions represented a new dawn in the field of hypertension. Today ambulatory blood pressure monitoring (ABPM) is a tool available not only in specialized clinics but also in many segments of primary care. A large number of studies have demonstrated the better reproducibility and the prognostic superiority of BP values obtained by using ABPM as compared with the BP obtained from standard clinical measurements. The prognostic value of ambulatory BP was established for the general population as well as for hypertension in general or under specific conditions such as refractory hypertension, diabetes, chronic renal insufficiency, or pregnancy. Based on outcome specific conditions such as refractory hypertension, diabetes, chronic renal insufficiency, or pregnancy. Based on outcome specific conditions such as refractory hypertension, diabetes, chronic renal insufficiency, or pregnancy. Based on outcome specific conditions such as refractory hypertension, diabetes, chronic renal insufficiency, or pregnancy. Based on outcome specific conditions such as refractory hypertension, diabetes, chronic renal insufficiency, or pregnancy. Based on outcome specific conditions such as refractory hypertension, diabetes, chronic renal insufficiency, or pregnancy. Based on outcome specific conditions such as refractory hypertension, diabetes, chronic renal insufficiency, or pregnancy.

Because ABPM provides large numbers of measurements, researchers have been tempted to look for more information than just the average of BP values during 24 hours or over more restricted periods such as the day, night, or morning. Therefore, assessment of other BP parameters has been considered. Blood pressure changes during the 24-hour period, the so-called circadian variability, and BP variation among measurements, intrinsic variability, have received increasing attention. Although the significance of intrinsic variability has been challenged when BP is measured intermittently every 15 or 20 minutes, circadian variability has become an increasingly used parameter even though reproducibility has introduced some limitations. Clinical observations have identified subjects with a blunted decline in the physiological BP nocturnal fall, the nondipper pattern. As compared with subjects in which nocturnal BP reduction was “normal”, defined as a drop of more than 10% of the diurnal BP values, subjects displaying a nondipper pattern have more hypertension-induced organ damage such as left ventricular hypertrophy, microalbuminuria, and reduced arterial compliance. Furthermore, follow-up studies have demonstrated that nondipper subjects have worse prognosis in terms of cardiovascular events as well as a higher risk to develop diabetic nephropathy in normotensive type 1 diabetics.

The relative importance of each of the parameters obtained from ABPM has been controversial from the beginning. The average of 24-hour, daytime, nighttime blood pressure, and night–day ratio, an estimate of circadian variability, are related to each other. This sometimes makes it difficult to assess whether one is more important than the other in terms of prognosis and, consequently, whether it should be specifically targeted.

A small number of studies has found that nocturnal BP is superior to daytime BP. Superiority of nocturnal BP has been claimed using 2 different approaches, calculating the slope of the regression line between the given BP value and the number of events, and by regression models. A stepper regression line between the nocturnal BP values and the rate of events as compared with that obtained with daytime, 24-hour, or office BPs, indicates a better association. Displacement of other BPs values by nocturnal BP in multiple regression models has been claimed to be superior as well. Whether or not the superiority observed has a mathematical explanation and no biological significance has been a matter of debate. The distribution of nocturnal BP is much narrower than that observed for diurnal BP and, consequently, steeper regression lines can be obtained when BP values and event rates are plotted or when values are introduced into regression models.

Although some of the studies claiming the superiority of nocturnal BP have a large number of subjects and events, statistical power has been limited to differentiating the degree of association among highly correlated parameters. Collecting individual information from several studies can improve this limitation. In the present issue of Hypertension, Fagard and coworkers assessed the prognostic significance of nighttime and daytime ambulatory blood pressure by performing a metaanalysis on individual data of 3468 patients from 4 prospective studies performed in Europe. Two of them were among those previously referenced claiming superiority for nocturnal BP. The prognostic value for mortality and cause-specific cardiovascular events in hypertensive patients without major cardiovascular disease at baseline was analyzed not only for the values but also for their ratio. Daytime and nighttime systolic blood pressure predicted all-cause and cardiovascular mortality, coronary heart disease and stroke, independent of office blood pressure and confounding variables. Although nighttime blood pressure predicted all outcomes, daytime blood pressure did not add prognostic precision to nighttime pressure. The systolic night–day blood pressure ratio predicted all outcomes, which only persisted for all-cause mortality after adjusting for 24-hour blood pressure.
pressure. The authors concluded that nighttime blood pressure is in general a better predictor of outcome than is daytime pressure in hypertensive patients, and the night–day blood pressure ratio only predicts mortality. These results seem to be similar for men and women, in younger and older patients, and in treated and untreated patients although splitting a population in subgroups reduced the statistical power.

Assuming the results are correct, what do they mean and what is the clinical utility of this information? Although high nocturnal BP is sometimes accompanied by a nondipping pattern, both are not always present together and the significance of nocturnal BP and the nondipping pattern differs. Nocturnal BP present in resting conditions, sleeping and repose, represents the minimal BP that the subject needs for adequate organ perfusion. Maintaining high BP at night, however, overloads the cardiovascular system with a negative impact on the heart and vascular structures. Likewise in the kidney the resting period is when the afferent arteriolar tone is lower allowing for a more direct transmission of the systemic BP to the glomerulus.14 Consequently, high BP at night impacts the heart, the vasculature, and the kidney, boosting damage and increasing risk for developing clinical events. Therefore, nocturnal BP should be targeted to reduce cardiovascular and renal risk.

The nondipping pattern, once excluded bad quality of sleep, reflects an inadequacy of the mechanisms regulating BP. It can be the consequence of baroreflex or autonomic dysfunction, relative nocturnal volume overload, and abnormal sodium handling. Long-standing or severe hypertension, hyperaldosteronism, diabetes, autonomic dysfunction, and chronic renal disease have been associated with a higher prevalence of nondipper pattern.14 In an individual, one or more mechanisms can be operating simultaneously, but in the majority of the cases the pattern represents the consequences of the underlying disease. This may explain why night–day ratio is a prognostic marker for cardiovascular events. If a nondipper pattern is present, it indicates that the patient is at a more advanced stage of organ damage as compared with the dipper pattern, and therefore a higher risk patient. In this case, a nondipper pattern is valuable information above and beyond of BP values. For a given BP value, subjects displaying the nondipper pattern have higher risk as compared with those in which the physiological nocturnal fall is maintained. Consequently, ABPM can refine the prognostic assessment in hypertension not only by providing BP value, that is the average of a large number of BP measurements, but also by assessing circadian variability, a parameter which requires ABPM. Targeting the nondipper pattern by itself, however, is not enough to protect against the harmful effects of high nighttime BP.

From the results available up to now, it would seem that nocturnal BP is more related to risk than to its diurnal counterpart, and that circadian variability can refine the evaluation of hypertension risk. Whether or not nocturnal BP is superior to diurnal BP in its pathophysiological consequences may be difficult to demonstrate; however, reducing BP throughout the 24 hours, both diurnal and nocturnal, is the way to antihypertensive treatment success.2

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References
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