Impact of the Morning Surge in Blood Pressure

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Thus, previous studies have suggested a parallel relationship between the early morning BP surge and cardiovascular outcomes but have been lacking in event numbers and enough statistical power to clarify at what level of the morning BP surge the risk will appear to become excessive. In this issue of Hypertension, Yi et al.11 have used the International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcome to address these questions. It is clear that their analyses have more advantages than previous studies: first, the population is large and heterogeneous (5645 people, and more than half are women from 8 countries on 3 continents); second, the follow-up period and event numbers are substantially greater than all of the previous studies with 11.4 years of median follow-up and >600 cardiovascular events. The investigators used 2 different definitions of the morning surge in BP; the first was called the “sleep-through morning surge” and was defined as the difference between the morning BP before awakening and the BP during the first 2 hours before awakening. The top decile for these 2 definitions of morning BP surge was associated with a 30% to 45% increase in hazard for cardiovascular events. Of note, both definitions were fairly robust and similar for cardiac events but not for stroke events. The investigators used 2 different definitions of the morning BP surge the risk will appear to become excessive. In this issue of Hypertension, Yi et al.11 have used the International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcome to address these questions. It is clear that their analyses have more advantages than previous studies: first, the population is large and heterogeneous (5645 people, and more than half are women from 8 countries on 3 continents); second, the follow-up period and event numbers are substantially greater than all of the previous studies with 11.4 years of median follow-up and >600 cardiovascular events. The investigators used 2 different definitions of the morning surge in BP; the first was called the “sleep-through morning surge” and was defined as the difference between the morning BP before awakening and the BP during the first 2 hours before awakening. The top decile for these 2 definitions of morning BP surge was associated with a 30% to 45% increase in hazard for cardiovascular events. Of note, both definitions were fairly robust and similar for cardiac events but not for stroke events. The reason for this is unclear, but the authors did note demographic differences, because subjects in Asian countries were at a significantly higher risk for hemorrhagic stroke in the top morning surge decile but not for ischemic strokes, a finding at odds with the study by Kario et al.8 Of interest from the clinical perspective is the analysis of Yi et al.11 to determine the “cutoff” point at which cardiovascular harm begins to occur. Using both definitions, the authors suggest that a systolic morning BP surge by either definition of <20 mm Hg is unlikely to be associated with increased risk. This is useful, and it would be important to know what absolute systolic BP correlates with the surge values used to plot against the adjusted hazard ratios. Lacking in this analysis, however, is characterization of the population as it relates to the morning BP surge. Might individuals with

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(Hypertension. 2010;55:835-837.)

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Hypertension is available at http://hyper.ahajournals.org

DOI: 10.1161/HYPERTENSIONAHA.109.148908
A history of previous vascular events or major cardiovascular comorbidities (eg, diabetes mellitus or chronic kidney disease) show increased risk with lesser morning BP surge values compared with a healthier hypertensive patient group.

A substantial number of investigations have been conducted on the mechanism of the morning surge in BP and its potential relationship to cardiovascular harm. Increased, sympathetic nervous system activity and activation of the renin-angiotensin system have both been determined to be possible contributors to increases in vascular resistance and the morning BP surge. Whether these mechanisms of morning BP elevation independently convey vascular harm is not clear but is of theoretical concern, because it is known that \( \alpha \)-adrenergic stimulation and renin-angiotensin-aldosterone activation can increase vascular tone, coronary vasospasm, and prothrombotic tendencies in the early morning period (see Figure).

Now that there is better characterization of the evidence linking an exaggerated morning BP surge of 28 to 37 mm Hg to cardiovascular morbidity and mortality, it seems reasonable to consider targeting this time of day with antihypertensive drug therapy. In fact, a substantial attempt to evaluate the benefit of a therapy that targeted BP and heart rate in the early morning period with controlled-onset extended-release verapamil versus conventional diuretic and/or \( \beta \)-blocker therapy on early morning cardiovascular events was initiated 12 years ago. The Controlled Onset Verapamil Investigation for Cardiovascular Endpoints Trial was a 17 000-patient study that defined morning cardiovascular events as those occurring in the first 6 hours postawakening and originally should have had enough statistical power to evaluate this prespecified outcome on targeted versus nontargeted therapy. Unfortunately, because of premature discontinuation of the trial 3 years early by the study sponsor, there were not nearly enough events to make any assessment of the early morning event outcomes.

It seems unlikely that another large-scale trial will be conducted to evaluate whether reduction of the morning surge in BP will reduce cardiovascular morbidity and mortality because, that trial would have to have an enormous sample size and be carried out for many years at a substantial cost. There are, however, a number of studies that demonstrate that it may not be difficult to intervene in morning BP surge values with targeted antihypertensive therapies. \( \alpha \)-Adrenergic blockade at bedtime may be an effective means to both lower the morning BP surge and reduce left ventricular mass index, as well as microalbuminuria, in patients with uncontrolled “morning hypertension.” In addition, renin-angiotensin blocking agents that maintain pharmacodynamic effects into the early morning period have been shown to have a significant effect on the morning surge in BP. Because the early morning period coincides with the end of the dosing period of once-daily medications, attenuation of antihypertensive efficacy is relatively common. On the basis of the results of this important new study by Yi et al, more scrutiny should be given to control of the early morning BP, especially in patients at high risk for cardiovascular diseases and those who continue to smoke cigarettes.

**Sources of Funding**

This work was supported by National Institutes of Health grants RO1 AG022092 and 5R01 DA24667-2 and the Donaghue Medical Research Foundation (West Hartford, CT).

**Disclosures**

None.

**References**


The Risk of Waking-Up: Impact of the Morning Surge in Blood Pressure
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Hypertension. 2010;55:835-837; originally published online March 8, 2010;
doi: 10.1161/HYPERTENSIONAHA.109.148908

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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World Wide Web at:
http://hyper.ahajournals.org/content/55/4/835

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