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REVIEW PAPER

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Clinical significance of nocturnal home blood pressure monitoring and nocturnal hypertension in Asia

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Abstract

Nocturnal home blood pressure (BP) monitoring has been used in clinical practice for ~20 years. The authors recently showed that nocturnal systolic BP (SBP) measured by a home BP monitoring (HBPM) device in a Japanese general practice population was a significant predictor of incident cardiovascular disease (CVD) events, independent of office and morning home SBP levels, and that masked nocturnal hypertension obtained by HBPM (defined as nocturnal home BP ≥ 120/70 mmHg and average morning and evening BP < 135/85 mmHg) was associated with an increased risk of CVD events compared with controlled BP (nocturnal home BP < 120/70 mmHg and

average morning and evening BP < 135/85 mmHg). This evidence revealed that (a) it is feasible to use a nocturnal HBPM device for monitoring nocturnal BP levels, and (b) such a device may offer an alternative to ambulatory BP monitoring, which has been the gold standard for the measurement of nocturnal BP. However, many unresolved clinical problems remain, such as the measurement schedule and conditions for the use of nocturnal HBPM. Further investigation of the measurement of nocturnal BP using an HBPM device and assessments of the prognostic value are thus warranted. Asians are at high risk of developing nocturnal hypertension due to high salt sensitivity and salt intake, and the precise management of their nocturnal BP levels is important. Information and communication technology-based monitoring devices are expected to facilitate the management of nocturnal hypertension in Asian populations.

1 | INTRODUCTION

Nocturnal blood pressure (BP) measured by ambulatory BP monitoring (ABPM) is a better predictor of future cardiovascular disease (CVD) events than daytime BP in both general and hypertensive populations.[1-6] Although ABPM has historically been the gold standard for the measurement of nocturnal BP levels, nocturnal BP measured by a home BP monitoring (HBPM) device has been used in clinical practice over the past two decades.[7] A 2017 meta-analysis showed that the clinical significance of nocturnal BP measured by HBPM is comparable to that of nocturnal BP measured by ABPM.[8] Compared to ABPM, HBPM has been widely adopted in clinical practice due to its wide availability, simplicity, convenience, and tolerability, and it is unanimously recommended by major hypertension guidelines.[9-14] However, the evidence concerning nocturnal BP measured by an HBPM device has been relatively limited. In addition, the precise management of nocturnal BP levels is especially important in Asians, who are at high risk of nocturnal hypertension due to high salt sensitivity and salt intake. In this review, we summarize the remaining clinical issues, the latest findings regarding nocturnal BP measured by HBPM, and its clinical implications. Little is known regarding the clinical significance of nocturnal BP measured by HBPM, and we wrote this review with a primary focus on the results of our own researches. Based on the results, our goal was to ensure that appropriate future research into HBPM-measured nocturnal BP is performed and that the results of such research be appropriately interpreted in order to assist physicians in the management of hypertension.

2 | NOCTURNAL HOME BLOOD PRESSURE MONITORING

2.1 | Definition of nocturnal hypertension

Nocturnal hypertension is defined as a BP value of ≥120/70 mmHg[10,11,13] or ≥110/65 mmHg in the 2017 American College of Cardiology/American Heart Association BP guidelines.[9] Although these thresholds were set based on previous studies using ABPM, 2017 meta-analysis revealed that nocturnal BP values measured by HBPM and those measured by ABPM were almost the same; the differences in systolic BP (SBP) and diastolic BP (DBP) between them were 1.4 mmHg (95% confidence interval [CI]: 0.3 to 2.6) and −0.2 mmHg (95% CI: −0.9 to 0.6).[8] Thus, the same definition of nocturnal hypertension obtained by ABPM has been used in the definition of nocturnal hypertension obtained by HBPM.

In the J-HOP (Japan Morning Surge Home Blood Pressure) Nocturnal BP study (n = 2,545, mean age: 63 years; antihypertensive medication use: 83%), we observed that nocturnal hypertension obtained by HBPM (defined as nocturnal SBP ≥ 120 mmHg) and masked nocturnal hypertension obtained by HBPM (defined as nocturnal home BP ≥ 120/70 mmHg and the average of morning and evening BP < 135/85 mmHg) were present in 49.3% and 26.7% of a Japanese general practice population, respectively.[15,16]

2.2 | Measurement schedules

In nocturnal BP measurements by ABPM, the term “nocturnal” has been defined by self-reported, fixed-time, or actigraphy-based approaches, and nocturnal BP values were automatically measured at regular intervals (e.g., 30 min) throughout the participant's time spent sleeping. In HBPM, the participants must wrap the BP cuff around the upper arm by themselves and press a button to start the timer before going to bed. It is easy to set the cuff by oneself since the procedure is the same as the usual HBPM of morning and evening BPs. The nocturnal BP values are then automatically measured based on the participant's specified bedtime (eg, 2, 3, and 4 h after the chosen bedtime) or measured at fixed time points (eg, 2:00, 3:00, and 4:00 a.m.).

Although recently developed HBPM devices permit participants to set the nocturnal BP measurement schedule freely, there are no established criteria regarding when and at what time intervals the nocturnal BP measurements should be taken in one night. We previously compared the reliability of different schedules of multiple nocturnal home BP readings measured based on the participants' specified bedtimes and those measured at fixed time points.[17] The reliability of the nocturnal home BP values measured using

bedtime-based measurements and that of the values measured using fixed-time measurements were similar. That study also revealed that multiple measurements (≥2 times) in a single night could provide reliable information about the nocturnal home BP values.

In the J-HOP study, we asked study participants to measure their nocturnal home BP at three fixed time points (2:00, 3:00, and 4:00 a.m.).[15] There was no difference between nocturnal SBP at 2:00 a.m. and 3:00 a.m., whereas at 4:00 a.m. the nocturnal SBP values were slightly, but significantly, higher by 1.5 mmHg. It is necessary to have further discussions about when nocturnal home BP should be measured.

Another matter of debate has been how many times nocturnal home BP must be measured within 1 week for a reliable assessment of nocturnal BP levels. We demonstrated that two nights of nocturnal home BP measurement in 1 week should be recommended in consideration of its feasibility.[17] Kollias and colleagues also showed that a schedule of three automated measurements at intervals of 1 h on each of two nights was the minimum requirement for the reliable assessment of nocturnal home BP values.[18] Taking these findings into consideration, two nights of nocturnal home BP measurement in 1 week would be reliable and feasible in clinical practice. However, further study is necessary to establish the necessary number of nocturnal home BP measurements per night and the number of nights per week, in order to gather more robust evidence for the use of HBPM to measure nocturnal BP.

2.3 | Measurement conditions

Measurement conditions are also essential factors affecting nocturnal BP levels. Saeki and colleagues demonstrated that (a) a 1°C lower nighttime bed temperature was significantly associated with 0.019 mmHg higher nocturnal SBP; (b) a 1°C lower indoor temperature was significantly associated with a 0.18% greater fall of nocturnal BP; and (c) a 1°C lower ambient temperature was significantly associated with a 0.21% greater fall of nocturnal BP, independently of traditional CVD risk factors (all BPs were measured by ABPM).[19] Tabara and colleagues also showed that the nocturnal BP fall assessed by an HBPM device differed according to the season, with a higher frequency of riser and non-dipper patterns in the summer.[20] These studies showed that attention must be paid to environmental factors when patients are told to measure their nocturnal BP at home.

The posture during nocturnal BP measurements might also affect the BP level. Since the arm-cuff height of an HBPM device differs between the supine position and the lateral position when measuring nocturnal BP, the nocturnal BP levels might be measured in different positions. In addition, during the supine position of sleep, nocturnal BP levels vary depending on the position of the arm cuff of the upper-arm device or wrist-type BP device and the position of the palm when using a wrist-type BP device.[21,22]

These various factors affect nocturnal BP measurements and may not reflect "inherent" BP levels.

2.4 | Association with target organ damage

In regard to the associations between nocturnal home BP and hypertensive target organ damages (TODs), we demonstrated that nocturnal home SBP levels were significantly correlated with the urinary albumin/creatinine ratio (UACR), left ventricular mass index (LVMI), and brachial-ankle pulse wave velocity (baPWV) even after adjustment for morning, evening, and office BP levels.[15] Studies comparing the association of hypertensive TOD with nocturnal BP measured by HBPM and the association of hypertensive TOD with nocturnal BP measured by ABPM reported that the correlation coefficient between nocturnal home SBP and UACR was significantly greater than that for the relationship between nocturnal ambulatory SBP and UACR.[23,24] This result is likely attributed to the superiority of nocturnal BP measured by HBPM compared with nocturnal BP measured by conventional ABPM in terms of measurement frequency, reproducibility, and acceptability. Further studies are needed to confirm the superiority of nocturnal home BP measurement compared with nocturnal ambulatory BP measurement in terms of the association with hypertensive TODs.

2.5 | ICT-based home BP monitoring device

The technological advances over the last two decades have been remarkable, enabling the measurement of nocturnal home BP levels with information and communication technology (ICT)–based HBPM devices.[25,26] This ICT-based approach has allowed us to obtain reliable nocturnal home BP data that are transmitted automatically to a cloud server. This technological revolution brings light to nocturnal BP measurement, once a "dark spot," and it is expected to be widely adopted in clinical practice in the future.

3 | PATHOPHYSIOLOGY AND CLINICAL CHARACTERISTICS

Various factors account for the increase in nocturnal BP. First, the increases in the circulating volumes of blood and interstitial fluid, particularly in patients with heart and/or renal failure when they are supine, cause an increase in sleep/nocturnal BP. During sleep, venous return from the lower body is increased by the body's supine position, which in turn increases nocturnal BP levels. Second, autonomic neuropathy would cause an increase in nocturnal BP. Usually, sympathetic activity is reduced during the nighttime compared with daytime, since there is little external stimulation during sleep. However, sympathetic tone during sleep is elevated, especially in patients with diabetes or insomnia, and elevated sympathetic tone causes an abnormal circadian BP pattern and increased nocturnal BP levels. Third, obstructive sleep apnea (OSA) is a significant risk factor for nocturnal hypertension. In patients with OSA, repetitive OSA episodes produce hypoxia, which induces transient sympathetic overactivation. The sympathetic overdrive causes nocturnal BP surges, and this nocturnal BP surge may be a trigger for the onset

of CVD events during the night. Fourth, in patients with cerebrovascular disease, persistent sympathetic overactivity, impaired endothelial function, platelet activation, and enhanced inflammatory response have been reported to be responsible for a nocturnal BP increase.[27] Various other factors such as depressive state/anxiety, cognitive impairment, and lifestyle habits (alcohol intake, insufficient sleep time/poor sleep quality) can also cause a nocturnal BP elevation.[28] As such, nocturnal BP should be actively measured in patients with those factors.

The timing of antihypertensive medication administration would also affect nocturnal BP levels. The bedtime administration of antihypertensive medications has been shown to lower nocturnal BP compared with morning administration in some, but not all,[29] studies. The HERMONY (Hellenic-Anglo Research into Morning or Night Antihypertensive Drug Delivery) trial demonstrated that the timing of antihypertensive medication administration (morning or evening) did not affect nocturnal BP levels.[30] We previously demonstrated that there were no significant differences in nocturnal BP reduction between morning and bedtime administrations of an angiotensin II receptor blocker (ARB)/calcium-channel blocker (CCB) combination in the ACROBAT (ARB and CCB Longest Combination Treatment on Ambulatory and Home BP in Hypertension With Atrial Fibrillation Multicenter Study on Time of Dosing (ACROBAT) trial).[31] We also observed that the morning administration of ARB/CCB was not inferior to the bedtime administration in the terms of the reduction in not only nocturnal brachial but also central BP levels.[32] These studies vary in several respects, including the populations, baseline comorbidities, and treatment regimens, which might have contributed to the inconsistent results. Further evidence is needed to determine when to take antihypertensive medications to control nocturnal BP levels.

4 | CLINICAL RESEARCH AND THE LATEST FINDINGS OF NOCTURNAL HOME BP MONITORING

Table 1 shows the up-to-date publications on nocturnal HBPM. The schedules (ie, timing and number) of the measurement of nocturnal home BP differ among the studies, indicating that there is no established method for conducting nocturnal home BP measurement. In addition, among these 33 studies, 27 were conducted in Japan, including most of the clinical trials concerning nocturnal HBPM. Japanese individuals are very tolerant of home BP measurements and widely accept them as a daily activity to track their health. In addition, Japanese medical device manufacturers are focusing on clinical research and investing significant effort into the development of new nocturnal HBPM devices.

There have been only four randomized control clinical trials (RCTs) using nocturnal HBPM devices[25,26,33,34] and one RCT using a hypoxia-triggered nocturnal HBPM device[35] to compare the effects of two different classes of antihypertensive medications on nocturnal BP lowering. All of these trials demonstrated that it was possible to have participants self-measure their nocturnal BP at home. Nocturnal HBPM devices could thus have the potential to be an alternative to ABPM for the measurement of nocturnal BP. Further clinical studies are needed to verify the tolerability of nocturnal HBPM with these devices and to determine antihypertensive medications that can effectively reduce nocturnal BP levels.

5 | NOCTURNAL HOME BP MONITORING IN ASIA

There is strong evidence of a causal relationship between salt intake and BP increase. Asians are likely to have a genetic predisposition to salt sensitivity,[36] and salt sensitivity is an independent risk factor for cardiovascular events and a strong predictor for total mortality in both hypertensive and normotensive patients.[37] This is of importance particularly in Asian populations as their salt intake is higher compared with other populations, and excessive salt intake remains a societal problem.[38] This excessive salt intake causes nocturnal hypertension via an increase in the circulating volume during the nighttime. In other words, nocturnal hypertension is considered to be one of the phenotypes of increased salt sensitivity. Salt restriction should thus be an important strategy for the management of nocturnal hypertension in Asian populations.

We recently demonstrated that nocturnal SBP measured by an HBPM device was a significant predictor of incident CVD events independent of office and morning home SBP levels in a Japanese general practice population of the J-HOP Nocturnal BP Study.[39] In the same J-HOP study participants, we observed that masked nocturnal hypertension obtained by home BP monitoring (defined as nocturnal home BP ≥ 120/70 mmHg and average morning and evening BP < 135/85 mmHg) was associated with an increased risk for total CVD events compared with controlled BP (nocturnal home BP < 120/70 mmHg and average morning and evening BP < 135/85 mmHg).[16] This means that even in individuals with controlled daytime BP, those with increased nocturnal BP have a significant CVD risk. This evidence emphasizes the importance of nocturnal HBPM in clinical practice.

In a direct comparison with ABPM in the J-HOP Nocturnal BP study, nocturnal hypertension (nocturnal home SBP ≥ 120 mmHg) obtained by HBPM was independently associated with CVD events, and there was no association between nocturnal hypertension (nocturnal ambulatory SBP ≥ 120 mmHg) obtained by ABPM and CVD events. These results indicate that it is worthwhile to measure nocturnal home BP in addition to the morning and evening home BP levels. Knowledge of patients' nocturnal HBPM would be useful for identifying patients with high CVD risk and could be used widely in daily clinical practice, especially for Asian populations.

6 | CONCLUSIONS AND PERSPECTIVES

Nocturnal HBPM values and the management of nocturnal hypertension are important for hypertensive patients. Due to high salt sensitivity and salt intake, Asians are at high risk of nocturnal

TABLE 1 The up-to-date evidence of nocturnal home blood pressure monitoring

Year	Authors	Study participants (age, years; % female)	Device	Schedule of BP measurement	Main findings
Observational study					
2001	Chonan et al[40]	49 hypertensive patients (details unknown)	HEM-747IC-N (Omron Healthcare)	2 a.m, 10 days	Complete vigilance during BP measurement led to a nocturnal BP increase at 2 a.m.
2006	Shirasaki et al[41]	16 patients with OSA (22-79 years, 25%)	HEM-770 (Omron Healthcare) hypoxia-triggered BP measurements	1 day (at the time of heavy hypoxia episode)	The midnight BP surge was associated with the severity of OSA
2007	Hosohata et al[42]	556 general population (62 ± 11 years, 71%)	HEM-747IC-N (Omron Healthcare)	2 a.m., 2 times (5.9 days interval)	The reproducibility was poor in the participants who experienced different sleep qualities
2009	Ushino et al[43]	40 healthy participants (25 ± 1 years, 30%)	HEM-5041 (Omron Healthcare)	6 times at 1-h intervals, 7 days	The nocturnal BPs measured by HBPM were not significantly different from those measured by ABPM, and HBPM was more comfor*table* for patients than ABPM in measuring nocturnal BP
2011	Shirasaki et al[44]	23 patients with OSA (58 ± 13 years, 9%)	HEM-780 (Omron Healthcare) hypoxia-triggered BP measurements	1 day (at the time of heavy hypoxia episode)	Hypoxia-triggered BP monitoring was able to detect severe OSA-related BP surge
2012	Ishikawa et al[23]	854 patients with CV risk factors in the general practice population (63 ± 11 years, 53%)	HEM-5001 (Omron Healthcare)	3 points (2 a.m., 3 a.m., 4 a.m.) at night, 14 days	Nocturnal home BP measured by HBPM was comparable to nocturnal BP measured by ABPM and associated with hypertensive target organ damage
2012	Stergiou et al[45]	81 hypertensive patients (58 ± 11 years, 47%)	WatchBPN (Microlife)	3 points (2, 3, 4 h after going to bed) at night, 3 days	Nocturnal HBPM was reliable and well-accepted by users as an alternative to ABPM
2013	Stergiou et al[46]	39 patients with OSA (49 ± 11 years, 28%)	WatchBPN (Microlife)	3 points (2, 3, 4 h after going to bed) at night, 3 days	Nocturnal HBPM was feasible and related to the severity of OSA
2015	Kario et al[15]	2,562 patients with CVD risk factors in general practice population (63 ± 10 years, 51%)	HEM-5001 (Omron Healthcare)	3 points (2 a.m., 3 a.m., 4 a.m.) at night, 14 days	Nocturnal home BP was associated with hypertensive target organ damage independently of office BP, morning home BP, and evening home BP
2016	Andreadis et al[24]	131 untreated hypertensive patients (52 ± 12 years, 42%)	WatchBPN (Microlife)	3 points (2, 3, 4 h after going to bed) at night, 3 days	HBPM and ABPM appeared to be equally reliable for the evaluation of nocturnal BP, the detection of nocturnal hypertension and non-dippers, and the determination of preclinical target organ damage
2016	Lindroos et al[47]	248 general population (58 ± 13 years, 55%)	WatchBP Home N (Microlife)	3 points (2, 3, 4 h after going to bed) at night, 2 days	HBPM and ABPM produced similar mean nocturnal BP values that had comparable associations with hypertensive end-organ damage
2017	Kuwabara et al[48]	147 patients with OSA (59 ± 14 years, 14%)	HEM-780 (Omron Healthcare) hypoxia-triggered BP measurements	2 days (at the time of heavy hypoxia episode)	Hypoxia-peak nocturnal BP was much higher than the mean nocturnal BP measured at 30-min intervals, and it was as reproducible as mean nocturnal BP

(Continues)

TABLE 1 (Continued)

Year	Authors	Study participants (age, years; % female)	Device	Schedule of BP measurement	Main findings
2018	Kuwabara et al[49]	116 patients with OSA (58 ± 14 years, 15%)	HEM-780 (Omron Healthcare) hypoxia-triggered BP measurements	2 days (at the time of heavy hypoxia episode)	Among polysomnography-derived parameters, lowest SpO2, defined as the minimum SpO2 value during sleep, was the strongest independent determinant of hypoxia-peak SBP and nocturnal SBP surge measured by nocturnal HBPM
2018	Fujiwara et al[17]	48 hypertensive patients (77 ± 8 years, 56%)	HEM-7252G-HP (Omron Healthcare)	3 points (2, 3, 4 h after going to bed) at night for 7 days and 3 points (0 a.m., 2 a.m., 4 a.m.) at night for another 7 days, total of 14 days	The reliability of nocturnal HBPM was similar between nocturnal HBP adapted to the chosen bedtime of participants (2, 3, 4 h after going to bed) and that measured at fixed time points (0 a.m., 2 a.m., 4 a.m.)
2018	Matsumoto et al[50]	5,959 general population (58 ± 12 years, 69%)	HEM-7080IC (Omron Healthcare)	3 points (0 a.m., 2 a.m., 4 a.m.) at night, the last 1 night of 7 days	Lower sleep quality, particularly frequent nocturnal urination, was a strong determinant for increase in nocturnal BP
2018	Kollias et al[18]	94 untreated hypertensive patients (52 ± 11 years, 43%)	WatchBP Home N (Microlife)	3 points (2, 3, 4 h after going to bed) at night, 3 days	A two-night home BP schedules (six readings) appears to be the minimum requirement for a reliable assessment of nocturnal home BP, which gives reasonable agreement with ABP and association with preclinical organ damage
2018	Tabara et al[20]	4,780 general population (59 ± 12 years, 69%)	HEM-7080IC (Omron Healthcare)	2 points (2 a.m., 4 a.m.) at night, the last 5 nights (day 3 to day 7)	The nocturnal BP fall was largely different by season, with a higher frequency of riser and non-dipper patterns in the summer
2018	Imai et al[51]	57 hypertensive patients (64 ± 10 years, 47%)	Arm-cuff system: HEM-7080IC (Omron Healthcare); wrist-cuff system: HEM6310F-N (Omron Healthcare)	Arm-cuff system: 2 points (2 a.m. and 4 h after going to bed) at night, 2 days; wrist-cuff system: every 30 min during night, 2 days	The SBP/DBP values obtained using the wrist-cuff system were 5.6/6.4 mmHg higher than those obtained using the upper arm-cuff system. The wrist-cuff system caused fewer sleep disturbances and was more accepted and tolerated by the participants, compared with the arm-cuff system
2019	Tamura et al[52]	78 severe AS patients (79 ± 6 years, 56%)	HEM-5041 (Omron Healthcare)	8 times at 1-h intervals from 11 p.m. to 6 a.m., 1 day	Higher nocturnal BP was independently associated with BNP in AS patients with preserved EF
2019	Lindroos et al[53]	180 general population (57 ± 13 years, 62%)	WatchBP Home N (Microlife)	3 points (2, 3, 4 h after going to bed) at night, 2 days	A good agreement between ABPM and HBPM in detecting nocturnal hypertension was observed. A two-night HBPM seems to offer an inexpensive, feasible, and reliable method for the diagnosis of nocturnal hypertension
2019	Matsumoto et al[54]	5,854 general population (58 ± 12 years, 69%)	HEM-7080IC (Omron Healthcare)	3 points (0 a.m., 2 a.m., 4 a.m.) at night, the last 5 nights (day 3 to day 7)	Low sleep efficiency was a strong determinant of increased nocturnal BP and decreased nocturnal BP drop
2019	Maruhashi et al[55]	169 hypertensive patients (70 ± 9 years, 38%)	HEM-7252G-HP or HEM-7080IC (Omron Healthcare)	4 points (2 a.m., 3 a.m., 4 a.m., 5 a.m.) at night, 7 days	baPWV was higher in the sustained hypertension (daytime SBP ≥ 135 mmHg and nighttime SBP ≥ 120 mmHg) group than in the isolated nocturnal hypertension (daytime SBP < 135 mmHg and nighttime SBP ≥ 120 mmHg) group after adjustment for mean BP at the measurement of baPWV
2019	Kario et al[39]	2,545 patients with CVD risk factors in the general practice population (63 ± 10 years, 51%)	HEM-5001 (Omron Healthcare)	3 points (2 a.m., 3 a.m., 4 a.m.) at night, 14 days	Nocturnal SBP measured by HBPM is a significant predictor of incident CVD events, independently of office and morning home SBP

(Continues)

TABLE 1 (Continued)

Year	Authors	Study participants (age, years; % female)	Device	Schedule of BP measurement	Main findings
2020	Fujiwara et al[16]	2,745 patients with CVD risk factors in the general practice population (64 ± 10 years, 51%)	HEM-5001 (Omron Healthcare)	3 points (2 a.m., 3 a.m., 4 a.m.) at night, 14 days	Participants with masked nocturnal hypertension defined by HBPM (nocturnal HBP ≥ 120/70 mmHg and average morning and evening SBP < 135/85 mmHg) are at high risk of future CVD events
2020	Hosohata et al[56]	55 general population (65 years, 78%)	HEM-747-IC-N (Omron Healthcare)	1 point (2 a.m.), only time	Since no significant difference was found in nocturnal BP between HBPM and ABPM, HBPM may be a reliable alternative to ABPM for the assessment of nocturnal BP levels
2020	Mokwatsi et al[57]	1,005 patients with CVD risk factors in general practice population (63 ± 11 years, 50%)	HEM-5001 (Omron Healthcare)	3 points (2 a.m., 3 a.m., 4 a.m.) at night, 14 days	Nocturnal hypertension defined by HBPM (≥120 mmHg) is a significant predictor of future CVD events. On the other hand, nocturnal hypertension defined by ABPM is not
Clinical trials					
2010	Kario et al[58]	161 hypertensive patients (67 ± 13 years, 53%)	HEM-5001 (Omron Healthcare)	3 points (2 a.m., 3 a.m., 4 a.m.) at night, 7 days	In home BP-guided antihypertensive treatment, bedtime dosing of an ARB might be superior to awaking dosing for reducing microalbuminuria, even when a similar reduction in office and home BP, including nocturnal BP, is achieved
2014	Ishikawa et al[33]	50 hypertensive patients (59 ± 10 years, 56%)	HEM-5001 (Omron Healthcare)	3 points (2 a.m., 3 a.m., 4 a.m.) at night, 7 days	The reduction in nocturnal BP measured by HBPM is significantly correlated with the reduction in left ventricular hypertrophy
2014	Kario et al[35]	11 patients with OSA (65 ± 13 years, 27%)	HEM-770 (Omron Healthcare) ; hypoxia-triggered BP measurements	2 days (at the time of heavy hypoxia episode)	The nighttime dosing of a vasodilating or a sympatholytic antihypertensive drug may be an effective option for controlling nocturnal BP in hypertensive patients with OSA
2017	Kario et al[25]	411 patients with nocturnal hypertension (63 ± 12 years, 45%)	HEM-7252G-HP (Omron Healthcare)	3 points (2 a.m., 3 a.m., 4 a.m.) at night, 5 days	The ARB/CCB combination was superior to the ARB/diuretic combination for reducing nocturnal home BP, independently of sodium intake, despite the similar impact of the two combinations in patients with higher salt sensitivity
2018	Fujiwara et al[26]	129 patients with morning hypertension (68 ± 12 years, 57%)	HEM-7252G-HP (Omron Healthcare)	3 points (2 a.m., 3 a.m., 4 a.m.) at night, 3 days	Although the nocturnal home SBP was significantly decreased in the ARB/diuretic combination group compared with the ARB/CCB combination group, there were no significant differences in the reduction in morning home BP surge between the two combination groups
2018	Kario et al[34]	78 diabetic patients with nocturnal hypertension (69 ± 10 years, 41%)	HEM-7080-IC (Omron Healthcare)	3 points (2 a.m., 3 a.m., 4 a.m.) at night, 5 days	The addition of an SGLT2 inhibitor to standard antihyperglycemic therapy marginally reduced nocturnal home SBP and significantly reduced morning/evening home SBP and NT-proBNP levels, compared with intensified antihyperglycemic therapy
2020	Fujiwara et al	129 patients with morning hypertension (68 ± 12 years, 57%)	HEM-7252G-HP (Omron Healthcare)	3 points (2 a.m., 3 a.m., 4 a.m.) at night, 3 days	In preparation for publication. (the BP-lowering effect of the ARB/CCB combination was more dependent on baseline nocturnal home SBP than that of the ARB/diuretic combination.)

Note: ABP indicated ambulatory blood pressure; ABPM, ambulatory blood pressure monitoring; ARB, angiotensin II receptor blocker; AS, aortic stenosis; baPWV, brachial-ankle pulse wave velocity; BP, blood pressure; CCB, calcium-channel blocker; CVD, cardiovascular disease; DBP, diastolic blood pressure; EF, ejection fraction; HBP, home blood pressure; HBPM, home blood pressure monitoring; NT-proBNP, N-terminal pro-brain natriuretic peptide; OSA, obstructive sleep apnea; SBP, systolic blood pressure; SGLT2, sodium-glucose cotransporter 2.

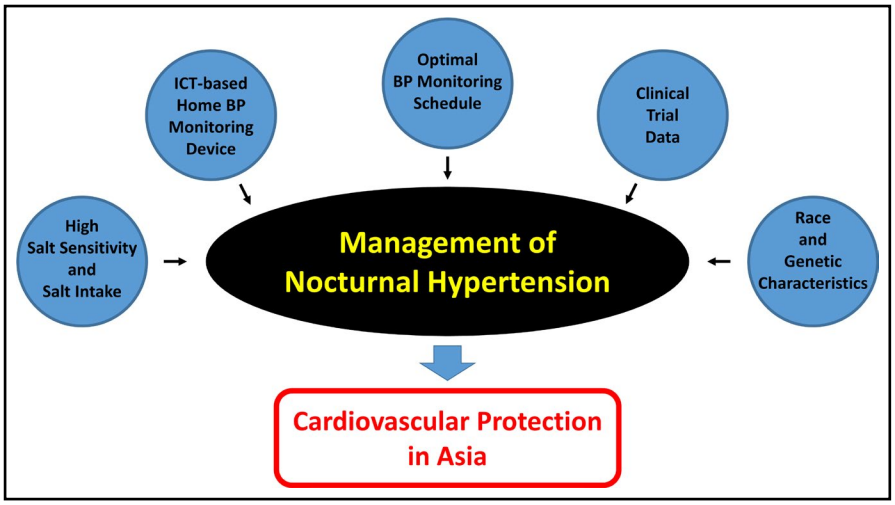

FIGURE 1 The management of nocturnal hypertension in Asia

hypertension, and a precise management of nocturnal BP levels is crucial (Figure 1). The ICT-based approach could be a revolutionary approach for the management of nocturnal home BP. This technological innovation improves nocturnal BP measurement, and it is expected to be ripe for wider adaptation in clinical practice in the future. Nocturnal HBPM could thus have the potential to be an alternative to ABPM for the measurement of nocturnal BP. Further research on how to measure nocturnal BP and assessments of its prognostic values is warranted. Lastly, data on the clinical significance of nocturnal BP measured by HBPM in other racial and ethnic groups will be needed.

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CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

T. Fujiwara conceived and designed the study. T. Fujiwara, S. Hoshide, N. Tomitani, H.-m. Cheng, A. A. Soenarta, Y. Turana, C.-H. Chen, H. V. Minh, G. P. Sogunuru, J. C. Tay, T.-D. Wang, Y.-C. Chia, N. Verma, Y. Li, J.-G. Wang, and K. Kario drafted the manuscript or critically revised the important intellectual content. T. Fujiwara, S. Hoshide, N. Tomitani, H.-m. Cheng, A. A. Soenarta, Y. Turana, C.-H. Chen, H. V. Minh, G. P. Sogunuru, J. C. Tay, T.-D. Wang, Y.-C. Chia, N. Verma, Y. Li, J.-G. Wang, and K. Kario approved the final version of the manuscript.

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