Sleep and nocturnal hypertension: Genes, environment, and individual profiles

Kazuomi Kario MD, PhD, FACC, FAHA, FESC

Jichi Medical University School of Medicine, Tochigi, Japan

Correspondence
Kazuomi Kario, Division of Cardiovascular Medicine, Jichi Medical University School of Medicine, 3311-1, Yakushiji, Shimotsuke, Tochigi 329-0498, Japan. Email: kkario@jichi.ac.jp

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Nocturnal hypertension is emerging as a residual cardiovascular risk.1,2 There is much evidence that nocturnal hypertension is associated with organ damages such as left ventricular hypertrophy, silent cerebral disease, and albuminuria, as well as with subsequent atherosclerotic cardiovascular disease and stroke.3,4 In this issue, Huang JF and associates extensively investigate the association between isolated nocturnal hypertension and determinates such as clock genes, environmental factors, and patient characteristic.5

There are two definitions of nocturnal hypertension: a BP-level definition, and a definition based on diurnal rhythm (Figure 1). The former definition is straightforward: nighttime BP (during sleep) ≥ 120/70 mmHg, regardless of the BPs measurements in other time periods (ie, regardless of office BP, morning and evening home BP or daytime ambulatory BPs). Building on this definition, Li Y and associates introduced the concept of isolated nocturnal hypertension, which they defined as nocturnal BP ≥ 120/70 mmHg and daytime BP < 135/85 mmHg by ambulatory BP monitoring (ABPM). In a study in a Chinese population, they demonstrated that isolated nocturnal hypertension is associated with increased arterial stiffness,6 and in a study utilizing the international ABPM database, they confirmed that isolated nocturnal hypertension confers a risk of cardiovascular events.7

The second definition of nocturnal BP exploits the concept of disrupted circadian rhythm. O’Brien first used the two-group classification of “non-dipper” versus “dipper” patterns, which he determined using ABPM based on a cut-off value of 10% reduction of nighttime BP from daytime BP.5 Extending his concept, we devised a four-group classification by extracting two extreme pathological edges from the two-group classification (a “riser” pattern from the “non-dipper” pattern, and an “extreme-dipper” pattern from the “dipper” pattern) to better clarify the pathogenic implications of disrupted circadian rhythm of BP, and found that both these extreme pathological edges, ie, the “riser” pattern and the “extreme-dipper” pattern, are associated with silent cerebral disease and future clinical stroke.9–12 More recently, in a large, nationwide multicenter prospective study called JAMP (the Japan Ambulatory Blood Pressure Monitoring Prospective study) (6359 patients; follow-up: 4.5 years), in which we used the same ABPM device, measurement schedule, and diary-based approach to process the data across all study centers, we showed that the “riser” and “extreme-dipper” patterns are associated with different phenotypes of cardiovascular disease. Namely, the “riser” pattern was associated with a risk of heart failure, while the “extreme-dipper” pattern was associated with stroke, in patients with well-controlled 24-h BP.13

Considering that both isolated nocturnal hypertension and the riser pattern are associated with hypertensive organ damage and future cardiovascular disease, including heart failure, we consider that nocturnal hypertension, whether from the viewpoint of higher nighttime BP level or the viewpoint of disrupted circadian rhythm, seems to be associated with increased cardiovascular risk, regardless of daytime BP or 24-h BP levels.

The determinants of nocturnal hypertension include genetic factors, environmental factors, sleep, salt, medical diseases (sleep apnea, diabetes, chronic kidney disease, etc), and antihypertensive medication (Figure 1). Huang JF and associates found that higher nighttime heart rate, shorter sleep duration, and higher humidity were all determinants

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of isolated nocturnal hypertension, but they found no association with genetic factors.5 Higher nighttime heart rate and increased heart rate variability are known to be associated with sleep apnea and heart failure. In part, therefore, increased nighttime heart rate may be partly a reflection of poor sleep quality. Higher humidity may also have a negative impact on sleep quality. Thus, both duration and quality of sleep seem to be important determinants of nocturnal hypertension. However, single nucleotide polymorphisms (SNPs) of clock genes have not been directly associated with isolated nocturnal hypertension. In addition, no significant interaction between clock genes and sleep has been observed in isolated nocturnal hypertension.

In regard to shorter sleep and nighttime BP, the J-HOP Nocturnal BP study using nocturnal home BP monitoring demonstrated that short sleep duration (< 6 versus ≥ 6 and < 9 h/night) was significantly associated with the risk of stroke (HR 2.47). When nighttime systolic BP was < 120 mmHg, those with a sleep duration of < 6 versus ≥ 6 and < 9 hr/night had a significantly higher risk of coronary artery disease events (HR: 3.24). Even patients with “optimal” sleep duration (≥6 and < 9 h/night) were at significantly higher risk of stroke when nighttime systolic BP was uncontrolled (HR: 2.76).14 These findings highlight the importance of both optimal sleep duration and control of nocturnal hypertension for reducing the risk of cardiovascular disease. In addition, the riser/non-dipper patterns of heart rate as well as BP are additively associated with cardiac overload15 and cardiovascular events, particularly heart failure.16,17

Isolated nocturnal hypertension and a riser pattern of disrupted circadian rhythm are emerging residual risk of cardiovascular disease even in normotensives and hypertensive patients well-controlled for office and daytime BPs. ABPM is clinically used to assess nighttime BP. Recently, nocturnal BP has also been measured using home BP. Wearable cuff-less BP monitoring is ideal to minimize sleep disturbance, but it is not recommended in clinical practice.18 Wearable wrist-type oscillometric home BP monitoring is validated, and its accuracy is comparable to the upper-arm device.19,20 In addition, it is much less likely to disturb sleep, compared with upper-arm device.19,20 Sleep quality and quantity seem to be the key factors determining nocturnal hypertension.21 The detection of nocturnal hypertension by ABPM or home BP and the improvement of sleep hygiene by digital therapeutics22 may achieve more effective prevention of cardiovascular disease.

CONFLICTS OF INTEREST

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ORCID

Kazuomi Kario MD, PhD, FACC, FAHA, FESC https://orcid.org/0000-0002-8251-4480

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