

Clock time-based hourly blood pressure surge around 6 AM: Blood pressure dynamics specific to awakening or endogenous circadian rhythm?

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In a sub-study from J-HOP data, Wanthong et al, reported that the hourly blood pressure (BP) surge (HBPS) at around 6 AM from a night-time trough was associated with left ventricular mass index (LVMI) independent of covariates, including clinic and 24 hour BPs.¹ In this study, about half of the patients were awake at 6 AM and HBPS at 6 AM is characterized with steepest slope of HBPS as shown in fig 1. This finding is partly consistent with the previous study showing that the rate of rise in morning BP is highest when the BP curve is aligned to the midpoint of the morning rise according to waking time.² Considering that most of the subjects were in a pre-awakening state at 5 AM, the study finding supports that the HBPS in this study is more closely related to a BP rise in the post-wakening period than in the pre-awakening period.^{3,4}

So, the BP surge at around 6 AM shown in this study can be an awakening-specific phenomenon on one hand or might be a circadian rhythm-specific phenomenon on the other hand. In terms of the HBPS being a dynamic parameter of BP rise in the morning, the steepest HBPS rise might not always be observed at around 6 AM because the mean awake times could be different among populations. So whether the correlation to HBPS observed at 6 AM is incidental to the mean waking time or instead due to the intrinsic circadian rhythm is not known and warrants further studies.

Resultantly, this study shows that the level of HBPS is highest at 9 AM. It has also been reported that the human endogenous circadian rhythm also shows the greatest platelet activity at around 9 AM.⁵ Interestingly, also in this study by Scheer et al, the maximal slope of increasing platelet activity or epinephrine level could be observed around 6 AM. The most interesting finding of the study by Wanthong et al, is not that the highest level of HBPS at 9 AM but that the most dynamic time interval of HBPS at 6 AM is independently associated with target organ damage. As for circadian rhythmometry, this result shifts our attention from the acrophase to the tangent or gamma representing the slope of BP rise. And because the steepest slope fits best for 6 hour earlier to the

acrophase in the 24-hour single-component cosinor-based model, the result of the study fits better for 12-hour cosinor or two component models.⁶

In general, the morning BP surge (MBPS) in a population is defined by the amount of rise during the 2 hour period after the diary based awakening time. Compared to the earlier hour of MBPS, the slope of the BP surge seems to be blunted in the latter hour as shown in fig 1. Even though there are few studies concerning the dynamics of HBPS in the morning and its related factors, many factors are known to be associated with the amount of MBPS.^{7,8} For example, with a simple calculation, higher nocturnal BP related to salt sensitivity could mean a lower HBPS by simple subtraction from a higher trough BP level. Alternatively, considering physiologic explanations, a BP surge could be even more exaggerated or steeper in response to stimuli because of increased cardiac output and peripheral resistance. In this regard, MBPS can be exaggerated by winter, PM 2.5, smoking, alcohol, or salt. And this is hypothesized to be associated with cardiovascular events.⁹ The association between the clock time-based HBPS with steepest increase and LVMI as shown in this study could be in line with the exaggerated MBPS hypothesis.

In the study by Wanthong et al, LVMI was the only target organ damage independently associated with HBPS, but related mechanisms seem to be unclear. Increased wall tension by preload could increase LVMI. Whether dynamics or slope in the increase of afterload could also increase LVMI independently of average increase of afterload is not known. By the way, HBPS or increased LVMI could be the result of ventriculoarterial interaction with stiffer aorta. As shown in previous studies,^{10,11} in this age range, there seems to be a close association between LVMI and aortic stiffness. Individual susceptibilities of myocardial response to the hemodynamic stress caused by HBPS need to be considered. In this regard, obesity could still be an important confounding factor. However, measurements using brachial-ankle pulse wave velocity to determine the degree of

aortic stiffness might not be accurate enough to determine a statistical significance in the relationship between HBPS and arterial stiffness.

Even though the proportion of the awakening subjects seems to be more closely related to the level of surge in this study, the BP level of the pre-awake state could influence the observed HBPS around 6 AM. From a statistical viewpoint, the individual variation of the HBPS at around 6 AM seems to be high enough to effectively test for any association with organ damage. In this regard, possible mechanisms related to a pre-awake BP surge deserve consideration. Rapid eye movement (REM) sleep could be associated with a high pre-awake BP level.¹² Recent big data analysis showed that a misalignment between the internal physiologic rhythms vs externally imposed timing in the “owl chronotype” correlated to higher mortality.¹³ Blood pressures measured around 6 AM could also reflect a more stressful awakening because of short sleep duration and/or restless terminal insomnia due to depression.

In summary, Wanthong et al demonstrated HBPS at around 6 AM is associated with LVMI independently of BP level. It shows new aspect of blood pressure dynamics in the morning because clock time-based HBPS implies the role of endogenous circadian rhythm, whereas diary based HBPS after awakening suggests the role of external stimuli. But there is a possibility that clock time-based HBPS could be different among populations and that it can be linked to awakening time. More studies from various populations will be needed.

CONFLICT OF INTEREST

I declare that I have no conflict of interest.

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