Editorial Comment

The Clinical Significance of Diurnal Blood Pressure Variations
Dippers and Nondippers

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In this issue of Circulation, Verdecchia et al1 suggest that the diurnal pattern of blood pressure, evaluated by noninvasive ambulatory monitoring, may be an important factor in determining the extent of left ventricular hypertrophy (LVH) in hypertensive patients. It illustrates the point that the introduction of a new diagnostic technique often raises as many questions as answers. The rationale for the introduction of ambulatory monitoring as a clinically useful diagnostic tool was provided by both the increasing awareness of the intrinsic variability of blood pressure and the disturbing fact that the conventional clinic measurements of pressure, which have formed the mainstay of our knowledge of the risks associated with hypertension, may in some patients be quite unrepresentative of their overall level of pressure.2,3

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Before this came about, the only effective way to describe an individual’s blood pressure was to take the average of a few clinic measurements. With ambulatory monitoring, it is possible to obtain up to 100 readings over a period of 24 hours, which may include the full range of normal daily activities. This plethora of data raises an important but still unanswered question—which measure of pressure gives the best prediction of risk? Is it the average level obtained over a prolonged period of time, or is it perhaps some measure of variability such as the peaks of pressure? There is, of course, not necessarily any simple answer to this question because it is quite conceivable that different aspects of blood pressure might be responsible for different pathogenic effects. It might be, for example, that the average level is more important in producing LVH,4 whereas the peaks trigger the rupture of an atheromatous plaque.5 By correlating the different measures of blood pressure with target organ damage or prognosis, ambulatory monitoring offers the possibility of providing some answers.

The most consistent variations of blood pressure occur as a result of the diurnal rhythm of pressure, which typically has an amplitude of 20–30 mm Hg.6 In most individuals, the highest pressures are seen during the morning hours, and the lowest during sleep. In hypertensive patients, this pattern is generally preserved, with an upward shift of the diurnal profile. While this has been known for many years, the more extended use of ambulatory monitoring has identified many conditions in which this pattern is not seen, and the blood pressure remains elevated throughout the night. Such is the case with a minority of patients with essential hypertension, as described by Verdecchia et al.1 It also has been described for many diverse conditions, including malignant hypertension,7 sleep apnea syndrome,8 pheochromocytoma,9 toxemia of pregnancy,10 Cushing’s syndrome,11 diabetes,12 orthostatic hypotension,13 cardiac transplantation,12 and congestive heart failure.14 These observations raise additional questions. Why does blood pressure not fall during sleep in some patients? And what are the clinical implications?

The mechanism of the fall of blood pressure during sleep is not well understood, although it is clear that there is a close link between the two: In subjects who remain awake during the night, little happens to their blood pressure. The onset of sleep is associated with a gradual fall of blood pressure, which then remains low until the moment of awakening, when it promptly rises.15 The most obvious explanation for the fall of pressure during sleep is a reduction of sympathetic nervous activity paralleling the change of arousal, and it is certainly true that many indexes of sympathetic activity, such as plasma catecholamines, heart rate, cardiac output, and peripheral resistance, are all lower.16 This mechanism also would explain why no nocturnal fall of pressure is seen in patients with orthostatic hypotension, whose sympathetic nervous system is effectively denervated. The fact that some patients with pheochromocytoma, whose catecholamine levels remain high throughout the night, show no fall of blood pressure would also be consistent with this view; it would not explain, however, why
many others, with equally high nocturnal catecholamine levels, still show a normal nocturnal fall of pressure.  

Other mechanisms may be involved. Normally, glucocorticoids are not regarded as having a major influence on blood pressure regulation, and cortisol secretion is highest during the latter part of the night, when blood pressure is low. This makes all the more intriguing the recent observation that patients with Cushing’s syndrome show a persistently elevated blood pressure throughout the night, despite a normal fall of heart rate.  

Cortisol levels are, of course, high in such patients throughout the night, and a direct causal link with blood pressure is suggested by the observation that when patients with glomerulonephritis are treated with prednisone, their blood pressure no longer falls at night.  

A major role for the renin-angiotensin system seems unlikely. While there is a tight relation between renin secretion and sleep cycles, renin tends to increase during the latter part of the night, and treatment with angiotensin converting enzyme inhibitors does not alter the diurnal profile of blood pressure.  

So far, the pathogenic significance of the absence of the nocturnal fall of blood pressure has remained obscure. It is reasonable to suppose that a hypertensive patient whose blood pressure remains high throughout the night will fare worse over the long term than the patient whose pressure falls. No prospective data are available to answer this question, which means that one must fall back on cross-sectional studies, with all their limitations. A considerable number of studies have shown that the average ambulatory blood pressure gives a better correlation with target organ damage (most commonly measured as LVH) than clinic pressure, which comes as no great surprise given the unreliability of clinic pressure and the fact that the ambulatory pressure is based on a much larger number of readings. Previous studies, however, including our own of 100 patients, have for the most part not shown a better correlation with sleeping than with waking blood pressure.  

Two explanations for the difference with Verdecchia et al’s results can be offered. First, the earlier noninvasive ambulatory recorders were relatively bulky and noisy. Many subjects complained that they could not sleep well during a recording period, and in our early studies we noted that the standard deviation of the blood pressure readings taken during the night was much higher than would be expected from our knowledge of the relatively low variability of pressure during sleep. The newer recorders, such as the one used by Verdecchia et al, have been shown not to interfere with the nocturnal fall of blood pressure. Second, the correlation between night-time blood pressure and LVH will depend on the population studied. If all the patients in the study show a normal nocturnal fall of blood pressure, the correlations with LVH will be approximately the same for the daytime and nighttime pressures. If, however, as in Verdecchia et al’s study, a substantial portion of the hypertensive patients (in their case, approximately one third) do not show such a fall, we may expect to see a difference in the correlations.  

The most reasonable interpretation of the finding of Verdecchia et al, that a patient whose blood pressure remains high during the night will have more LVH, is that it is the average level of blood pressure over prolonged periods of time that determines the amount of LVH. This interpretation seems more plausible than the opposite one—that the presence of LVH prevents the blood pressure from falling at night; in fact, it has been previously reported that when hypertensive subjects with and without LVH are compared, their diurnal blood pressure profile is generally similar. However, this study also indicates that LVH can develop in the absence of a nocturnal pressure fall.  

Consistent with Verdecchia et al’s findings is an earlier report that an elderly patient whose pressure remains high at night is more likely to have more extensive vascular disease, although in this case, the “chicken and egg” debate is even more relevant. The new findings have further implications. They suggest that it may be clinically important to know which patients show a fall of blood pressure during the night (“dippers”) as opposed to those who do not (“nondippers”). The prevalence of nondippers in the hypertensive population is unknown, as are the factors that distinguish them. There is some evidence that there may be an increased prevalence of nondippers among blacks, and there are a number of studies that suggest that sleep apnea may be commonly associated with hypertension: It has been reported that as many as 80% of patients with sleep apnea are hypertensive and that 30% of hypertensive patients have sleep apnea. It is a condition that has largely been neglected by cardiovascular physicians, perhaps because it has hitherto required a specialized sleep laboratory for its diagnosis. It is becoming increasingly clear that where blood pressure is concerned, we should no longer ignore what happens during the night.

References

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