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REVIEW PAPER

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Role of ambulatory blood pressure monitoring for the management of hypertension in Asian populations

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Abstract

Out-of-clinic blood pressure (BP) measurement, eg, ambulatory BP monitoring, has a strong association with target organ damage and is a powerful predictor of cardiovascular events compared with clinic BP measurement. Ambulatory BP monitoring can detect masked hypertension or various BP parameters in addition to average 24-hour BP level. Short-term BP variability assessed by standard deviation or average real variability, diminished nocturnal BP fall, nocturnal hypertension, and morning BP surge assessed by ambulatory BP monitoring have all been associated with target organ damage and cardiovascular prognosis. Recently, the authors compared the degree of sleep-trough morning BP surge between a group of Japanese and a group of Western European untreated patients with hypertension and found that sleep-trough morning BP surge in Japanese persons was significantly higher than that in Europeans. Although Asian persons have been known to have a higher incidence of stroke than heart disease, the difference in characteristics of BP indices assessed by ambulatory BP monitoring might be the cause of racial differences in stroke incidence between Asian and Western populations. This review focuses on Asian characteristics for the management of hypertension using ambulatory BP monitoring.

1 | INTRODUCTION

Many studies have reported that out-of-clinic blood pressure (BP) measurement is a powerful predictor of cardiovascular events compared with clinic BP measurement. Although ambulatory BP monitoring (ABPM) and home BP monitoring (HBPM) are used to evaluate out-of-clinic BP, the position of these two techniques in clinical practice differs depending on the guidelines.

The Asian population has unique characteristics associated with the risk and incidence of cardiovascular disease (CVD) compared with Western populations. For the Asian population in particular, the management of hypertension is important because the prevalence of stroke events compared with coronary events are higher than in Western populations.[1] Moreover, the contribution of BP for CVD events are also higher in Asian populations than in Western populations.[2]

This review focuses on Asian characteristics and the management of hypertension using ABPM.

2 | POSITION OF ABPM IN HYPERTENSION GUIDELINES

ABPM has an increasingly defined and appropriate position within some, but not all, guidelines (Table 1). The Japanese Society of Hypertension (JSH) 2014 guidelines clearly state that home BP readings should be prioritized in the management of hypertension

compared with clinic BP readings when a discrepancy in BP values exists between home BP and clinic BP readings.[3] In addition, in the JSH 2014 guidelines, ABPM is recommended, if physicians can access the device with the following approved indications for the management of hypertension: (1) for the difficult decision in treatment strategy using home BP or office BP; (2) for patients with 125 to 135/80 to 84 mm Hg at home; (3) for patients with increased BP variability at home; and (4) for patients concerned with short-time BP variability, such as transient hypertension or hypotension, and instability of home and office BP measurement. The Japanese reimbursement system has approved ABPM for the management of hypertension since 2008. The 2013 European Society of Hypertension (ESH)/European Society of Cardiology (ESC) guidelines recommended both ABPM and HBPM to provide adjunct information to clinic BP[4] and demonstrated specific indications (Tables 1 and 2). The National Institute for Health and Care Excellence (NICE) in the United Kingdom recommends that ABPM be offered as a cost-effective technique to all persons suspected of having hypertension to exclude white-coat hypertension.[5] The Canadian Hypertension Education Program suggests that out-of-clinic assessment by ABPM is preferable to HBPM.[6] The National Heart Foundation of Australia in 2016 recommends that ABPM and/or home BP should be offered if clinic BP is >140/90 mm Hg.[7] Thus, three latter guidelines recommend that ABPM is useful to exclude white-coat hypertension. However, the guidelines of the American Joint National Committee (JNC) 8 did not mention either ABPM or HBPM based on the fact that these techniques have not been evaluated by randomized controlled trials.[8]

TABLE 1 Specific indications for ABPM in hypertension guidelines

Guideline	Year	Indication
Japanese Society of Hypertension[3]	2014	1. For the difficult decision in treatment strategy using home or office BP 2. For patients with BP 125 to 135/80 to 84 mm Hg at home 3. For patients with increased BP variability at home 4. For patients concerned with short-time BP variability
European Society of Hypertension[4]	2013	1. Marked discordance between office BP and home BP 2. Assessment of dipping status 3. Suspicion of nocturnal hypertension or absence of dipping, such as in patients with sleep apnea, CKD, or diabetes mellitus 4. Assessment of BP variability
National Institute for Health and Care Excellence[5]	2011	If clinic BP is ≥140/90 mm Hg, offer ABPM to confirm the diagnosis of hypertension
Canadian Hypertension Education Program[6]	2015	The out-of-office assessment should preferably be performed using ABPM
The National Heart Foundation of Australia[7]	2016	If clinic BP is 140/90 mm Hg or hypertension is suspected, ABPM and/or home monitoring should be offered to confirm BP level

Abbreviations: ABPM, ambulatory blood pressure monitoring; BP, blood pressure; CKD, chronic kidney disease.

TABLE 2 Association between morning BP surge assessed by ABPM and cardiovascular events

Year	Source	Population	Mean follow-up	End point	Findings
2003	Kario et al[36]	519 Elderly Japanese patients with hypertension	3.4 y	Stroke	Patients with sleep-trough morning BP surge (≥55 mm Hg: the highest decile) had a higher stroke incidence than those without
2011	Israel et al[37]	2627 Western population	22,353 person-y	All-cause mortality	There was a tendency for an increase in all-cause mortality in patients with sleep-trough morning BP surge (≥40 mm Hg), although not significant
2012	Verdecchia et al[38]	3012 Western patients with hypertension	8.4 y	Composite of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, and heart failure requiring hospitalization	Patients with sleep-trough morning BP surge (>44 mm Hg: the highest decile) showed a rate of cardiovascular events and total mortality that did not differ from values in patients without
2014	Bombelli et al[39]	2051 Community-dwelling white patients	16.0 y	All-cause mortality or cardiovascular mortality	No difference in the adjusted risk of all-cause or cardiovascular death was seen when the highest decile and other deciles of sleep-trough morning BP surge were compared

Abbreviations: ABPM, ambulatory blood pressure monitoring; BP, blood pressure.

2.1 | Masked hypertension and uncontrolled masked hypertension

Patients with masked hypertension have normotension based on their clinic BP but hypertension according to their out-of-clinic BP measurement. When these patients are receiving antihypertensive treatment, the ESH/ESC guidelines define this as uncontrolled masked hypertension.

There have been several reports of masked hypertension as defined by ABPM being associated with a worse cardiovascular prognosis, in a similar manner to sustained hypertension. Clement and colleagues[9] investigated whether ABPM could predict cardiovascular events or death in 1963 European patients with hypertension over 5 years. This study demonstrated that patients with 24-hour systolic BP (SBP) ≥135 mm Hg had an increased relative risk compared with those with 24-hour SBP <135 mm Hg and either clinic SBP <140 mm Hg or 140 to 159 mm Hg. In the group with clinic SBP ≥160 mm Hg, patients with 24-hour SBP ≥135 mm Hg had an increased relative risk compared with those with 24-hour SBP <135 mm Hg, after adjusting for cardiovascular risk factors. The Ohasama Study,[10] which comprised a Japanese community-dwelling population (n=1332) that was followed for 10 years, demonstrated that masked hypertension (daytime BP ≥135/85 mm Hg and clinic BP <140/90 mm Hg) as defined by ABPM had a higher risk of cardiovascular mortality and stroke morbidity than sustained normotension.

Although several cohort studies have shown an association between HBPM and cardiovascular prognosis,[11–14] only one study (SHEAF [Self-Measurement of Blood Pressure at Home in the Elderly: Assessment and Follow-Up])[11] has demonstrated that patients with uncontrolled masked hypertension (BP ≥135/85 mm Hg by HBPM and <140/90 mm Hg by clinic BP), as defined by HBPM, had a worse cardiovascular prognosis than patients with controlled hypertension (<135/85 mm Hg by HBPM and <140/90 mm Hg by clinic BP).[4] This study enrolled and followed 4938 patients with treated hypertension (average age, 70 years) during an average of 3.2 years. The results clearly demonstrated that uncontrolled masked hypertension was associated with a worse cardiovascular prognosis than controlled hypertension (hazard ratio [HR], 2.06; 95% confidence interval [CI], 1.22–3.47) after adjusting for covariates. In the PAMELA (Pressioni Arteriose Monitorate e Loro Associazioni) study,[12] which enrolled a regional population of 2051 individuals and followed them over an average of 12.3 years, masked hypertension increased the risk of cardiovascular death compared with the reference of normotension in an unadjusted model, although this association did not remain significant after adjusting for age and sex. Similarly, the Finn-Home study,[14] another long-term, multicenter, multinational study (n=2046) with a follow-up of 7.5 years, also found that masked hypertension was associated with an increased risk of cardiovascular death compared with normotension as the reference in an unadjusted model (HR, 2.99; 95% CI, 1.42–3.68). However, again, this association was not significant after adjusting for age and sex (HR, 1.39; 95% CI, 0.86–2.25). The smaller, multinational Didima study[13] (n=662), which had a follow-up of 8.2 years, demonstrated a similar result to both the PAMELA and Finn-Home studies.

The International ARTEMIS (Ambulatory Blood Pressure Registry: Telemonitoring of Hypertension and Cardiovascular Risk Project) study[15] revealed that masked hypertension and masked uncontrolled hypertension were more likely to be diagnosed in Asia than any other region. In a recent and relatively large US sample of employed adults without CVD and not taking antihypertensive medication, the clinic-ambulatory BP difference was high in the patients with low body mass index.[16] A pooled analysis of nearly 1700 population-based studies indicated that Asian populations have a lower body mass index compared with Western populations.[17] Lower body mass index might thus be the reason for the difference in the proportion of masked hypertension between Asian and non-Asian populations.

Taken together, although it is clear that out-of-clinic BP readings evaluated by both HBPM and ABPM are undoubtedly important in terms of prognosis of cardiovascular events in not only Asian populations but also Western populations, further investigation is required on whether masked HT evaluated by HBPM provides the prognostic power for cardiovascular events.

2.2 | BP variability

Short-term BP variability calculated by standard deviation (SD) or average real variability using ABPM has been reported to be associated with subclinical organ damage and cardiovascular events and mortality. Several studies about this issue in Asian populations have been reported. In the Ohasama Study, which enrolled 1542 Japanese persons in the general population including those with both normotension and hypertension with a follow-up of 8.5 years, when the patients were divided into quintiles of SD of SBP, the highest quintile of SD of SBP during daytime (>18.8 mm Hg) had a significant risk for cardiovascular mortality compared with the second quintile (11.5 to 13.9 mm Hg), and during nighttime, the highest quintile of SBP SD (>14.4 mm Hg) also had a significant risk for cardiovascular mortality compared with the fourth quintile (11.8 to 14.4 mm Hg).[18] In 300 Japanese patients with diabetes mellitus with or without hypertension, with a follow-up of 54 months, SD of SBP (5-mm Hg increase [HR, 1.08; 95% CI, 1.01–1.16]) and diastolic BP (5-mm Hg increase [HR, 1.13; 95% CI, 1.04–1.23]) during nighttime were independently associated with incident CVD.[19] In a cohort of Taiwanese participants (624 patients with normotension and 633 patients with untreated hypertension), high DBP variability assessed by average real variability (≥8.8 mm Hg) during 24 hours significantly predicted cardiovascular mortality compared with low BP variability (<8.8 mm Hg).[20]

The Syst-Eur trial, which investigated the efficacy of antihypertensive therapy in elderly patients (median age, 69.5 years) in a Western population, showed that the risk of stroke increased by 80% (95% CI, 17–176%) for each 5-mm Hg increment in BP variability assessed by SD during nighttime.[21] In 1280 European patients with hypertension without antihypertensive treatment, daytime SBP variability assessed by average real variability was an independent predictor of cardiovascular events during 4.8 years of follow-up.[22]

Although short-term BP variability assessed by ABPM has unsolved issues, such as methodology of calculation of BP variability

and its threshold, it may be a common risk factor for CVD in Asian and Western populations.

2.3 | Diurnal BP variation

ABPM is the only device available to evaluate the time course of BP during 24 hours. Patients with a normal diurnal BP profile typically have a nocturnal BP fall of 10% to 20%. There is substantial evidence to show that an abnormal fall in nocturnal BP corresponds with an increased risk of target organ damage or poor cardiovascular prognosis.[23,24] Even in Japanese patients with nonmedicated normotension (24-hour BP <125/80 mm Hg and clinic BP <140/90 mm Hg), those with a diminished nocturnal BP fall exhibited cardiac overload compared with those with normal nocturnal BP fall.[23,24] Wave 1 of the JMS-ABPM (Jichi Medical School Ambulatory Blood Pressure Monitoring) study investigated whether an abnormal BP dipping pattern would influence the prognosis of stroke in 575 Japanese elderly patients with hypertension over 41 months of follow-up; those with a riser pattern had the worst stroke prognosis, while an extreme-dipper pattern had the second worst prognosis.[24]

Several studies mentioned that Asians and blacks have less nocturnal BP fall than whites; however, the reproducibility of the nocturnal BP pattern has been debated.[25,26] Specifically, it has been reported that the dipper and nondipper patterns are not reliably reproduced. In contrast, an excessive abnormal diurnal BP pattern may be relatively well reproduced. The reason for the poor reproducibility of the nocturnal BP patterns could be the patients' daily activities. The effect of daytime naps may be especially important. In China and Taiwan, daytime napping is a well-accepted practice.[27,28] Differences in the nocturnal BP fall and the proportion of nondippers were reported between patients with BP defined by daytime and nighttime intervals and between patients who engaged in daytime napping and those who did not.[29] Most of the previous studies of nocturnal BP patterns did not consider daytime napping. In the future, the accurate evaluation of patients' daily activities including daytime napping (eg, by actigraphy) is necessary when measuring ABPM. In general, the recent focus on BP variability evaluated by ABPM has moved nighttime BP to the center stage, while attention has shifted away from diurnal BP variations.

2.4 | Nighttime BP

While awake BP is affected by various environmental factors, nocturnal BP is not. Recently, Stergiou and colleagues[30] reported that all clinic, home, or ambulatory BP readings were affected by seasonal changes, except for nighttime BP. Nocturnal BP may be the most reproducible physiological and "real" phenotype of individual BP among all BP indices. Previously, we reported that Japanese patients with masked nocturnal hypertension (home BP <135/85 mm Hg and ambulatory nocturnal BP ≥120/75 mm Hg) had greater intima-media thickness and relative wall thickness than patients with normotension (home BP <135/85 mm Hg and ambulatory nocturnal BP <120/75 mm Hg).[31] The IDACO (International Database of Ambulatory Blood Pressure in Relation to Cardiovascular Outcome) study,[32] an international database of ABPM, demonstrated that both awake and nocturnal BP were associated with poor cardiovascular prognosis in untreated patients, while in treated patients this association was observed only in those with abnormal nighttime BP. In previous studies that compared nighttime BP between Chinese populations in individuals with normotension, the whole-day and nighttime diastolic BPs were from 1 to 4 mm Hg and from 3 to 7 mm Hg higher than in five other population studies in white or Japanese patients.[33]

Recently, self-measured HBPM has become available for measuring nocturnal BP. In the J-HOP (Japan Morning Surge Home Blood Pressure) study,[34] nocturnal BP was measured using HBPM. The average nighttime BP measured at 2 AM, 3 AM, and 4 AM was independently associated with organ damage (urinary albumin creatinine ratio, left ventricular mass index, and brachial-ankle pulse wave velocity) after adjusting for covariates including clinic BP and morning or evening home BP. In addition, the relationship between nighttime BP, measured by HBPM, and urinary albumin creatinine ratio was significantly greater than that of the relationship between nighttime BP measured by ABPM and urinary albumin creatinine ratio.[35]

At present, the use of home BP measurement to measure nighttime BP is limited to only Japan. There is also no consensus on the optimal number of measurements per night or the number of recording nights using HBPM. ABPM is still acknowledged as a superior method compared with HBPM for the evaluation of nocturnal hypertension, as it can provide accumulating evidence. In addition, ABPM can be used to evaluate 24-hour BP levels, diurnal BP variation, morning BP surge, and BP variability, all of which can be used clinically, whereas HBPM cannot be used for these purposes. Further research is needed to establish the relationship between nighttime BP measurements by HBPM and cardiovascular prognoses.

2.5 | Morning BP surge

We previously reported that sleep-trough morning BP surge (morning BP minus the lowest nocturnal BP) was associated with a significant risk of stroke in Japanese elderly patients with nonmedicated hypertension, independent of 24-hour BP level and nocturnal BP dipping.[36] However, several studies conducted in Western countries demonstrated discrepant results (Table 2).[37–39] The different characteristics of the populations under study might explain this discrepancy. The populations of the three above-cited studies consisted of more general populations than those seen in clinical practice, whereas our study was of elderly patients with hypertension. In addition, there might be racial differences in morning BP surge between Asian and Western populations. Lately, when we compared the degree of sleep-trough morning BP surge between groups of Japanese and Western European patients with untreated hypertension, we found that sleep-trough morning BP surge in Japanese persons was significantly higher than that in Europeans independent of age, 24-hour BP, and lowest nocturnal BP (40.1 mm Hg [95% CI, 39.0-41.2] vs 23.0 mm Hg [95% CI, 22.4–23.5]; $P<.001$).[40] An international ABPM database (which included data from a general population and not from patients with hypertension only) demonstrated that the threshold value of the

highest decile of sleep-trough morning BP surge of white (European and South American) and Asian (Japanese and Chinese) patients in the same database had ≥35 mm Hg and ≥43 mm Hg, respectively. Asian persons have been known to have a higher incidence of stroke than of heart disease.[1] Higher morning BP surge in Asian populations compared with Western populations might be the cause of racial differences in stroke incidence between Asian and Western populations.

In the above-cited studies of Western populations that demonstrated negative results of the association between morning BP surge and cardiovascular outcomes, the primary outcomes were all-cause mortality,[37] a major composite cardiovascular event (ie, cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, and heart failure requiring hospitalization),[38] and cardiovascular or all-cause death.[39] Thus, in Asian populations, it might be more important to evaluate morning BP surge using ABPM as a means to prevent the occurrence or recurrence of stroke. Morning BP surge is currently only detectable by ABPM. In the future, however, this parameter may become evaluable by HBPM.

3 | CONCLUSIONS

Undoubtedly, measuring out-of-clinic BP using ABPM is useful for cardiovascular risk stratification. In Asian patients with hypertension, there is robust evidence on the association between BP indices assessed by ABPM and target organ damage or cardiovascular prognosis. Masked hypertension, nocturnal hypertension, and morning BP surge might be important for the management of hypertension to prevent stroke because they are strong predictors of stroke incidence. Although the mechanism of these two BP indices assessed by ABPM remains unclear, the challenge now, and in the future, is to conquer these important factors in the Asian population.

CONFLICTS OF INTEREST

The authors have no financial conflicts of interest to disclose.

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