Review Paper

Early Morning Blood Pressure Surge

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Alterations in the circadian rhythm of blood pressure, whether a loss of the nighttime dip or an exaggeration of the early morning increase that occurs upon rising, indicate increased cardiovascular risk. Estimates of the magnitude of the blood pressure surge on rising vary depending on technique and population, but it is usually around 10–30 mm Hg systolic and 7–23 mm Hg diastolic. The magnitude of the surge increases with age, alcohol consumption, and smoking and is greater in whites. Blood pressure variations and morning plasma aldosterone are closely correlated. A high morning surge is linked to increased target organ damage as well as strokes and other cardiovascular complications. Therapeutic options exist to reduce the magnitude of the morning blood pressure surge—notably, the use of drugs with a long duration of action, the use of medications that specifically antagonize the morning surge (such as α blockers), and the administration of drugs upon awakening but before rising. (J Clin Hypertens. 2006;8:584–589) ©2006 Le Jacq

Blood pressure (BP) variation is a phenomenon that has been well known for many years, which to date has mainly been considered in relation to its consequences for the reliability of measurements. However, this variability also appears to be linked to the cardiovascular complications of hypertension, independent of the average BP level. Ambulatory techniques for monitoring BP are now facilitating the investigation of this phenomenon, in particular its circadian component. Two aspects of this circadian variation have been the subject of studies; however, results may seem contradictory. The loss of the nyctohemeral cycle of BP (nondipper profile) is accompanied by increased cardiovascular risk. The excessive morning BP surge, on rising, also appears to increase risk. This report summarizes the available data on the morning BP surge and its consequences and examines the relationship of the risks of this surge with the dangers of the nondipper profile.

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CIRCADIAN VARIATIONS OF BP

The development of automatic monitoring has led to the description of the circadian variation of BP. We must recall the pioneering work of Richardson and colleagues[1] who, with the assistance of an automatic device using the oscillometric method and the simultaneous recording of the electroencephalogram (EEG), wrote: "The pressure fell before EEG evidence of sleep, fell further during sleep and rose sharply in the morning after the subject woke." Fundamentally important observations were made by the use of continuous, uninterrupted, intra-arterial measurements using methodology developed by the Oxford team,[2,3] which clearly showed that BP was at its lowest during nighttime and rose in the morning to reach its highest values at midmorning.[4] These studies suggested that a BP surge in the early morning before waking was the result of an internal clock. This notion has been widely held for many years, but is an artifact that results from the likelihood that individuals who were studied awakened at different times. When the results are expressed in relation to the time of waking rather than the time of day, there is no longer any marked BP surge preceding this arousal.[5,6]

Several studies[7,8] (such as Richardson's initial report) have shown that the essential mechanism of the morning BP surge is waking and, undoubtedly even more important, rising.[9,10]

IMPORTANCE OF THE PRESSURE SURGE ON RISING

Several methods of measuring BP on rising have been described. For many years, we have asked patients who are fitted with ambulatory BP monitoring devices to measure BP on rising in the morning, at the point when they put their feet on the floor, and in the evening, just after going to bed. The initial aim was to accurately evaluate these two points, which are essential for calculating pressure averages during activity and at rest.[11,12] This method can be used to calculate the BP surge on rising as the difference between the measurement taken on rising and the last measurement recorded by the apparatus in the previous half hour during sleep. In a population of normotensive subjects, the increase in BP on rising measured in this way is on average 11 mm Hg for systolic BP (SBP) and 12 mm Hg for diastolic BP.[6] In a population of hypertensive patients it is basically similar: 14 mm Hg for systolic pressure and 12 mm Hg for diastolic pressure, but with extremes that can reach 80 mm Hg for systolic pressure.[13] Figure 1 shows the distribution of the SBP surge values on rising in a population of 507 untreated hypertensive patients.

Since 1996, we have been using an ambulatory BP monitoring device equipped with a positioning sensor (Diasys Integra, Novacor, France), which automatically records BP at the point when the patient gets up. The results obtained are similar to those produced by manual monitoring.[13] One of the advantages of an automatic sensor is that it also allows any effects of a siesta to be taken into consideration. Rising after a siesta is also accompanied by a BP surge, although this is smaller.[14] Another approach consists of defining the morning BP as the average of the pressures over a certain period (2–4 hours) after rising and the BP preceding rising as the average over an identical duration before rising. The morning surge is then defined as the difference between these two averages.[10,15] A third approach is based on defining the minimum nighttime BP as the average of three measurements: the lowest and the two measurements on either side of this. The BP surge on rising is then calculated as the difference between the average of the measurements in the 2 hours following rising and the minimum BP. These different methods of calculation produce estimates of the pressure surge on risings that are significantly different (Table I).

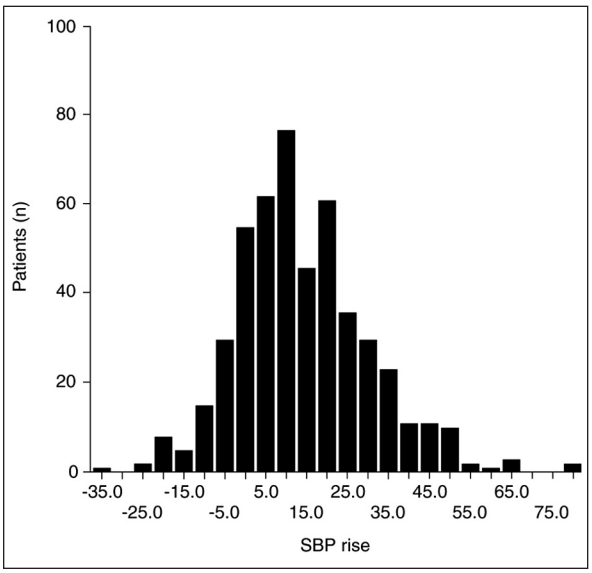

Figure 1. Distribution of the systolic blood pressure (SBP) surge on rising in a population of 507 untreated hypertensive subjects. Data derived from J Hypertens. *2004;22:1113–1118.*[13]

Table I. Magnitude of the Blood Pressure (BP) Surge (mm Hg) on Rising Reported in Normotensives and Hypertensives Using Different Techniques

	Normotensives			Hypertensives		
	N	SBP	DBP	N	SBP	DBP
Rising BP/pre-awakening BP (one measure)						
Gosse et al.[6,13]	233	11±14	12±13	507	14±16	12±12
Baumgart and Rahn[60]	111	14	13	109	16	13
Morning BP (2 h)/pre-awakening BP (2 h)						
Kario et al.[15]	—	—	—	466	9±14	6.5±9
Morning BP (4 h)/pre-awakening BP (4 h)						
Leary et al.[10]	—	—	—	420	23±13	15±10
Morning BP (2 h)/lowest night BP						
Kario et al.[15]	—	—	—	466	29±13	17±10
Gosse et al.[16]	—	—	—	1419	29±13	24±10

Data are mean or mean ± SD. SBP=systolic BP; DBP=diastolic BP

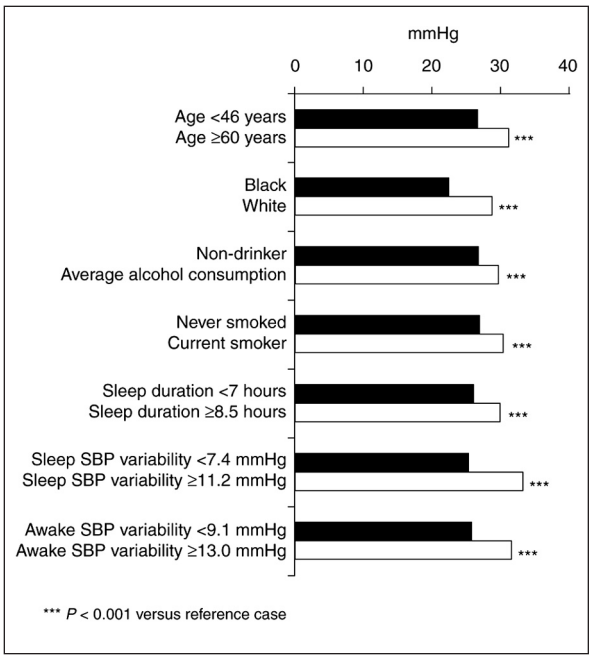

Figure 2. Magnitude of systolic blood pressure (SBP) surge in patients with essential hypertension. SBP variability is defined as the SD of hourly means during either the sleep or awake periods (excluding the 2-hour intervals around going to sleep and waking). Data derived from J Hypertens. *2006;24(suppl 4):S301.*[16]

The BP surge on rising does not seem to be influenced by gender.[13,16] In our experience, the SBP surge on rising is loosely correlated with age. In a large pooled analysis of 1419 patients with hypertension, we found that the magnitude of the SBP surge increased from 26 mm Hg in patients younger than 46 to 31 mm Hg in patients 60 years of age or older.[16] No such increase was observed in diastolic BP surge. Ethnicity, alcohol consumption, smoking status, and duration of sleep also affected both SBP and diastolic BP.

The strongest predictor for the morning surge was BP variability during sleep expressed by the SD of individual measurements: the lowest quartile of BP variability during sleep had a BP surge of 25/20 mm Hg compared with 33/29 mm Hg in the highest quartile (Figure 2).[16] Similar results have been observed previously, along with a strong link to the difference in BP level between activity and rest.[13] Although the surge is accompanied by an increase in cardiac rate, there is no significant correlation between the variations in BP and heart rate on rising.[13,16] We also found a significant correlation between BP and the level of morning plasma aldosterone, but none with cortisol. A preliminary study shows that the SBP surge on rising could be associated with a degree of hostility.[17]

CONSEQUENCES OF BP SURGE ON RISING

The morning period is accompanied by a peak in incidence of cardiovascular complications. Ischemic changes on Holter electrocardiographic[18] recordings, episodes of unstable angina,[19] vascular cerebral accidents,[20–24] myocardial infarction, and sudden death[25,26] have all been observed. The period that follows rising is accompanied by an increased risk of cardiovascular complications of 30%–40% in comparison with other periods of the day[27]; it is therefore logical to associate this with the sudden and daily BP surge on rising. This hypothesis is reinforced by demonstrating the parallelism between BP, activity, and the incidence of cardiovascular events, with a dual peak found in countries where siestas are a normal custom.[24,28,29] Another disconcerting fact is that the morning BP surge seems to be highest on Mondays; this is also reflected in the incidence of cardiovascular complications.[30] It is difficult, however, to prove that the BP surge is directly responsible. In fact, the morning period is accompanied by various changes that could also play a role in the increase of cardiovascular events: activation of the sympathetic nervous system,[31–34] increase in cortisol, increase in platelet aggregability,[35] activation of the angiotensin–renin system, and reduction in endothelial function.[36,37]

A few studies have provided some proof of the relationship between BP surge and increased cardiovascular events. The BP surges on rising may affect left ventricular mass and the degree of left ventricular hypertrophy independent of the average BP over 24 hours.[13,38–42] The BP surges may also contribute to increasing the carotid artery intima–media thickness.[43,44] This correlation between the BP surge in the morning and target organ damage, independent of the average BP level over 24 hours, provides indirect proof that the daily BP surge may have hemodynamic consequences. Two studies have now reported a connection between the SBP surge on rising and the incidence of cardiovascular complications in the hypertensive subject, independent of the average BP level over 24 hours.[13,15,45,46]

MORNING RISER AND NONDIPPER: CAN THE TWO CONCEPTS BE RECONCILED?

Subjects presenting a profile of a nondipper type, with lack of a BP decrease during sleep, do not present any significant BP surge on rising although their cardiovascular risk is clearly increased.[46] The contradiction is only apparent, rather than real; both BP elevation and high BP variability should be considered factors in evaluating risk. Morning BP can rise moderately without any significant

Table II. Comparison of Blood Pressure (mm Hg) According to Dipper and Riser Status in Patients With Essential Hypertension[16]

	Dipper/Moderate Riser (n=357)	Dipper/Extreme Riser (n=595)	Nondipper (n=255)
24-H mean	145/92	147/92	151/93*
Wake mean	153/99	156/99**	152/94†
Sleep mean	130/80	128/77	147/90*
Nighttime low	124/74	118/69**	136/81*,†
Early morning mean	144/94	157/100**	155/97*
Morning surge	20/21	40/31**	19/16†
Wake variability	10.6/8.2	11.6/8.7**	11.6/9.1*
Sleep variability	8.7/7.6	9.9/8.3**	10.1/8.1*

Dipper=sleep mean systolic blood pressure (SBP) <90% of wake mean SBP *and* sleep mean diastolic blood pressure (DBP) <90% of wake mean DBP; moderate riser=morning surge (SBP) <28 mm Hg (median); extreme riser=morning surge (SBP) ≥28 mm Hg (median); nondipper=sleep mean SBP ≥90% of wake mean SBP *and* sleep mean DBP ≥90% of wake mean DBP; *p<0.0001 in test regarding SBP between nondipper and dipper/moderate riser; **p<0.0001 in test regarding SBP between dipper/extreme riser and dipper/moderate riser; †p<0.0001 in test regarding SBP between nondipper and dipper/extreme riser. Data derived from *J Hypertens.* 2006;24(suppl 4):S301.[16]

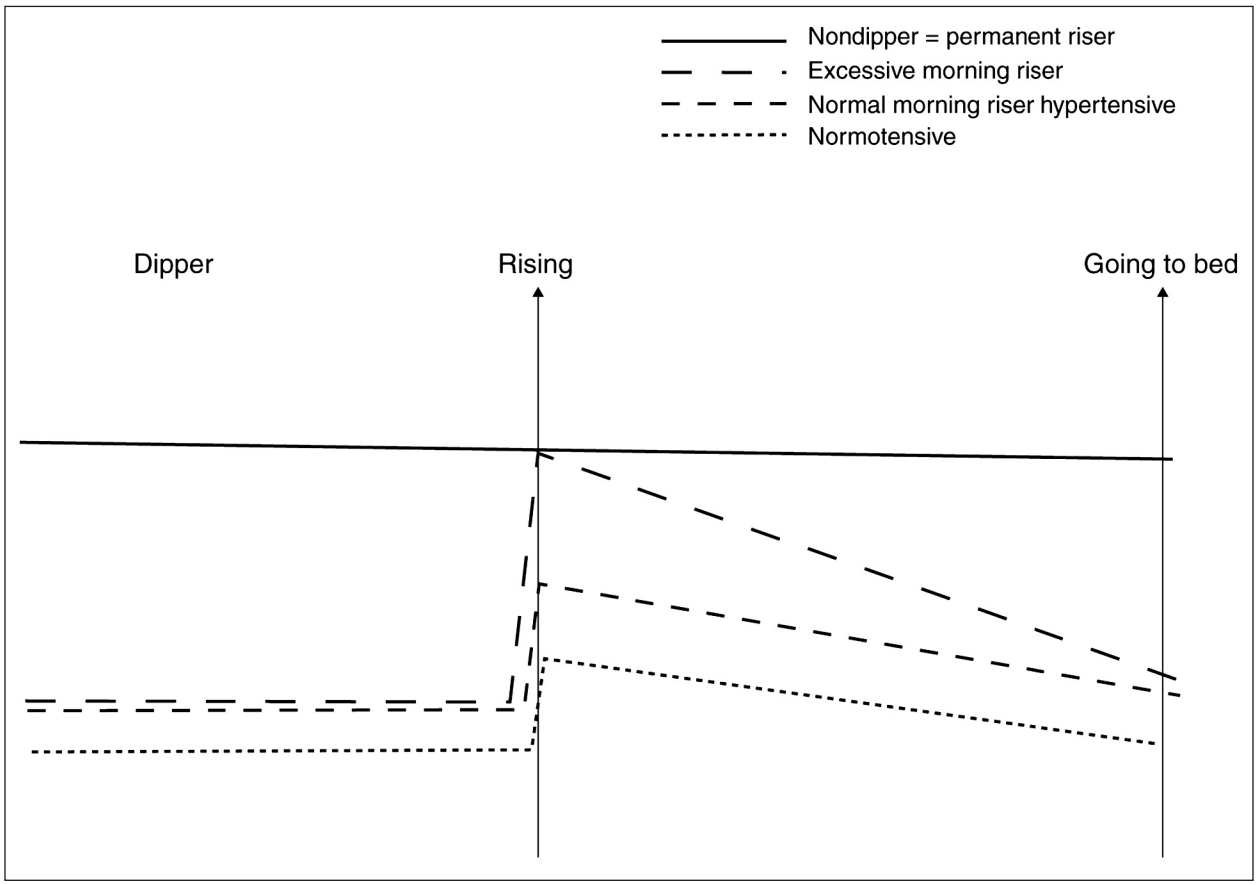

Figure 3. Diagrammatic representation of the modes of blood pressure surge over 24 hours

increase in variability (moderate morning riser hypertensive), may surge extremely on rising (extreme morning riser) with increased BP variability during sleep and when awake, or permanently stay at an elevated BP level (permanent riser/nondipper), which also appears to be connected to increased variability (Table II). The risk appears to be increased between the first and the second and probably between the second and the third groups (Figure 3). However, this hypothesis remains to be confirmed in larger groups of patients.

THERAPEUTIC APPLICATIONS

If we accept the possible causal link between the BP surge on rising and the occurrence of cardiovascular complications, we must then consider this

surge as a therapeutic target. This is all the more important given that antihypertensive medications are usually taken in the morning, after rising. Consequently, the BP surge on rising occurs at the time when the treatment taken the previous day may be less effective. Several strategies have been proposed to date:

- Administration of treatment in the evening rather than the morning. So far, this strategy has not produced very convincing results for controlling BP on rising.[47–53]
- The use of an extended-action drug, taken in the morning, but whose effect continues for longer than 24 hours[54–57]
- The use of drugs that are more specifically effective against the BP surge on rising, such as α blockers[58] and central α_2 agonists[59]
- The administration of drugs on awakening, before rising[60,61]

The relative advantages of these different strategies is difficult to evaluate. To date, one single study appears to favor a benefit linked directly with reducing the morning BP peak, with the observation of a significant correlation between the decrease in this peak and the reduction of the carotid artery intima–media thickness.[43] Whatever the case, the morning period should receive special attention when antihypertensive strategies are evaluated.

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